BRIAN SANDOVAL
Governor

RICHARD WHITLEY, MS
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NOTICE OF PUBLIC MEETING – DRUG USE REVIEW BOARD

AGENDA

Date of Posting: **October 5, 2018**

Date of Meeting: **Thursday, October 18, 2018 at 5:15 PM**

Name of Organization: **The State of Nevada, Department of Health and Human Services, Division of Health Care Financing and Policy (DHCFP), Drug Use Review Board (DUR).**

Place of Meeting:
Grand Sierra Resort and Casino
2500 E 2nd St.
Reno, NV 89595
Phone: (800) 738-1410

Webinar Registration

https://optum.webex.com/optum/onstage/g.php?MTID=e089cb784258780a111f2a9af1200c0c1

Or go to www.webex.com and enter the Event Number listed below.

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Event Number: **645 452 368**

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For Audio Only:

Phone: 1-763-957-6300
Event: 645 452 368

AGENDA

1. **Call to Order and Roll Call**

2. **Public Comment on Any Matter on the Agenda**

3. **Administrative**

   a. **For Possible Action:** Review and Approve Meeting Minutes from July 26, 2018.

   b. Status Update by DHCFP

4. **Clinical Presentations**

   a. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for Immunomodulator Drugs.

      i. Public comment on proposed clinical prior authorization criteria.
      ii. Presentation of utilization and clinical information.
      iii. Discussion by Board and review of utilization data.
      iv. Proposed adoption of updated prior authorization criteria.

   b. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for opioid use in members under 18 years of age.

      i. Public comment on proposed clinical prior authorization criteria.
      ii. Presentation of utilization and clinical information.
      iii. Discussion by Board and review of utilization data.
      iv. Proposed adoption of updated prior authorization criteria.

   c. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for CGRP (Calcitonin Gene-Related Peptide Receptor) Inhibitors.

i. Public comment on proposed clinical prior authorization criteria.
ii. Presentation of utilization and clinical information.
iii. Discussion by Board and review of utilization data.
iv. Proposed adoption of updated prior authorization criteria.

5. Public Comment on any DUR Board Requested Report

6. DUR Board Requested Reports

a. Prior Authorizations on High Dollar Claims
   i. Discussion by the Board and review of utilization data.
   ii. **For Possible Action**: Requests for further evaluation or proposed clinical criteria to be presented at a later date.

b. Opioid Utilization – top prescribers and members
   i. Discussion by the Board and review of utilization data.
   ii. **For Possible Action**: Requests for further evaluation or proposed clinical criteria to be presented at a later date.

c. Antibiotic Utilization
   i. Discussion by the Board and review of utilization data.
   ii. **For Possible Action**: Requests for further evaluation or proposed clinical criteria to be presented at a later date.

d. Oncology Medication Utilization
   i. Discussion by the Board and review of utilization data.
   ii. **For Possible Action**: Requests for further evaluation or proposed clinical criteria to be presented at a later date.

7. Public Comment on any Standard DUR Report

8. Standard DUR Reports

a. Review of Prescribing/Program Trends.

   i. Top 10 Therapeutic Classes for Q4 2017, Q1 2018 and Q2 2018 (by Payment and by Claims).
   ii. Top 50 Drugs of Q4 2017, Q1 2018 and Q2 2018 (by Payment and by Claims).

b. Concurrent Drug Utilization Review (ProDUR)

   i. Review of Q2 2018.
   ii. Review of Top Encounters by Problem Type.

c. Retrospective Drug Utilization Review (RetroDUR)

i. Status of previous quarter.
ii. Status of current quarter.
iii. Review and discussion of responses.

9. Closing Discussion

a. Public comments on any subject.

b. Date and location of the next meeting.

i. Discussion of the time of the next meeting.

c. Adjournment.

PLEASE NOTE: Items may be taken out of order at the discretion of the chairperson. Items may be combined for consideration by the public body. Items may be pulled or removed from the agenda at any time. If an action item is not completed within the time frame that has been allotted, that action item will be continued at a future time designated and announced at this meeting by the chairperson. All public comment may be limited to 5 minutes.

This notice and agenda have been posted at http://dhcfp.nv.gov and http://notice.nv.gov

Carson City Central office and Las Vegas DHCFP. The agenda posting of this meeting can be viewed at the following locations: Nevada State Library; Carson City Library; Churchill County Library; Las Vegas Library; Douglas County Library; Elko County Library; Lincoln County Library; Lyon County Library; Mineral County Library; Tonopah Public Library; Pershing County Library; Goldfield Public Library; Eureka Branch Library; Humboldt County Library; Lander County Library; Storey County Library; Washoe County Library; and White Pine County Library and may be reviewed during normal business hours.

If requested in writing, a copy of the meeting materials will be mailed to you. Requests and/or written comments may be sent to Robyn Heddy at the Division of Health Care Financing and Policy, 1100 E. William Street, Suite 101, Carson City, NV 89701, at least 3 days before the public hearing.

All persons that have requested in writing to receive the Public Hearings agenda have been duly notified by mail or e-mail.

Note: We are pleased to make accommodations for members of the public who have disabilities and wish to attend the meeting. If special arrangements are necessary, notify the Division of Health Care Financing and Policy as soon as possible and at least ten days in advance of the

meeting, by e-mail at robyn.heddy@dhcfp.nv.gov in writing, at 1100 East William Street, Suite 101, Carson City, Nevada 89701 or call Robyn Heddy at (775) 684-3678.

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DRUG USE REVIEW BOARD

Meeting Minutes

Date of Meeting: **Thursday, July 26, 2018 at 5:15 PM**

Name of Organization: **The State of Nevada, Department of Health and Human Services, Division of Health Care Financing and Policy (DHCFP), Drug Use Review Board (DUR).**

Place of Meeting: **Hyatt Place Reno-Tahoe Airport**
1790 E. Plumb Ln
Reno, NV 89502
Phone: (775) 826-2500

ATTENDEES

Board Members Present
Paul Oesterman, Pharm.D., Chairman
James Marx, MD
Jennifer Wheeler, Pharm.D.
David England, Pharm.D
Netochi Adeolokun, Pharm.D.

Board Member Absent
Marta Bunuel, MD
Michael Owens, MD
Yvette Kaunismaki, MD

DHCFP
Holly Long, Social Services Program Specialist III
Jodi Patton, Social Services Program Specialist III
Andolyn Johnson, Senior Deputy Attorney General

OptumRx
Carl Jeffery, Pharm.D.

Managed Care Organizations
Thomas Beranek – Silver Summit Health Plan
Ryan Bitton – Health Plan of Nevada
Jeannine Murray – Anthem

Public
Ann Nelson, Vertex
Jamie Tobitt, Vertex
John Sandstrom, Shire
Lori Howarth, Bayer
Ryan Morris, Bayer
Joe Lasky, Children's Specialty Center
Holly Frye, Red Chip
John Scott, Novo Nordisk
Jason Russell, Bioveratio
Bill Robie, NHF
Brian Roeder, Ferrari Public Affairs
T. Carsten, DHCFP
Rebecca Reynold, Abbvie
Paige Barnes, Crowley and Ferrato
Pauline Whelan, Orexo
Betsy VanDeusen, Nevada Chapter NHF
Rob Booth, Allergan
Karen Campbell, Allergan
Amy Roonby, Allergan
James Wilson, MD, UNR
Kelly Gonzalez
Amber Federizo, Hemostasis and Thrombosis Center of NV
Jennifer Roberts, Hemostasis and Thrombosis Center of NV
John Zabukouz, Conduent

AGENDA

1. Call to Order and Roll Call

Ryan Bitton,
Jeannine Murray
Thomas Beranek
Jodi Patton
Holly Long
Carl Jeffery
Paul Oesterman
Andolyn Johnson
James Marx
Jennifer Wheeler

Netochi Adeolokun
David England (teleconference)

2. Public Comment on Any Matter on the Agenda

Paul Oesterman: Is there any public comment?

Jennifer Roberts: I am Jennifer Roberts with hemostasis and thrombosis of Nevada. I would like to review the availability of options we can provide as a carve-out option. We are required to submit annually how we have met over 25 measureable quality measures to remain eligible for grants. As the only Federally designated hemophilia treatment center in the State, we have very high standards of care of our patients and subject to audits for HRSA and the OPA as well and many other insurers. We take our program very seriously, conduct monthly self-audits, and third party audits every two years. All factor sales are considered program income and therefore the revenue is restricted. All revenue generated is required to go back to patient care services for example to overcome transportation services, we offer Uber to all our available clinics.

Amber Federizo: My name is Amber Federizo and I am the co-medical director for the Hemostasis and thrombosis center of Nevada. We provide flights via SouthWest for these patients to be evaluated. That is a completely free service that we provide. This provides a better quality of life and outcomes and no cost to the State. We are able to provide amicable solution to our patients at no charge. Our patients struggle with this medication and some pharmacies do not like to service them. We use contract pharmacies that can provide medications at cost savings by allowing a 3% pass-through pricing. We closely monitor that the patient is able to get their needed medications. We are currently partnering with Aeva health to provide factor in the home and self-infusion classes on a monthly basis. As a carve-out, we are willing to negotiate a lower reimbursement on these medications. We can offer significant savings statewide. When a patient has access to a provider in a timely manner, it reduces the number of visits to emergency departments. We would like to suggest carving-out factor products.

Paul Oesterman: Thank you. I have one question. I understand what you are asking, but I do not think that falls under the purview of the DUR Board.

Amber Federizo: Correct, this is an additional agenda item. We have additional information for the prior authorization discussion.

Paul Oesterman: For us to be able to act upon anything, it must be on the agenda.

Amber Federizo: Correct, and hopefully in the future it could be on the agenda.

Paul Oesterman: Thank you. Any other public comment?

3. Administrative

a. **For Possible Action:** Review and Approve Meeting Minutes from April 26, 2018.

A motion to approve as submitted. Seconded. Voting.

Minutes are approved.

b. Status Update by DHCFP:

Holly Long: I am Holly Long with DHCFP. I have a couple of updates. In June, preventative services updated their billing restrictions. I have a website where it is posted if anyone is interested. The instructions are intended to be more clear and easy to follow. It is on the Medicaid Nevada website. On June 28, 2018, Medicaid announced that behavioral health providers are invited to attend the monthly DHCFP webinar. The DHCFP behavioral health unit is inviting provider-type 14, which is behavioral health outpatient treatment, and provider-type 82, behavioral health rehabilitative treatment to a monthly behavioral health webinar. These monthly webinars are intended to provide policy training and education to behavioral health providers. A Q&A forum will be available during the event to get real time responses to provider questions. I also have that link if anyone is interested in registering and they can pass along the information.

4. Clinical Presentations

a. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for Hepatitis C Direct-Acting Antivirals.

Paul Oesterman: Just for a little background, this was kind of a homework assignment that was put out by the board at the last meeting, we asked our three managed care organizations to try to work together to make a consolidated approach to the prior authorization and apparently, they have worked at this and have come to no compromise. With that being said, what did you come up with?

Ryan Bitton: It is not that we didn't come to a compromise; we did meet with the goal of seeing if we can consolidate these things. We were doing that. We've had difficulties, having all of our documentation different in the sense of the way it flowed, the way it was set up, all of those have one thing wrong, hepatitis-C and some of us had separate ones by each drug and as we went through the process, we didn't see an easy way. A decent amount of effort from each of our organizations and retooling the processing part of them that need prior authorization or individual states that we cover. We couldn't come up with a pass-through to that.

Jeannine Murray: It's fair to say when we looked at the criteria and we compared the criteria, this is all in a different look or format, but the elements of the criteria are similar. We did like a grid to see who had what and it seems very similar as far as the requirements of the criteria to better read through it; the documents all look different.

(Indiscernible speakers)

Ryan Bitton: The intent of how we covered them is similar to the way that OptumRx covered it so our thought was, we are covering them similarly as per the DUR guidelines so it allows separate documents and support separate processes.

Paul Oesterman: Okay, I appreciate your efforts.

Carl Jeffery: As you know, we have brought these back a couple of times. I have brought forward some proposed criteria from Optum, which is probably unfortunately similar to what the other ones are. After seeing their recommendations from the MCO as saying that they would just like to keep this criteria. Chapter 1200 as it is currently written is confusing and so we are going to go down the road of having individual agents. We still do not have criteria for the two newest agents, Mavyret and Vosevi. Therefore, we still need some coverage criteria for those if we are going to have those covered, as well. It would be simpler for the chapter 1200 criteria to be listed by drug, and that way they're easier to update and easier when a provider wants to treat hep-C; they have an idea of what drug they want to use, they look at the specific guidelines. I think as a reference document easier to use if it's listed by drug. We have all the different proposed criteria listed in the binder; probably half the binder here. The first couple are the OptumRx proposed criteria that is just listed by drug.

Paul Oesterman: I guess at this point, I would ask our managed care organizations, how do you feel about the proposed prior authorization criteria that as listed by drug?

Jeannine Murray: That is how Anthem has it listed. You would look for the specific drug. If you are wanting to prescribe Mavyret, you would go to Mavyret and pull that criteria and that's what you would submit off of and it probably looks very similar to what the other criteria is except for it has a few more genotypes that are available for it.

Paul Oesterman: Okay, so that's Anthem's take on it. How about HPN?

Ryan Bitton: We've got one document with all of them. The criteria is similar, so even though my document may be 20 pages. I'm okay with the criteria that is proposed for Vosevi and Mavyret, but we tend to put them in one bucket.

Thomas Beranek: Ours are similar they don't look exactly the same but as Carl stated, ours are individual, as well, so they look is similar. Silver Summit would be fine with the proposed criteria.

Holly Long: How would the Optum proposed criteria look, does that include, I see Mavyret, but is Vosevi in there, as well?

Carl Jeffery: Vosevi's mentioned, yeah.

James Marx: It would seem to me, since these are pretty complex patients anyway and have a high likelihood of ending up on fee for service regardless, it would seem to me simplistic just to use the Optum that's already a part of fee for service as the managed care organization want to get rid of these patients anyway, we know that, and they not really excited about taking up hep C, so why not just use the Optum criteria from the very start? It looks like a lot of work on their part, and have a unified approach rather than attempt to try to go through the various iterations of who does what and which is preferable to another when they are going to end up in fee for service regardless, why not just start out that way and be done?

Carl Jeffery: Yeah, and that is a valid point. We can look at the utilization so here's the utilization of the different products, this is for fee for service here but you can see, you know, it's hard for me to look around and turn around like that but, here between 5 and 45 claims per month we're

seeing so we're not seeing a whole lot of claims. Here's Anthem's utilization and theirs is formatted a little bit differently.

Paul Oesterman: I think one thing to note also is that the number of claims for the hepatitis C drugs is on the decline, too, because patients are being treated, they are being cured, and so we're having fewer and fewer claims. So at this point, we do have a proposed prior authorization guideline in front of us from Optum. It sounds like our managed care organizations are okay with what's being proposed here. We've gone through this several times. We will ask that the chapter 1200 be updated to reflect by drug. Do we have a motion to approve the proposed prior authorization guidelines, the Optum guidelines for the hepatitis-C direct-acting antivirals?

Motion to accept as presented.

Second.

Voting – Ayes unanimous. The motion carries.

b. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for antibiotics.

Jim Wilson: My name is Jim Wilson, I'm a pediatrician in Northern Nevada Hopes. I am also on faculty with the University of Nevada Reno, Department of Pediatrics and Health Sciences and the directives of the National Developing Center. My background is in health security intelligence, I led the teams with substantial intel on the expansion of H5N1. I did provide warning of the 2009 H1N1 pandemic and was involved in the investigation of the Haiti Cholera disaster. About 25 years of history in health security intelligence. My role here today is I'm the co-chair of the Nevada and Civil Stewardship Program. I do have these handouts. I was hoping to provide you all some context as to why we are talking about this in the context of antimicrobial stewardship. The first slide here is that this kind of reviews where we in comparison to the rest of the country in terms of the antimicrobial consumption. We're 15th in the nation overall for all antibiotic classes in the outpatient sector. The next slide is for cephalosporin. We are 15th in the nation and 20th in the nation for quinolone respective. So, that's pretty good. I want to acknowledge the CDCs assessment of our state in terms of consumption. Now we're getting to some of the interesting stuff. The next slide, unfortunately, though we are number one in the nation for carbapenem resistance. Additionally, that is the last functional line of drugs we have to treat gram-negative infections. This is a big deal. We also on top of this do have evidence of (indiscernible) resistance. Some of this is due to infection control issues. Some from reported cases from foreign countries. We are the first State in US history to report the death of someone from pan-resistant bacteria. We are a hot zone for drug resistance. The next slide, this is actual data from our acute care, SNF's. Basically, we have multi-drug resistant e. coli here. Our most common bacteria that we isolated in medicine is multi-drug resistant. It has been so for about 10 years, which means it is resistant to five different class of antibiotics. The trend lines are not reassuring. We do not have statistical evidence yet of the effects of antimicrobial stewardship in our facilities. Next slide, this is what acinetobacter looks like. This is an important gram-negative pathogen for LTACs. If your patient's on a ventilator and you're trying to figure out how to treat them upfront for infection involving the acinetobacter good luck. The cephalosporins, why are we focusing on the third generation cephalosporins? Because we're losing control of our third

generation cephalosporins and that is why it shows that across multiple gram-negative species and streptococcus pneumonia, we are really concerned about our ability to be able to continue using this drug in the acute care setting or long-term acute care setting in a skilled nursing facility. So really what we're trying to focus on here is making sure that we're using third generation cephalosporins in the outpatient environment appropriately. I can tell you as a pediatrician, we are seeing these used inappropriately and the studies have currently shown that. This is really a call for us to be on the same page initially with these drugs judiciously, appropriately, and in accordance with the IDSA guidelines as well as the local intel. Next slide, the fluoroquinolones, if you are trying to get the fluoroquinolones up front to treat infections, better check your cultures and sensitivities. We have some facilities reporting 30% success. We have come to understand that Cipro is used quite frequently and is a frontline medication often inappropriately for things like asymptomatic bacteria, uncomplicated urinary tract infections, again in contrast to what the IDSA recommends so again, lots of inappropriate usage which promotes the development of tremendous resistance. Levaquin is the next one. Levaquin is supposed to be reserved for use in serious bacterial pneumonia. This is where these patients might be going to the ICU and have lost control of that medication, as well. This proposal here is an attempt to help us get control of the problems as an outpatient prescribing behavior. We can use all the help we can get.

Paul Oesterman: I think we all recognize in practice that antimicrobial stewardship has become a leading concern for all of us and I know in my facility, we have dedicated physicians, pharmacists, nurses. It's going to be an uphill battle. It's one definitely worth looking at and I think your advice about possible limitations or guidance for use of the third generation cephalosporins in the outpatient basis is very well warranted. Thank you for sharing that. We have in front of us, proposed criteria for coverage/noncoverage of third generation cephalosporins and the fluoroquinolone, oxazolidinones and Carl I will let you go over the criteria since you've got it.

Carl Jeffery: It's up on the screen here for those who want to see it. I was working with Dr. Wilson. He came to me several months ago with the concern he just expressed here and so based on some of his studies that he's been putting together, put together some simple criteria. Basically, it's fairly simple as far as requiring prior authorization, which our prior authorizations are turned around in 24 hours and so that's faster than cultures come back. The criteria that I proposed and put together was the culture and sensitivity-proven susceptibilities suggest the drug is necessary. And that really is the criteria, there's some exception criteria so if it's prescribed by an infectious disease specialist or cefixime for gonococcal infection or ceftriaxone isn't available or if the recipient resides in one of the following: Acute care, long-term care facility, and skilled nursing. Those would go through without any kind of PA. Right now, we're just starting with the third generation cephalosporins and the fluoroquinolones on specific medications are there. I know this is a big step, this would be a pretty significant impact, but I think it's what Dr. Wilson said, I think it's pretty important in regards to this.

James Marx: Why are the last two exceptions on there, I think that would be more critical than otherwise?

Paul Oesterman: I'll speak towards the LTAC because that's where I practice and we do have the cultures and sensitivities right there so we're on this.

James Marx: It's not all will and some won't so that's my concern.

Paul Oesterman: Well that's where the antimicrobial stewardship team I think will intervene and they do and they are. Joint Commission now has mandated a lot in that direction.

Carl Jeffery: So that's pretty much the proposal. I don't think the MCOs have any kind of suggestions with these.

Ryan Bitton: I think HPN was worried about prior authorization on every antibiotic, but the focus on specific agents makes sense toward antibiotic stewardship. So the prior auth would just require the culture and sensitivity.

Carl Jeffery: Right, they would have to know what bug it is and they'd have to know it's sensitive to the requested agent.

Jim Wilson: So just to reassure you, we really are sticking with IDSA guidelines, we are finding in the field, they are not being adhered to. If you look in Epocrates, which is the number one mobile app for prescribing for frontline physicians, so that's what we're using now. We find that a lot of physicians are just going with whatever they are used to and they're not really taking a minute to just go in and hit the brakes and they're not aware of what is going on in the SNFs or LTACs. Many folks are not getting cultures when they should so this is sort of an encouragement to get back to the standards that we were trained in for medical school, we should have them.

Jeannine Murray: Will there be education or some kind of campaign from other providers on this or will it just be a provider bulletin?

Paul Oesterman: I think this is one that because it is so significant, that a letter should go out to providers.

Holly Long: I do, too. We can definitely work on a letter, we'll always have a web announcement, but regardless of whatever we decide on, we'll provide a lot more detailed information and maybe go to the next step in providing some kind of link for a webinar or provider training that is specific to this and give more detail around the purpose for it.

James Marx: I think this is the first criteria that's coming out totally backwards. You're looking at sensitivity. I say we should be looking at resistance and that there's no other viable products that could be use because there are a lot of garden-variety infections from sensitivity. Some say, well I got a culture and sensitivity, and therefore I could be approved, so I mean that's totally, I don't say ass-backwards but I think ass-backwards. If you're looking at resistance, those are the only suitable treatment rather than on the basis of resistance rather than sensitivity. I would say that that criterion should be revised.

Carl Jeffery: I'll ask our resident expert here, Dr. Wilson.

Jim Wilson: Okay, so the IDSA guidelines, I'll give you an example, uncomplicated cystitis, the number one recommended treatment is Macrodantin, nitrofurantoin, right? That's what should be using with resistance patterns here in the states support that, right? The reassuring

thing is the data is supporting the standard national guidelines, which should have been using anyway, right? So that's the point of reassurance and I do agree that the language should be revised to reflect that we're actually using a couple different data, of course, but we do want to encourage providers that if they feel like they need to pull that particular antibiotic to use on a patient that they would be able to justify either against the IDSA guidelines or that they do have cultures and sensitivity on the patient back. There are times when we don't, we can't get cultures and sensitivities done.

Paul Oesterman: So, possibly to support Dr. Marx's comment, maybe we could revise the criteria. Bullet point number one, to read culture and sensitivity, proven susceptibility and resistance to other agents, suggesting the requested drug is necessary.

Jim Wilson: Susceptibilities does imply that.

Paul Oesterman: I want to cover both ends of the spectrum.

Motion to accept as amended.

We have a motion to approve the proposed criteria with the amendment that I just stated, do we have a second.

Second.

Voting – Ayes unanimous. The motion carries.

Holly Long: Paul, do you mind repeating the amendment.

Paul Oesterman: Sure, bullet point number one is to read culture and sensitivity-proven susceptibilities and resistance to other agents suggests the requested drug is necessary.

Holly Long: And what would you like from, what would the Board like from DHCFP as far as provider information?

Paul Oesterman: I'd say just a letter letting them know that increased support antimicrobial stewardship efforts.

Jim Wilson: I am funded by the State, so I am here to help.

c. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for medications used in the treatment of hemophilia.

Paul Oesterman opened up for public comment.

Amber Federizo: (indiscernible). Amber Federizo, Provides overview of services and locations of sites. States an overly aggressive prior authorization process may impede services. But there are some processes that could be put in place to see some cost savings. A factor product that has been negotiated at a special price could be used. They have lost some services to specialty pharmacies. States she is the only dual certified provider in the State. Recently

contracted with the department of corrections and have been able to save them money. Recommends to look at guidelines and implement rules related to those guidelines. Limit prescribing to specialists.

Paul Oesterman: Just one point. Our prevue is not necessarily cost at this committee, so keep that in mind.

Kelly Gonzalez: I am Kelly Gonzalez, although I have had fancy title of PharmD and N.P., it seems like other MBA and (indiscernible) I am a mother. I support and I have some things to talk to you about with consideration to prior authorization guidelines. I wanted to show you slides. I'm just going to show you picture of my daughter a year ago. This is my child that has a severe bleeding disorder. I have 5 children, 4 of which have bleeding disorders. My daughter had to go to the hospital because she broke her arm and anyone that knows anything about bleeding disorder knows that any healing to the bone itself requires appropriate clotting factors and she did not have that. This is my daughter 4 months after her emergency surgery at the hospital, I don't know if you can see that through the bleeding, she had appropriate care. We went to the hospital and in the hospital, she underwent the surgery, right after arriving at the hospital. And what happened, we had blessed, because what happened is that immediately they called and they got authorization because they knew they would need this post-surgery. They were able to obtain prior authorization because of the insurance (indiscernible). Even with that 4 months later, she has a circumference of a 17-inch arm because of swelling and inflammation even with the appropriate medications. I want you to imagine my child and what would have happened to her had she been in the hospital, had they done the surgery, and they called for a PA to have this quantity of medication on hand at the house, when she is released 24 hours later and for them to say she was going to be in for 72 hours, or hey this is going to take another week or this is Thursday and we can't process this until Monday. I want you to imagine that even with the appropriate treatment, she has limited motion and she went through all of the appropriate channels. Imagine if she didn't have access to treatment with the prior authorization being delayed. I have my older child who has two severe bleeding disorders, and her PA's were delayed significantly, and that resulted in us going to the ER. It's about quality of life. It does come down to cost. As you move forward and you're going to decide and talk about prior authorization and what states appropriate time-frame for people with bleeding disorders and our hemophilia community, I want you to consider the quality of life that my children, one of which had even though she had access to treatment right away, she still had problems healing because of her bleeding disorder, and then imagine if you were in my other daughter's place, what she had to go through with the ER. If my daughter that had access, she had to go to the ER every time. As you move forward and you consider adopting prior authorization for these, I want the people in the hemophilia community, this isn't about prior authorization, this is about prior authorization because I needed to a hysterectomy. This is about prior authorization for something that needs immediate treatment, so the longer that we delay treatment, it's problematic to the quality of life for persons like my daughter/my children, I'm not opposed to saying like hey, I know that there is inappropriate use. I'm not saying that there's not, I'm not saying that people should have people should have a lot on hand, I'm not saying that. What I'm saying is that, you know, our genetics dictate to what our bleeding type is, this is what our bleeding disorders are and our genotype is monitored by our provider and this is what clinically presents and this is what we need on-hand. That's not going to change. My diagnosis is not going to change. It's in my genetics. I have the genetics and neither will for my child, neither will it for some on our committee who have severe hemophilia, there is

0% factor level is still 0% factor level. Take into consideration that say we're going to require it every whatever, the frequency might be, take it into consideration that you know, we're not opposed to saying, hey, we'll come in for a clinic and go through a P.A. that you're going to say, well we'll PA you for three months or six months, the quality of life that patients in our situation have and take that into consideration. But I don't understand PA's that take weeks and we have to do every month for every single issue. Thank you.

Bill Robie: Hi, good evening. My name is Bill Robie. I represent the National Hemophilia Foundation. I work in our public policy department. Our organization is based in New York. I work out of my home in Bend, Oregon and cover about 19 states. We submitted a letter for the record expressing our concerns about clotting factors for PDLs and prior authorization criteria so I'm not going to rehash that I just wanted to take a few minutes and give you a little bit of background on our organization and bleeding disorders in general. We are to ensure the individual affected by hemophilia and related to bleeding disorders that timely access to high-quality medical care and services regardless of financial service deficits, were in place for residents. NAHF has a medical and scientific advisory council that issues guidelines for the care and treatment of hemophilia, and their recommendations are for individuals with bleeding disorders, they have to have access to the full range of FDA approved clotting factor therapy as determined by their treating physician regardless of financial circumstance or type of insurance coverage, if they need access to a federally funded hemophilia treatment center providing collaborate integrated coordinated care, and access to at least one specialty pharmacy provider and 340b program. Hemophilia and other bleeding disorders most importantly fortunately are rare conditions. Also, they are inherited conditions. They are genetic. In most cases, it is passed from mother to son but women also have bleeding disorders. I will refer to hemophilia most generally as that's what people are familiar with. The main symptom of hemophilia and other bleeding disorders is uncontrolled and often spontaneous bleeding and internal bleeding into the joints which result in pain, swelling, and even cartilage damage. They are rare conditions. There's about 20,000 people in the U.S. at any given time that have hemophilia. When you include other bleeding disorders, that number goes higher, probably the most common bleeding disorder is VonWillibrands disease, and that is spread equally between men and women in the population. Hemophilia occurs in about 1 in every 5000 births and while in most cases it runs in the family and is passed on, there are cases of spontaneous mutations so there are new cases developing every day. There's no cure. There's also no prevention. If you have hemophilia, you have a disease where you have it your entire life, so treatment is never an option. That treatment is lifelong infusions of replacement by factor therapies. These are from human plasma or using recombinant technology. Many of our patients, certainly the most severe from a prophylactic type of treatment, so they're infusing regularly to prevent bleeds. Those in milder conditions may have the luxury of treatment on demand but most of our severe patients are between prophylactically prevent bleeds to begin with. People did start learning to infuse themselves at about age 7 or 8 and then they spend the rest of their lives infusing themselves so most of our patients are infusing at home, some people infuse, I've seen videos of people infusing in the middle of a lake, so home fusion is the typical treatment standard for most of our patients. We are an expensive population. As been indicated, treatment costs for an average hemophiliac patient is about 350,000 dollars a year. For severe patients, it's about twice that and if you've got an inhibitor, it's probably at least a million dollars a year. The good news is for our patients, if they have access to the medication that works for them, they feel otherwise normal lives, being productive, tax-paying citizens running businesses, having a job, having a family and things like that, case in point, Chris Bombardier, a member of our

community in Colorado climbed Mt. Everest last year and was infusing the entire time in his tent on the way to the summit. So, our patients are very adept to taking care of themselves as long as they have access to the medications.

Paul Oesterman: You have about 1 minute left.

Bill Robie: Again, for most of our patients, the most serious concerns are bleeding at the joints, into the organs, into the brain and as a consequence, people either are not having access to the right medication, they're not having timely access. For many of our patients, our concern about not having the medication prescribed by their physician is they experience some increased bleeding or doesn't control their bleeding entirely; the treatment protocol is more infusions. Some of our patients are not necessarily on proper medications and the result of costing more because of simply infuse more to take care of bleeding episodes. Again, we have a letter submitted as part of the record.

Betsy VanDeusen: I am the executive director of the nation chapter of the National Hemophilia Foundation. Our mission is to improve the quality of life for your members with bleeding disorders. We represent over 600 households and an estimated 60% of our members are on Medicaid. I am here to advocate for our members to have access to all approved therapies for the treatment of bleeding disorders. I am requesting access without undue barriers that may compromise the quality of care or increase hospitalization and ultimately result in higher costs. I request prior authorization criteria to be as direct and open as possible and for as long as a period as possible, six to 12 months. We request additional barriers such as preferred drug list or quantity limits not be imposed due to their documented negative effects of health outcomes. We would be in favor or moving hemophilia treatments to fee for service because it would provide with the most timely access to treatment. As far as what Amber shared, the National Hemophilia Foundations supports the federally designated treatment center model and our stance is that we request to have at least two pharmacy options available to our patients and one be a 340b program. Thank you.

John Sandstrom: I'm John Sandstrom with Shire. We represent a large number of products. Our company manufacturers products for hemophilia A, hemophilia B, (indiscernible). I will not talk about how clotting factors are different. I think my colleagues have already addressed that. One thing that I will point out is that our two products, Advate and Adynovate. Advate is the standard half-life therapy available since 2003 with a full complement of real world evidence study and clinical studies supported. In 2018, the FDA approved (indiscernible), the first and only FDA-approved software device. They're based on a pharmacokinetic model for the management of dosing as well as the interval of therapy. This in conjunction with management of vial sizes can have an impact on the disease state management with respect to cost and efficacy and can be used as part of a disease-state management program. Our extended half-life products, the Adynovate is a factor 8 for the treatment of hemophilia A. I wanted to point out that in a recent peer-reviewed publication, that categorizes extended half-life products, there's a number of products that claim to be extended half-life products. In this article, they categorize Adynovate and some other products as our pegylated form of extended half-life product as an extended half-life product. Also in our profile, with respect to our clinical trials for Adynovate, we have shown to provide a reliable and predictable twice-weekly dose in patients in the trial, when we had to adjust their dose with 2% of the population.

Kelly Gonzalez: I know that you guys mentioned that you said earlier like cost isn't a factor. But I don't understand because why would PA be required if cost isn't a consideration? Isn't the PA required to reduce unnecessary usage and what is…

Paul Oesterman: Unnecessary usage and inappropriate…. You heard about the antimicrobials? Inappropriate use. That's kind of what we're looking at.

Kelly Gonzalez: Because inappropriate use as effective use would be a cost hindrance. From my perspective as a patient, as a parent, it does come back to cost and it does come back to wanting to work with our insurance companies to make sure that the PA that's put in the process, that's for quality of life for patients but at the same time, cost effectiveness. I just wanted to add that part of it.

Carl Jeffery: We'll talk briefly about what we have going here. The Optum criteria is in there. It's very simple. It requires a diagnosis and FDA approved or some kind of other peer review literature and make sure it's appropriately being used, the dose is appropriate, and the duration is appropriate and really there is no quantifying it in our criteria that I put together so it's really up to the provider to say that and the pharmacist will be reviewing the PA. The dispensing provider basically makes a promise that they will monitor how much product that the member has on hand; I've heard horror stories of pharmacies that just drop ship factor regardless of how much the patient may have on hand. We want to get away from that and make sure that the provider is following up with the member and finding out so they don't have that overstocked and then that the prescriber is a specialist in treating hemophilia. The criteria that was submitted by the MCO I think are much more extensive, very specific, so they're good criteria and much more lengthy.

Jeannine Murray: Well I think they're put together by drug and they align with what the FDA lists as approved.

Paul Oesterman: Looking at the proposed criteria from Optum here, it looks like pretty much the diagnosis is required and is supported, the prior authorization covers pretty much every drug available right? Am I correct? On our managed care organizations, all of them are covered, just to confirm. We don't have an issue with drug cost selectivity there. My only question might be in regards to the proposed approval length of just being 3 months? I would recommend a longer period.

Speaker: National guidelines suggest patients under 18 year old see their provider every 6 months and adults every year. So, if they were to extend that to coincide with provider visits, that would advantageous.

James Marx: Prior authorizations keep me working until 8:30 every night, so I think putting unnecessary prior authorizations is just a lifelong process is typically not going to change so I'm not sure why we need; 6 months is a reasonable expectation.

Paul Oesterman: I would go with a year.

Amber Federizo: For continuity of coverage of a year, I would not want to see them not go through the prior authorization for a change in medication. I do see a lot of inappropriate

utilization around the state. I see a lot of money being wasted. I don't think a change in dose should require a new prior authorization, but the initial approval should be for one year.

Carl Jeffery: And the way our PAs work, if they were approved for a single one agent, they could go up and down on the dose for that one agent, but if they change from like Kogenate, to something else, that would require….

Speaker: (indiscernible)

Carl Jeffery: Those PAs get complex. I don't know what the MCOs do as far as when they enter those specific quantities, they're allowed specific….

Jeannine Murray: I'm pretty sure you can find the number of units even though the PA lengthened for a year, but I think the PAs enter by hand.

Paul Oesterman: So, if I'm hearing you correctly, you're kind of not suggesting but asking that we maybe consider limitations of 3% variance…

Amber Federizo: I am asking because as some pharmacies are better than others in how they adjust the dose. A prescriber may not really evaluate the refill request from a pharmacy and just sign it off.

Carl Jeffery: We do have the utilization numbers in there. (slide presentation) This is for the fee for service. It's broken out by product. We have several patients in fee for service that are on hemophilia products. It kind of goes down. AmeriGroup is in there. It's carried over to the next page and so by far, fee for service has way more claims than the MCOs but I think that's most of the sicker patients come to fee for service.

Holly Long: Was there a reason behind Optum proposing the three-month duration?

Carl Jeffery: I'm not opposed to 12 months or 6 months.

Paul Oesterman: What I'm hearing is that the proposed criteria that we have is to amend the approval length to one year from prior authorization and that a new prior authorization would be required for any dose adjustment, and I'm going to go liberal, in excess of 5%, either increase or decrease.

Motion made to approve amended criteria.

Second

Voting: Ayes are unanimous, motion carries.

d. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for medications used in the treatment of irritable-bowel syndrome.

Opened up for public discussion.

Carl Jeffery: Trulance is an existing medication. It's been on the market for a while. It's got a new indication for irritable bowel syndrome so that's why we're just going to add it to our existing criteria or with Linzess and Amitiza. It follows the same steps. In addition to its chronic idiopathic constipation diagnosis, we're going to add the IBS-C. This is the chapter 1200 criteria that is proposed in here. I just copied it over and then added the generic name for the Trulance. That's the only change, just adding because the other ones had a max daily limit.

Ryan Bitton: For HPN, this aligns with what we have already.

Motion to accept the criteria as presented.

Second

Voting: Ayes are unanimous, the motion carries.

e. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for tezacaftor/ivacxaftor (Symdeko®).

Opened up for public discussion.

Speaker: (indiscernible) I am the director of the CF Center for Reno and a pediatric pulmonologist. I would like to thank the Board for considering the prior authorization process for Symdeko and give the patients the opportunity to have this medication in addition to Orkambi. Any questions you may have, I am happy to answer.

Jamie Tobitt: My name is Jamie Tobitt. I am a MSL with Vertex Medical Affairs. I just wanted to introduce that I'm here and will answer any questions. I know how pretty complicated the drugs are, as well.

Carl Jeffery: This is a new criteria because this is a newer medication on the market, similar to the other agents that are currently available. It follows the same kind of standard guidelines that we have set for the other ones. We've got 12 years of age or older, that's what it's approved for currently. They're probably working for younger ages. The diagnosis of CF and then one of the following, they've got the F508 deletion mutations. So this is where maybe it's a little bit sticky because I tried to come up with some language that didn't list out every single mutation because that's what we struggle with is the added new mutation, we have to bring it back to the Board and add that to the criteria. I tried to add language that would include all the mutations as they are added and so I put language in there so if the patient has one FDA-approved package insert listed mutation on at least one allele of the CF transmembrane conductance regulator. I try to get that so read through that and make sure it makes sense. That's my own language so I won't be too offended if you want to make some updates to that or anything but prescribed by or in consultation with the pulmonologist or a CF care specialist, somebody affiliated with the CF care, and then it will be approved for 12 months. The reauthorization criteria is on the very bottom of the page. It's kind of hard to see, but basically it's just documented benefits they are getting from the medications.

Holly Long: I think we're on the page mostly with the MCO's and I apologize I didn't make my charts with the comparisons for the MCOs and the fee for service, but there are different durations. For example, Silver Summit and Fee For Service, we're seeing the duration for treatment early approval of the prior authorization being either 6 or 12 months, is there any information around that why it should be six or 12 months?

Carl Jeffery: I had suggested 12 months because I think that's what we have for the other ones, but I don't know, is there some reason you guys have 6 months versus 12 months.

Tom Beranek: I don't know, I couldn't respond why. If this is the corporate policy, it isn't one we did for this account.

Ryan Bitton: HPN normally approves things for 3 to 6 months initially, we have the authorization criteria still in the reauthorization, then we will go to 12 months to make sure it is effective.

Paul Oesterman: So, for consistency, should we consider our initial authorization to be a 6-month period and then additional refills and reauthorization be 12 months?

Speaker: I would suggest doing it for the 12 months' duration rather than the 6 months' because we do know that these medications are really expensive and we do not start these medications unless they really as a provider that they will really benefit the patient. So, not having to go through the process for 12 months would be really beneficial, I would like to ask the board to consider 12 months.

Paul Oesterman: I guess this is a question from my end, if we approve it as 12 months and your criteria is 6 months…

Holly Long: It's updated. Their criteria can't be more stringent.

Paul Oesterman: They can't be more stringent than we are.

Holly Long: They'd have to change theirs.

Paul Oesterman: They have to change. Okay.

Holly Long: Part of the reason that I ask is as I'm looking at other states like the other states that have the prior authorization, most of them have 12 months.

Motion to approve the criteria as presented.

Second

Voting: Ayes are unanimous, the motion carries.

f. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria for ivacaftor (Kalydeco®).

Opened for public discussion.

Jamie Tobbit: Jamie Tobbit from Vertex. We also make Kalydeco, so I am here for any questions. The FDA indications are spelled out in the package insert and this medication should only be used in patients with those mutations.

Carl Jeffery: This is real simple, just like the Symdeko, uses kind of the similar language and just updated so instead of listing every single gene mutation, in reference to FDA-approved package insert so that's the language that was added in there.

Paul Oesterman: You're going to modify and take this out?

Carl Jeffery: Well, that's Amerigroup's criteria. I guess they'll have to take it out. The list of all the gene mutations.

Jeannine Murray: Aren't those the same?

Carl Jeffery: They are and in reference to the FDA. It doesn't have to be in there.

Jeannine Murray: We're not more restricted by them.

Carl Jeffery: Right, so you can have them in there. This is my criteria here. This is the only thing; this is the chapter 1200 criteria here and all I did was remove the… There were a lot of mutations that were listed there and I just changed to list it in the FDA-approved package insert.

Paul Oesterman: This one piece I've noticed is not on here is the renewal.

Carl Jeffery: Yeah and since this was an old chapter 1200 criteria, we can add renewal criteria on there to say the patient had similar to the Symdeko and there's a clinical benefit.

Paul Oesterman: And that would be for 12 months, also?

Carl Jeffery: Yes.

Paul Oesterman: Do we need this to be prescribed by a pulmonologist or specialist, also?

Carl Jeffery: I think it's a good idea. Like I said, we've got an opportunity to update it and we might as well add that same language to it and the Symdeko and we can add that criteria, too, so pulmonologist and specialist affiliated with the CF care center.

Paul Oesterman: We have in front of us the proposed criteria with two modifications. One is the who can prescribe it and the second is the approval line for reauthorization if a patient shows a positive clinical response.

Motion to approve criteria as amended.

Second.

Voting: Ayes are unanimous, the motion carries.

Holly Long: I just wanted to clarify on Carl's statement that a reauthorization is for the one year duration?

Paul Oesterman: Correct.

g. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria for topical immunomodulators.

Opened for public discussion.

Carl Jeffery: We have a new agent in this class, which it's been a long time since we've seen a new agent in here, but Eucrisa is wildly popular topical immunomodulator and we see quite a bit of it. If you look at the utilization numbers on there, we're actually seeing it quite a bit. You can see on the popularity of it going up. So the Eucrisa is very popular lately. This is the chapter 1200 criteria existing. We're just going to add the Eucrisa on there. It's also has similar indications, mild to moderate atopic dermatitis for 2 or more year old.

Paul Oesterman: Do you know if there's any head-to-head studies between Elidel and Eucrisa?

Carl Jeffery: I'm not aware of any but I can almost guarantee that there's not.

Paul Oesterman: Eucrisa does not have a black box warning.

Carl Jeffery: Yeah, I don't know that off the top of my head.

Paul Oesterman: I don't think so.

Holly Long: I don't see any black box warnings with this.

Paul Oesterman: Okay, thank you.

Speaker: Under A, the patient must have a failure of a topical steroid. Is there a timeframe associated with that? Like within 6 months they have tried and failed a topical steroid?

Carl Jeffery: Right, and you want to quantify, like how long they need to try this, maybe they tried it for a day, maybe they didn't have good results within a day so they wanted to… No, I think that's good. I don't know what a good 10 days of therapy or something? Two weeks?

Paul Oesterman: Fourteen days.

Carl Jeffery: A 14-day trial within the last 6 months?

Speaker: Yeah.

Paul Oesterman: So, we've added to the proposed criteria that the patient must have a therapeutic failure with the use of a topical steroid for 14 days within the immediate prior 6 months. Do we have any other proposals or changes?

Motion to accept as amended

Second

Voting: Ayes are unanimous, the motion carries.

h. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for compounded medications.

Opened for public discussion.

Carl Jeffery: This is a new one and a new set of criteria for us. This is something we've been a little bit struggling with for the last couple of years because there's a lot of . . . I think it kind of comes in waves and pharmacies that do this compounding, it will compound a lot of stuff that's kind of similar to commercially available stuff but they tweak it just enough to get by the rules. We're an advantage within Medicaid and this may change in the future is that the manufacturers that make like the powders, like the PCAA and Letco and those types of companies, they don't participate in the Federal Drug Rebate Program so we don't pay for most of these anyway, so a lot of what is billed is the pharmacies only get a portion of the ingredients because they're only getting paid for what is rebatable. But, to head these off, I think to get with it, there are a lot of inappropriately used that are still used tablets and capsules and use those in compounding and get reimbursed for that when they probably should not be compounding it, so here is the criteria here. You can read through it real fast but it's basically that each ingredient is FDA approved because we see there's a lot of ketamine being used now and some others, topical Ativan that is being applied. I'm not sure it has any data to show that it's effective, so it's FDA approved, or National Compendia supports its condition, the therapeutic amounts are also listed in the National Compendia peer review literature.

James Marx: I think the specific amounts but also the combination, we're seeing all kinds of crazy combinations and there's not any peer review support for those combinations. I think that may be an out as well, because I mean, there's all kinds of stink oil preparations that are being done. It may be a great idea, but it's not really supported by any sort of science. So, I think that's part of it, too, some sort of support or the combination.

Carl Jeffery: Therapeutic amounts and combinations are supported?

Speaker: Yeah.

Carl Jeffery: And then any prescription ingredient requires authorization and/or steps so if there's not a way to get around the PA for other medications by just compounding it and cannot include any drug that has been withdrawn from the market due to safety reasons or the patient has tried and failed therapy or had a tolerance to two FDA approved commercial available prescription therapeutic alternatives and it then lists out….unless one of the following criteria, and it has some exceptions there, so if they have an allergy or if it's not commercially available

for example, and then the compounded drugs must not be used for cosmetic purpose, and the last one is the compound is subjected to drug specific targeted compound program, they meet all the specific drug criteria below. The last sentence doesn't make sense now, but it made sense when I wrote it. I think it's a remnant of the criteria that I was kind of plagiarizing. I would just strike that number 7.

Paul Oesterman: Did we have a list of commonly compounded…

Carl Jeffery: There's utilization numbers in here of what medications are being used. Ora-Plus Interestingly enough, it's not rebatable but we got an exception from CMS to cover that one because so many children's medications are being used to compound and the next is lidocaine and then again another Ora-Plus similar, so really not too many and we don't see a whole lot of the real high-priced ones here because like I said, most of them are non-rebates so we don't pay for them.

Paul Oesterman: When looking over the list, it looks like a lot of them who used a compound and things like Magic Mouthwash or GI cocktail… Diclofenac gel, that's available from market….That's available commercially, 1%. Interesting that we, Cialis, Viagra, Revatio.

Carl Jeffery: I think those are mostly used, they are compounding them, I hope, is that they are using those for PAH in children.

Holly Long: So Carl, originally when we talked about this, we talked about the dollar amount correct?

Carl Jeffery: And we can certainly go down this path. I know we've talked about cutting just claims over 500 dollars. I am not opposed to having it applied to all of them.

Ryan Bitton: For HPN, we have a $200 limit. So, anything less than that, it isn't worth the PA effort. We have had $50, but we are at $200 now.

Jeannine Murray: Amerigroup has also moved it down over time, we are at $200 now too.

Holly Long: That's what I saw across this board was a lot of the states started higher and then had to move it down, and so generally I think the average that I found was around 200 and they're starting to move it to 100 which I believe Silver Summit is at 100 right now.

Jeannine Murray: You asked about how many claims we had for 500, for compounds; do we have any compounds claim, but we had only 19 over $500, so they are able to get it. They just need a PA for it. We don't have specific criteria, they just submit a universal request.

Ryan Bitton: For HPN, we also reference the FDA do not compound list. And the FDA not approved for topical use. I'm not sure how expansive you want the criteria. We have it there to help guide the pharmacists and providers. I don't know if that is viewed as more restrictive, they are FDA lists that guide compounding. As we move forward with more or less-restrictive, it might help to align it, so something to consider if we have to take it out.

Paul Oesterman: In particular, one of those in here is Prograf or Tacrolimus. As we move into USP 800, the facilities are going to be able to compound that are going to be extremely limited and I would not want to see claims from John's Independent Pharmacy for this when they're not going to be able to safely process these prescriptions. We see a fair amount of tacrolimus suspension but because of the carcinogenic risks, USP 800, pharmacies are not going to be able to compound it unless they have chemo hood and all the requirements to handle that.

James Marx: I don't see a distinction here between sterile injectable vs. oral or topical compounding. I think that's really an important distinction that maybe these need to be addressed, as well, especially with 504 c and d going on and all kinds of problems with compounding sterility issues. I think we really want to make sure that the pharmacy that's doing this is really properly certified to produce that actual product.

Carl Jeffery: Yeah. We only look at oral and topical utilization for this report, but I think you have a valid point there, too. Although, the Board of Pharmacy may have more power over the pharmacies to enforce that.

James Marx: I know that there's a lot of controversy about how well Boards of pharmacy can do that sort of oversight.

Carl Jeffery: Yeah, because there's also the USP 797, I think it's the rule that makes all the compounding the sterile…

Paul Oesterman: That is changing the USP 800, next year. So, we have in front of us criteria that will be recommending the approval of 6 months unless the provider requests a shorter length of therapy, and we have 6 different criteria. We've amended criteria bullet point number 2 to include the therapeutic amounts and combinations are supported by National Compendia or peer review literature for the condition being treated. My question, I've heard talk about a dollar limitation, and I know that's not under the purview of this committee to necessarily talk cost of medication. It sounds like they are dropping, so…

Carl Jeffery: The limits are dropping.

Paul Oesterman: The limits are dropping.

Carl Jeffery: I think as far as this goes, you can't make any decisions to PA drugs based on its cost. I think is what the rule is. So, I think you setting a dollar limit is okay.

James Marx: For example, the number 2 drug in the over 500 list. The 2% is not a whole lot more effective than the 1.5% or Omeprazole 20mg capsule, what do you need to compound that for?

Paul Oesterman: Oral suspension; the patient has a core track and they can't…

(indiscernible speakers)

Paul Oesterman: I think they use that to compound; that's what they use to compound suspension.

Carl Jeffery: And mixed with bicarb and that, especially my daughter was on a PPI when she was an infant.

Holly Long: I get calls all the time from parents that are trying to get certain compounds approved just by the pharmacy to get them to make it because they have complications, they have problems with it, and they're just trying anything so the child won't throw up or the child won't have side effects, sometimes it is the suspension that works and sometimes the tablet, you never know.

Paul Oesterman: On the fee for service slide, what are the row labels, what does that stand for?

Carl Jeffery: So, the top one is the topical, oral, so ex. is external, ij is injection and iv…you know, and OR is oral.

Paul Oesterman: XX is unknown?

Carl Jeffery: Yeah, they didn't specify it, kind of unknown.

Paul Oesterman: Do we ever claims for bio-identical hormone replacement therapy?

Carl Jeffery: We probably do but they're not paid because they're all non-rebate.

Paul Oesterman: I think this is still a pretty vague area and I know this is our first attempt to try and…

Carl Jeffery: If you read through, and I didn't honestly look at the MCOs criteria, I was just reading through the one of the United Healthcare ones next in line after ours, and this is just the first one I came to… I think it's very complete.

Holly Long: HPN definitely has a good middle-ground.

Carl Jeffery: It's the one titled…it's got United Healthcare on the top.

Paul Oesterman: Out of curiosity, are you finding that your claims for compounded medications are coming from necessarily limited number of providers and /or pharmacies?

Ryan Bitton: I think the answer is yes, but I don't have an official report. We normally see pharmacies that do more marketing and some issues. We see specialized pharmacies.

Jeannine Murray: I thought it was interesting when we looked at the, and the names are hidden, but there are two pharmacies that really stick out and there's really not prescribes that stick out as much the way the couple pharmacies do, it would be interesting if we can go back and see what those pharmacies are filling.

Paul Oesterman: And if it's the same limited number of compounds they're specializing in….

James Marx: I like the HPN criteria. The only question I have, the one issue is under 6B about, sentence 1, not intended to treat dermatologic conditions, scar treatments are considered cosmetic, I would say that that's generally true if you're talking about adults but if you have a child that has like a big gash on their forehead, I wouldn't really say that child is vain and wants to reduce the scar, so I think there has to be some sort of wiggle room in there for certain cosmetic sort of indications that maybe are outside the box, maybe let's say an adult, but I don't think they considered that at all.

Ryan Bitton: We have considered it but I think there might be a prior authorization override or something like that that we could have done…

Paul Oesterman: So, we have our Optum proposed criteria here with one modification and then possibly the addition of a cosmetic use for patients under the age of 18 as a waiver. This is relatively new to us and I'm sure we will be coming back to this and revising it to adjust as needed.

Carl Jeffery: Right, and then I would I think just for the call center's sanity, if you would also consider a 200-dollar limit so it would only apply for total claims that were over 200 dollars.

Andolyn Johnson: Since this is my first board meeting, I want to be consistent with what you all done in the past, but at what point we've made a lot of changes do you say, okay, we're going to wait on this and then come back to it after it's republished, because I'm just looking at it from a notice standpoint. I think in my gut, we're on the edge, but I want to be consistent with what you've guys done in the past so are you guys comfortable…

Paul Oesterman: Yeah, I don't think we've made really any major significant changes so… Thank you for your input.

Holly Long: It is new what's going along with what you're asking. I think I have more comfort in it knowing that when we do something like this, any changes that we make that Optum is going to go with it and watch the utilization and too many changes, no matter how much of a change we make if it doesn't make sense in the future. For example, if that 200-dollar limit isn't working, we can change that and we can bring that up at the next meeting.

Andolyn Johnson: Okay, great, thank you.

James Marx: Can we continue to monitor this…

Carl Jeffery: Yeah, we'll watch these and we'll include board request reports going forward at the next meeting.

Motion to approve the proposed criteria as presented with the two amendments and the elimination of line 7.

Paul Oesterman: Motion presented. The only discussion would be to bring the usage back to the next meeting so we can take a look and see, when's this going to be implemented? A couple of months, so like in two meetings from now, let's put it on the agenda to take a look at the usage.

Second

Voting: Ayes are unanimous, the motion carries.

i. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria for neuromuscular blocking muscle relaxants (botulinum toxin)

Opened for public discussion.

Karen Campbell: My name is Karen Campbell, PharmD, and Scientific director at Allergan. My testimony is specifically to address the criteria for coverage of Botox on botulinum toxin A (indiscernible). Allergan respectfully request the Board adopt the PAs criteria for chronic migraine coverage as stated in section 10 and 11 in the Nevada Medicaid botulinum policy. The Washington Medicaid criteria for chronic migraines are included in the policy only as a reference. However, if the Board is asked to consider adding the Washington Medicaid criteria for Nevada's Medicaid policy for chronic migraine coverage, I would like you to add the following comments: My first point is, Botox is the only toxin FDA approved for the prophylactic treatment of chronic migraines in adults. We agree that the United Healthcare policy statement included in the binder that the other agents are unproven and not medically necessary for the treatment of chronic migraines. There are three components to the Washington Medicaid Chronic Migraine Criteria. We will go through each separately and provide evidence against the addition of these criteria. Criteria number 1: The patient cannot continue treatment if "have shown an inadequate response to treatment defined as less than 50% reduction in pain per month after 2 treatment cycles." A post-hoc hoc analysis in 2017 provided data on patients that did not achieve the 50% responder rate after 2 cycles of Botox injections. It showed a significant decrease in severe pain days, these treatment refractory patients achieved significant treatment improvement from Botox even though they didn't meet the 50% responder rate criteria. The second criteria: Patients cannot continue treatment if "a change of episodic migraines as defined by 50 headache days per month for 3 consecutive months." The Washington Medicaid final revision release on July 15, 2018, a week ago, has removed this language. The treatment induced by the chronic migraine patients are still chronic migraine sufferers. Lastly, Washington Medicaid limits Botox use to only 5 treatment cycles, one year of therapy. Their policy does state that additional treatment cycles should be the plan's decision. A real-world open label study demonstrated the sustained headache free days through 9 treatment cycles, 2 years of Botox. This real-world study also shows continual improvement in functional disability, reduction in headache impact scores, and favorable long-term safety profiles with only 18% reported having 1 or more treatment-related adverse event. Neck pain was the most commonly reported side effect at 4%. There were no new safety signals identified. Once again, Allergan respectfully requests the Board adopt only the chronic migraine PA criteria for Botox, as stated in sections 10 and 11, and that the Washington Medicaid Criteria only for reference purposes.

Carl Jeffery: This was actually a request from the state. We've had the criteria in chapter 600 right now but the chapter 600 wasn't….

Holly Long: Administration says this is kind of inappropriately placed. It's there but they would like pharmacy to oversee the policy so they've asked that we would move it over to

chapter 1200 and there will be a reference within 600 stating the location of the policy. We didn't see any changes needed for the policy but I don't know if Optum has any recommendations or any of the MCO company recommendations for the policy.

Carl Jeffery: Yeah, and I didn't put any proposed changes in there. My thought was just to move the criteria directly over from chapter 600 to chapter 1200 without any changes, and that criteria is in the back, the last couple pages; it is in the back. None of this criteria addresses migraines?

Holly Long: Yes, it does.

Carl Jeffery: Oh it does. I see it, okay, yeah.

James Marx: Do we have the Washington mandates?

Carl Jeffery: No, I think that reference, and that's what I was talking to Janine about….

Jeannine Murray: The Washington reference is an Anthem policy. Anthem Washington has specific mandates to use with Botox so our policy said Washington Medicaid is not going to follow what the Anthem policy that you go all the way to the end of policy with what is Washington Medicaid's policy for migraines, and I think that's what the lady was referred to. So, we're not here to talk about Washington's policy. This is about in our policy so that we don't have to have a separate Washington policy.

James Marx: I think that's totally wrong. Having used Botox for 20 years, they don't get a 50% reduction but there is an improvement to quality of life and reduction in intensity and severity and frequency, about maybe 50% is an artificial benchmark that really isn't necessary.

Jeannine Murray: When she was referring to items 10 and 11; that was what our policy is and similar to yours for 15 days, how you define migraines.

Paul Oesterman: So, the proposal is just to move, make no changes to the botulinum toxin policy, it's just to move it from chapter 600 to chapter 1200.

Holly Long: Yes, so pharmacy will be managing it.

Paul Oesterman: It looks like our usage is like light…

Carl Jeffery: No, we don't see a whole lot of usage of this, even within the past year, 864 claims total for all of it so it's not a huge utilization of that.

Paul Oesterman: Do we have a motion to adopt the existing criteria from chapter 600 into chapter 1200?

James Marx: I still…I don't have a problem with 10, but I do have a problem with 11.

Carl Jeffery: That's Amerigroup's policy so a few more pages, you've got to go the other way… chapter 600. Prior authorization is not required. So under C? We're going to change that, too? And right now we don't have prior authorization.

Holly Long: Yes, so that they would require removal of it. If it was under pharmacy, it would require a prior authorization.

Paul Oesterman: So, we would be amending the criteria to say prior authorization is required and then how long do we want to make the prior authorization for. Twelve months?

Carl Jeffery: It really depends on what they're using it for. Sometimes it's a one-time administration and sometimes it's chronic.

Paul Oesterman: How do you guys handle the time frame?

Jeannine Murray: I think it's for 6 months. We cover Botox under our medical benefit.

Paul Oesterman: Six-month initial and then reauthorization at one year if somebody has to continue on it?

Ryan Bitton: It doesn't go to a year. We are six months for both.

Paul Oesterman: Six and six? Okay.

Jeannine Murray: It's 4 to 6 from the initial and then ongoing from there.

Paul Oesterman: The call center, which works best?

Carl Jeffery: Either way, it does depend on (indiscernible).

Paul Oesterman: On behalf of our practitioners that are having to get in trouble by the PA process, I know what the answer is 6 months and then 1 year….

James Marx: Yeah, I think that's fine. I think the only thing I really have trouble with is I think the Botox is very misunderstood molecule. It has other effects outside the neuro-blocking activity that isn't addressed here. I wouldn't be using these criteria, but I do use them for some of the central effects. If a provider wanted to use them under a different circumstance, there is no allowance for the use. I'm ok with the use as they are.

Paul Oesterman: So we need a motion to shift the criteria for botulinum toxin from chapter 600 to chapter 1200 with the change and policy of part C from prior authorization is required now that it is no longer not required and the initial prior authorization would be 6 months and reauthorizations would be good for one year.

Motion to accept as amended

Second

Voting: Ayes are unanimous, the motion carries.

j. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for opioid containing cough preparations.

Opened up for public discussion.

Carl Jeffery: I will give everybody a few minutes to read through the extensive criteria that I put together. The patient is a routine, so there's no allowance at all for this for under 18.

Paul Oesterman: The approval length, that would be my only question.

Carl Jeffery: So, there wouldn't really be a length because there would be an age restriction so as long as they're over 18, there's going to be the other criteria that we still have for all of the opioids so either the morphine equivalent dose or we put the codeine with promethazine quantity so they just have to follow those quantity limits and numbers. So we probably don't need the length of 6 months. There's no prior authorization with age restrictions.

Paul Oesterman: We do have a motion to approve. Do we have a second?

Ryan Bitton: Before we vote, can I throw out some MCO criteria? We limit it to a 30-day approval. We define limitations of 120 ml per fill and 360 per 30 days and require a failure of some non-opioid-containing cough syrup. At the end of our short-acting opioid protocol, so it's a little bit more extensive for 12 years of age for codeine containing products. I think there's a little bit more that could be put into the criteria like this. With the opioid crisis, we have some extensive programs and we try to not let kids get opioids. So we built a tougher approval for kids.

James Marx: Well, I think the opioid containing cough syrups is not the opioid crisis, it just hasn't been shown to be safe in kids. So opioid crisis or not, these are not safe in this population.

Holly Long: We do have the existing criteria for codeine for children that we put in place last October. The recipient must be 12 years of age or older… We do have that which takes precedent over as far as a different kind of limitation.

Ryan Bitton: Does it talk about non-opioids first and put limits on it?

Carl Jeffery: Yeah, we did that for both tramadol and codeine.

Holly Long: I have never seen prior authorization for 30 days. How does that work?

Ryan Bitton: There's not a lot of requests for opioids containing cough syrups now. We see the utilization drop off. I have not heard of anything.

James Marx: I think what we're doing is confusing and expectorants, they are two different things; I think we're getting off track here.

Paul Oesterman: At this point, we do have a motion to approve the criteria as presented. Do we have a second? Any further discussion on this motion which is just that the approval length would be for 6 months and the patient must be 18 years of age or over to receive an opioid cough medication without any quantity limitations.

Carl Jeffery: Well, not without meeting the previously established criteria.

Ryan Bitton: To be clear, so with the quantity limits, those were previously established?

Carl Jeffery: Yeah, previously established quantity limits so it various so the promethazine with codeine has quantity limits. There are other opioids who already have quantity limits so if they are getting something that has codeine in it, there's a limit to it.

Paul Oesterman: Do we have a motion and second.

Motion to accept the proposed criteria.

Second

Any further discussion? Seeing none, call for the question. All those in favor of the proposed opioid cough medication new criteria for patients requiring them to be 18 or over, please indicate so by saying "aye." All opposed say "nay."

Voting: Ayes are unanimous, the motion carries.

5. Public Comment on any DUR Board Requested Report

No public comments.

6. DUR Board Requested Reports

a. Pharmacy lock-in program:

Carl Jeffery: Holly put together the first page in there. It's the lock-in program comparison name; it compares the different programs and what their lock-in procedure is.

Paul Oesterman: For those in the audience not aware, the lock-in program is a program that requires recipients to obtain their pharmaceutical products from a particular pharmacy so that we try to minimize the pharmacy shopping, the doctor shopping, and the potential for abuse, misuse, and inappropriate use of their medications.

Carl Jeffery: I'll let Holly highlight these and then the biggest differences you will notice.

Holly Long: Sure, well I think the main reason, you wanted to be able to see all of the differences here and wanted to readdress the possibility of reviewing the clinical review after a recipient had been in the lock-in program for a certain amount of time. So, I created this so that you could see what the fee for service does compared to the MCO's, so the review is at the

end of the report. The fee for service is not currently doing a review and the MCOs are; they have their own criteria. One of the biggest differences is with HPN and their Holy Trinity that they refer to that Ryan can explain. Otherwise, they are fairly similar. There's much more detail in Silver Summit's, but I think everybody has the similar clinical review process and everybody is locking into one pharmacy and is everybody is given the opportunity to change the pharmacy? There's some differences in days but duration of time…

Ryan Bitton: Holy Trinity has kind of fallen out of favor. It was a national initiative and that is what it was called at the time. That is basically three medications used.

Carl Jeffery: Wasn't historically the Holy Trinity opioid, Ativan, and Soma?

Paul Oesterman: The Las Vegas cocktail.

Holly Long: I just talked to Kelli Wedge. She is the registered nurse that oversees the actual clinical review for every single recipient for the Lock-In Program. She is very against doing a review again. She doesn't think that there's any point in reviewing the recipients after a period of time, that they should always remain within the lock-in program indefinitely as long as they are a Medicaid recipient.

Carl Jeffery: So, you're forcing the members to go to one pharmacy. Of course, after 6 months they're only going to be going to one pharmacy.

Holly Long: So basing that off of good behavior, it's hard for us to justify that because you're forcing us to be in good behavior, it seems like it would be adding a lot more work for her to be able to re-review, and she does a really extensive clinical review every time.

Paul Oesterman: How often is she doing it? Like once a year?

Holly Long: We're not re-doing a review. We're keeping them on it indefinitely.

James Marx: When did she start doing that because actually I had two patients on lock-in and to this day, I still don't know why they were on lock-in, but I was always amazed why they would be on lock-in and the fact that their pharmacy would occasionally be out of stock, and we had to go to another pharmacy but…

Holly Long: It wouldn't be based on override but just because they are requesting the override.

James Marx: They would have to request it. Some of the pharmacies don't want to do it, there's a lock-in, because they think oh, there's a lock-in, you're a bad patient and most of these cases, they were not, I've never really understood why they were locked in but…

Holly Long: I mean, we could definitely touch base for a number of reasons and take a look at who the recipients are to validate it.

James Marx: One isn't on Medicaid, but the other is still in lock-in.

Holly Long: We can always ask for a re-evaluation if there are certain circumstances like that, and you can do that, and make sure that that happens and there's always an appeal process if the recipient wants to go through that. So, if for some reason they feel like that decision was not appropriate, there is a period of time where they have an appeal process, but we can definitely look at that.

James Marx: It definitely wasn't appropriate and I just wondered if that was just an isolated incident or if there are others, that was my concern. Both these cases, there were no indicators of abuse.

Holly Long: We would have to look at their specific case and see why. And Kelli keeps good records, so we could definitely do that and see if there's…

James Marx: I think in retrospect, we need to look at those patients and see how those came out.

Holly Long: You're the first person honestly that has come forward and said there's someone inappropriately placed. I appreciate your feedback. I'm happy to look back and re-evaluate it.

Paul Oesterman: So is Kelli overwhelmed or can she handle more patients?

Holly Long: Well, she is always willing to evaluate a patient, she just doesn't see any justification in re-evaluating them because we're forcing them to have that good behavior.

Paul Oesterman: Have we put anybody in the lock-in program recently? It's ongoing?

Carl Jeffery: Yeah. We add maybe 20 or 30 every month.

Paul Oesterman: Okay, perfect. That's my question. Thank you for the information. Anybody have any comments on the Lock-In Program?

Dave England: I'm just kind of curious of how well it's working and what the process is but sounds like it's working.

b. Opioid overdose deaths:

Carl Jeffery: This one is not in your binder it was a handout that I put out before the meeting entitled the Department of Health and Human Services Office of Analytics, Opioid-Related Overdoses and Deaths. For some reason, when I put the binder together initially, I could email it but when I added this one page, it put it over the limit and my email system was not sending it out. The one page must have been too much.

Holly Long: We're hoping this will teach Carl a lesson that no binders should ever be this big. So previously the Board had for the opioid-related overdoses and deaths. We're trying to compare between before quality limits and criteria were implemented in May 2017 to after and had some difficulty pulling information because we can't get toxicology reports clarifying what the cause of death was for a period of time usually from these 6 months. So, I apologize. I don't think this data is great. It is for a limited amount of time so what we're looking at is the

best that I can do. We're comparing an even amount of time before and after the implementation so we're looking at 8 months before compared to 8 months after. This is the information that DHHS was able to pull together. This is combined fee for service and MCO data so it's collected by the Department of Health and Human Services and their data analytic team. Just a few things for clarification. The opioid-related deaths on Medicaid, that is the number of deaths with drug poisoning with opioids listed as a contributing factor and those people had to be actively enrolled in Medicaid at the time of their death and then on the third table, this is Medicaid recipients who had an opioid-related overdose on the Medicaid claim and who had an opioid death. There are people who did not have a Medicaid claim with the diagnosis of opioid-related overdose who died due to drug poisoning where opioids were a contributing cause.

Paul Oesterman: This does not necessarily mean they were prescribed for them, but they consumed….

Holly Long: Yes, and I know we're trying to be able to pick that apart and identify that but it's hard to do. So, what I would like to do, I suggested that we can look at it in the future which I think we will have better numbers and an amount of time this works when the CDC reports come out, that those are going to be the best for us to look at and looking at least 12 months of time. But at least we have a start here.

Paul Oesterman: I think this is good information. The numbers are relatively small. I don't think there's a statistically significant difference between before and after and like you say, let's give it some more time to take a look and see because I think as we move forward, there's enough awareness of the opioid crisis that hopefully we'll see a reduction in the opioid-related deaths. Thank you for your efforts.

c. Opioid Utilization – Top prescriber and member, including more than four concurrent opioids

Paul Oesterman: We have a report here. Are there any significant changes?

Carl Jeffery: Yeah, we have a new number one. I don't know if it's good or bad. Several months ago, we sent out letters to the top ten prescribers that were on this report just to let them know. There was the one of the nurse practitioners in Las Vegas who had actually responded with a letter kind of justifying some of their prescribing habits which was good feedback. The instances have decreased. You can see going down in the bottom one here 218 claim or members and almost 2200 claims down to under 1000 and now they're under 1700 claims I don't know. I hope it's a good sign that they're seeing or maybe they're just not seeing Medicaid patients anymore so it's hard to say if it's intended consequences of this but we've got another anesthesiology specialist who is a D.O. in Henderson that's now moved up into number 1and they were number 3 before on that graph before.

Holly Long: So, the one that's number 1 now receives the letter sent before.

Carl Jeffery: And then we can go through the different MCOs, have them maybe go through their… do you guys want to speak to your numbers?

Jeannine Murray: Well, I realize that we need to look at that Wisconsin person and I meant to do that before I had talked about that on the last quarter; I forgot to look that up. We're thinking that that's an NPI which is the wrong address, but I looked at this data so long ago I can't think of what might have been outstanding at the time to look at it.

Ryan Bitton: I don't have anything on the HPN data.

Holly Long: I can't remember if we already talked about this. Have any of you ever sent letters out like we did? Notifying providers that they were in the top prescribing list?

Jeannine Murray: I don't think that we do send anything out like that that you're kind of a high flyer. The only thing that I can that we send out is more a letter about if it's their member, if it's a member and they're prescribing for a member is a high utilizer, but nothing focused on the physician's prescribing habits.

Ryan Bitton: We have run reports and we've tried to look at, okay yeah, you're our top utilizers but are these people writing more scripts than the partners in the same type of pain management or dental. The data is not perfect because it's hard to get prescriber specialty. So, we don't send out letters like that. We are trying to get better reports to identify those.

Carl Jeffery: Yeah, I think that was the emphasis of our letters, too, that we realize every practice is different and maybe you're completely appropriate, but we just wanted to let you know like where you are compared to your peers, so I think it's a constructive letter I think.

Thomas Beranek: We're not sending them to physicians, but we are sending mail to the patients. As a matter of fact, I finished a report yesterday. We're kind of right now, we're focusing on the Trifecta that we mentioned earlier and if the patient is getting one of those three classes of medications and getting it from two or more doctors, we're about ready to send both the patient and the physician a letter letting them, hey physician did you know, the patient is also getting this from the other doctor and then we wanted to let the patient know, pick one doctor and…

Paul Oesterman: I would be highly surprised if the prescribers were not aware since the requirement is per AB474 was that they look at the PMP before prescribing any controlled substance.

Thomas Beranek: I'm not going to argue but I'm, there's, I mean, from what little data we have compared to the other two MCO's, we're seeing some, I wouldn't say pattern yet because I just combined over the last three months, so our population is finally getting big enough now to where some of that actually looks like it might mean something. We've got a few numbers that keep going up, but everything was going up, so it didn't mean anything. We have a few members that look suspect to me.

Holly Long: Do your letters that each of you send refer to lock in or is that outside of a lock-in?

Thomas Beranek: Outside lock-in.

Paul Oesterman: I can't tell you what to do, but I think we've got very good feedback from the letters that went out and highly recommend similar be done. It's an educational opportunity.

Holly Long: Maybe looking at the top 10 or whatever number you decide on for over a period of time, if they're the top 10 prescribes for over a year, besides Ryan what you're doing to better those reports. That might be a good indication that some additional information or a letter can be sent out, and I'm happy to provide you the language that we used if you want to use that as a template, you can.

James Marx: I guess I'm a little bit concerned just about the focus on numbers and to tell you that we are constantly being contacted about patients to be tapered or reduced. We actually had a patient transferred to us from another pain practice who has a case of hypophosphatemia. There are eight other cases in the United States, but the bottom line is what this condition, you could walk down the street and start breaking bones because you don't have normal bone strength and they just break. He's not even on a high dose, what I would consider high dose, his pain management physician reduced him. We have other cases where patients are being reduced, what I would consider not even particularly high doses and seem to have fairly legitimate situations and we can't really take any more patients right now; we're just overblown because of overhead associated with providing care to these patients. As an unintended consequence, I think a lot of these patients will be diverted. You won't be paying for it; society will be paying for it because a lot of the patients will go up the street and will overdose and we will continue to see an increase in opioid overdoses.

Paul Oesterman: Any additional comments on our opioid concerns, utilizations?

d. Asthma and short-acting rescue inhaler utilization.

Carl Jeffery: For fee for service information, here's the first one. I first started by running a report of all the utilization for the past year of all the different short-acting albuterol products so you can see Proventil is our preferred agent, if it's not obvious and you can see the month over month. Then on the following page, I took a look at the other medications that are being used for maintenance and the other pretty low utilization of those medications. I think what it's telling is the next report after that. The members without maintenance medication/maintenance treatment so these are the members who had received albuterol more than once and who are not on any kind of long-term therapy. They're not really getting appropriate long-term maintenance therapy, so I randomized them into the top 17 on the page but I think there are more than this but I just picked the top numbers.

Paul Oesterman: It might be a good opportunity as a reminder for all of our practitioners to think about prevention, rescue inhaler use versus prevention inhalers and maybe a letter should go out?

Carl Jeffery: Yeah, and this is an ongoing RetroDUR activity, too, that we just watch these. I don't know if there's the…

Jeannine Murray: Like Carl said, we all see the different RetroDUR programs in aligned with the HEDIS measurement. We do have about 30% of the members that use rescue inhalers receive more than one inhaler per month, so they go in for the refill. If it was difficult for me, inhaled maintenance therapy, it looks like about 25% can actually get an inhaler that is maintenance

therapy or preventative, but there's 30%, they get Montelukast but I don't know how many of those really are for asthma versus allergies. It's hard for me to assess those.

Paul Oesterman: Silver Summit? Do we have info from them?

Ryan Bitton: Looking at May, you can see how many members got one or more than one script. Maintenance therapy take the total number of 5200 of total count members, albuterol, I did not look up maintenance specifically.

Paul Oesterman: That's pretty good actually. Pretty high ratio of maintenance.

Holly Long: Do you have prior authorization criteria for this? Is that what you said?

Ryan Bitton: No.

Holly Long: No, okay.

Carl Jeffery: These are the quantity limits right on albuterol?

Ryan Bitton: Yeah. On albuterol.

7. Public Comment on any Standard DUR Report

No public comment.

8. Standard DUR Reports

a. Review of Prescribing/Program Trends.

Top 10 Therapeutic Classes for Q3 2017, Q4 2017 and Q1 2018 (by Payment and by Claims).

Carl Jeffery: Nothing really remarkable. Same old kind of trends and we still see the number one as far as dollars goes is always our hemophilia medications, so they're always ranked up there, when we rank it by pharmacy paid. When look at the number of claims. The opioid claims are really decreasing which promising. We will see what Dr. Marx kind of eludes, there may be some unintended consequences with these but there are 10,000 fewer claims over the quarter in 2018 versus the third quarter 2017 so we're seeing a lot fewer. It's broken down by more specific drug classes and hemophilia medications are still one of our most costly classes of medications to cover.

Jeannine Murray: For Anthem, we don't really notice too many changes. We did review these statistics in the quality meetings every other month so there's really nothing that changing this as far as health and drug classes. Your comment about the opioid, that's one thing when I look at the drug-specific data, saw hydrocodone sitting I think ranked 19 but in our monthly meeting, it's finally fallen out of the top 25 so we don't have an opioid anymore on our top 25 for utilizations. We get excited about that.

Ryan Bitton: I don't' really have any specific commentary.

Thomas Beranek: Ours had held steady since the last meeting. I don't have a good example of changes with opioids, not good or bad.

Top 50 Drugs of Q3 2017, Q4 2017 and Q1 2018 (by Payment and by Claims).

Carl Jeffery: Top 50 is on there, too. Again, similar results to previous quarters. I don't think there's too much to remark on those.

Paul Oesterman: Looks like we've got pretty good usage of diabetic test strips and basal insulin.

b. Concurrent Drug Utilization Review (ProDUR)

Carl Jeffery: I don't have anything in there to say what we're working on as far as sending letters out with hep-C treatments and with the asthma medication and then starting to look at psychotropic usage again and see if there is some kind of letter we need to generate with those, but right now our still initial discovery phase of that.

Paul Oesterman: Is there anything the Board wants to request for the meeting next time?

Dave England: Not that I can think of, I think we have it pretty well covered.

i. Review of Q1 2018.
ii. Review of Top Encounters by Problem Type.

c. Retrospective Drug Utilization Review (RetroDUR)

i. Status of previous quarter.
ii. Status of current quarter.
iii. Review and discussion of responses.

9. Closing Discussion

a. Public comments on any subject.

b. Date and location of the next meeting.

i. Discussion of the time of the next meeting.

Paul Oesterman: Our next meeting will be October 18, 2018, it was moved up to avoid conflict with Nevada Day. Thank you everyone.

c. Adjournment.

Meeting adjourned at 8:13 PM

L. Immunomodulator Drugs

Therapeutic Class: Immunomodulators
Last Reviewed by the DUR Board: January 25, 2018

Actemra® (tocilizumab)
Amevive® (alefacept)
Arcalyst® (rilonacept)
Cimzia® (certolizumab pegol)
Consentyx® (secukinumab)
Enbrel® (etanercept)
Entyvio® (vedolizumab)
Humira® (adalimumab)
Ilaris® (canakinumab)
Kevzara® (sarilumab)
Kineret® (ankinra)
Orencia® (abatacept)
Remicade® (infliximab)
Siliq® (brodalumab)
Simponi® (golimumab)
Simponi® ARIA™ (golimumab)
Stelara® (ustekinumab)
Xeljanz® (tofacitinib)
Ilumya (tildrakizumab)
Inflectra (infliximab)
Olumiant (baricitinib)
Otezla (apremilast)
Renflexis (infliximab)
Taltz (ixekizumab)

Immunomodulator Drugs are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the SSA and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

Approval will be given if the following criteria are met and documented:

a. For all recipients:

1. The recipient has had a negative tuberculin test; and

2. The recipient does not have an active infection or a history of recurring infections; and

3. The approval will not be given for the use of more than one biologic at a time (combination therapy); and

4. Each request meets the appropriate diagnosis-specific criteria (b-j).

b. Rheumatoid Arthritis (RA):

1. The recipient has a diagnosis of moderately to severely active RA; and

2. The recipient is 18 years of age or older; and

3. The recipient has had a rheumatology consultation, including the date of the visit; and one of the following:

a. The recipient has had RA for ≤ six months (early RA) and has high disease activity; and an inadequate or adverse reaction to a disease modifying antirheumatic drug (DMARD) (methotrexate,

hydroxychloroquine, leflunomide, minocycline and sulfasalazine); or

b. The recipient has had RA for ≥ six months (intermediate or long-term disease duration) and has moderate disease activity and has an inadequate response to a DMARD (methotrexate, hydroxychloroquine, leflunomide, minocycline or sulfasalazine); or

c. The recipient has had RA for ≥ six months (intermediate or long-term disease duration) and has high disease activity.

c. Psoriatic Arthritis:

1. The recipient has a diagnosis of moderate or severe psoriatic arthritis; and

2. The recipient is 18 years of age or older; and

3. The recipient has had a rheumatology consultation including the date of the visit or a dermatology consultation including the date of the visit; and

4. The recipient had an inadequate response or a contraindication to treatment with any one nonsteroidal anti-inflammatory (NSAID) or to any one of the following DMARDs: methotrexate, leflunomide, cyclosporine or sulfasalazine.

d. Ankylosing Spondylitis:

1. The recipient has a diagnosis of ankylosing spondylitis; and

2. The recipient is 18 years or older; and

3. The recipient has had an inadequate response to NSAIDs; and

4. The recipient has had an inadequate response to any one of the DMARDs (methotrexate, hydroxychloroquine, sulfasalzine, leflunomide, minocycline).

e. Juvenile Rheumatoid Arthritis/Juvenile Idiopathic Arthritis:

1. The recipient has a diagnosis of moderately or severely active juvenile RA or juvenile idiopathic arthritis; and

2. The recipient is at an appropriate age, based on the requested agent, and:

a. Abatacept: Six years of age or older.

b. Adalimumab, canakinumab, etanercept, tocilizumab: Two years of age or older.

3. And the recipient has at least five swollen joints; and

4. The recipient has three or more joints with limitation of motion and pain, tenderness or both; and

5. The recipient has had an inadequate response to one DMARD.

f. Plaque Psoriasis:

1. The recipient has a diagnosis of chronic, moderate to severe plaque psoriasis; and

2. The recipient is 18 years of age of older; and

3. The agent is prescribed by a dermatologist; and

4. The recipient has failed to adequately respond to a topical agent; and

5. The recipient has failed to adequately respond to at least one oral treatment.

g. Crohn's Disease:

1. The recipient has a diagnosis of moderate to severe Crohn's Disease; and

2. The recipient is at an appropriate age, based on the requested agent:

a. Adalimumab, infliximab: Six years of age or older.

b. All others: 18 years of age or older.

3. And the recipient has failed to adequately respond to conventional therapy (e.g. sulfasalzine, mesalamine, antibiotics, corticosteroids, azathioprine, 6-mercaptopurine, leflunomide); or

4. The recipient has fistulizing Crohn's Disease.

h. Ulcerative Colitis:

1. The recipient has a diagnosis of moderate to severe ulcerative colitis; and

2. The recipient is at an appropriate age, based on the requested agent:

a. Infiximab: Six years of age or older.

b. All others: 18 years of age or older.

3. And the recipient has failed to adequately respond to one or more of the following standard therapies:

a. Corticosteroids;

b. 5-aminosalicylic acid agents;

c. Immunosuppresants; and/or

d. Thiopurines.

i. Cryopyrin-Associated Periodic Syndromes (CAPS): Familial Cold Autoinflamatory Syndromes (FCAS) or Muckle-Wells Syndrome (MWS):

1. The recipient has a diagnosis of FCAS or MWS; and

2. The recipient is at an appropriate age, based on the requested agent:

a. Canakinumab: Four years of age or older.

b. Rilonacept: 12 years of age or older.

j. Cryopyrin-Associated Periodic Syndromes (CAPS): Neonatal-Onset Multisystem Inflammatory Disease (NOMID):

1. The recipient has a diagnosis of NOMID.

2. Prior Authorization Guidelines

Prior Authorization forms are available at:
http://www.medicaid.nv.gov/providers/rx/rxforms.aspx

Prior authorization approval will be for one year.

Anthem Actemra (tocilizumab)

CG-DRUG-81

Override(s)	Approval Duration
Prior Authorization	1 year

Medications	Line of Business	Quantity Limit
Actemra (tocilizumab) vials	VA MCD and All L-AGP	May be subject to quantity limit
Actemra (tocilizumab) syringes	All MCD	

APPROVAL CRITERIA

I. Actemra (tocilizumab) may be approved for the treatment of an individual with giant cell arteritis when the following criteria are met:
   A. Individual is 18 years of age or older; **AND**
   B. Agent is used in combination with a tapering course of corticosteroids (such as, prednisone);
      OR
   C. Agent is used as a single agent following discontinuation of corticosteroids;

OR

II. Actemra (tocilizumab) may be approved for the treatment of an individual with moderately to severely active rheumatoid arthritis when the following criteria are met:
   A. Individual is 18 years of age or older; **AND**
   B. Agent is used for any of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **OR**
      3. To inhibit the progression of structural damage; **OR**
      4. To improve physical function;

   AND
   C. Individual has had an inadequate response to a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) of one or more disease modifying anti-rheumatic drugs (for example, methotrexate) or a tumor necrosis factor antagonist drug; **AND**
   D. May be used alone or in combination with methotrexate **or** with other nonbiologic disease modifying anti-rheumatic drugs; **AND**
   E. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred b**i**ologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria are met:
      1. Individual has been receiving and is maintained on a stable dose of Actemra (tocilizumab); **OR**

2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
    a. Known hypersensitivity to any active or inactive component which is not also associated with Actemra (tocilizumab); **OR**
    b. Individual's age; **OR**
    c. Pregnant or planning on becoming pregnant; **OR**
    d. Serious infections or concurrent sepsis;

OR

3. The individual has either concomitant clinical condition:
    a. Demyelinating disease; **OR**
    b. Heart failure with documented left ventricular dysfunction;

OR

4. The preferred agent(s) do not have activity against a concomitant clinical condition and Actemra (tocilizumab) does. An example includes but may not be limited to the following:
    a. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred;

OR

III. Actemra (tocilizumab) may be approved for the treatment of an individual with active polyarticular juvenile idiopathic arthritis when the following criteria are met:
A. Individual is 2 years of age or older; **AND**
B. Agent is used for any of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response;

AND

C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more nonbiologic disease modifying anti-rheumatic drugs (such as methotrexate); **AND**
D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria are met:
    1. Individual has been receiving and is maintained on a stable dose of Actemra (tocilizumab); **OR**
    2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Actemra (tocilizumab) does; **OR**
    3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with Actemra (tocilizumab); **OR**
        b. Individual's age; **OR**

c. Pregnant or planning on becoming pregnant; **OR**
d. Serious infections or concurrent sepsis;

OR

4. The individual has either concomitant clinical condition:
    a. Demyelinating disease; **OR**
    b. Heart failure with documented left ventricular dysfunction;

OR

IV. Actemra (tocilizumab) may be approved for the treatment of an individual with active systemic juvenile idiopathic arthritis when the following criteria are met:
A. Individual is 2 years of age or older, **AND**
B. Agent is used for any of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response;

AND

C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to 1 or more corticosteroids or nonsteroidal anti-inflammatory drugs;

OR

V. Actemra (tocilizumab) may be approved as subsequent therapy for the treatment of an individual with relapsed/refractory or progressive multicentric Castleman disease when all of the following criteria are met:
A. Used as a single agent; **AND**
B. Human immunodeficiency virus (HIV)-negative; **AND**
C. Human herpes-8 negative; **AND**
D. No concurrent clinically significant infection (for example, Hepatitis B or C); **AND**
E. No concurrent lymphoma;

OR

VI. Actemra (tocilizumab) may be approved for the treatment of cytokine release syndrome when all of the following criteria are met:
A. Individual 2 years of age or older; **AND**
B. Individual has chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome;

OR

VII. Actemra (tocilizumab) may be approved for the treatment of an individual with chronic active antibody-mediated rejection plus donor-specific antibodies and transplant glomerulopathy who has failed to respond to intravenous immune globulin (IVIg) plus rituximab therapy (with or without plasma exchange).

Requests for Actemra (tocilizumab) may **not** be approved for an individual with any of the following:

I. In combination with other biologic disease modifying anti-rheumatic drugs such as anti-CD20 monoclonal antibodies, IL-1R antagonists, Janus kinase inhibitors (for example, tofacitinib citrate), selective co-stimulation modulators, or TNF antagonists; **OR**
II. At initiation of therapy, absolute neutrophil count less than 2000/mm^3, platelet count less than 100,000/mm^3, or alanine aminotransferase or aspartate aminotransferase greater than 1.5 times the upper limit of normal; **OR**
III. Tuberculosis, invasive fungal infection, or other active serious infections or a history of recurrent infections; **OR**
IV. Individual has not had a tuberculin skin test or Centers for Disease Control and Prevention (CDC)-recommended equivalent to evaluate for latent tuberculosis prior to initiating tocilizumab (in a setting of non-emergent use only).

Request for Actemra (tocilizumab) may **not** be approved when the criteria above are not met and for all other indications, including but not limited to the treatment of:

I. Adult onset Still's disease; **OR**
II. Ankylosing spondylitis; **OR**
III. Crohn's disease; **OR**
IV. Takayasu arteritis; **OR**
V. Systemic lupus erythematosus; **OR**
VI. Tumor necrosis factor receptor-associated periodic syndrome; **OR**
VII. Unicentric Castleman disease.

Note: Actemra (tocilizumab) has a black box warning for risk of serious infections. Individuals treated with Actemra are at increased risk for developing serious infections that may lead to hospitalization or death. Most individuals who developed these infections were taking concomitant immunosuppressants. Reported infections include: Tuberculosis, invasive fungal infections (including candidiasis, aspergillosis, and pneumocystosis), and infections (bacterial, viral, or other) due to opportunistic pathogens. The risks and benefits of treatment with Actemra should be considered prior to initiating in individuals with chronic or recurrent infection. If a serious infection develops, Actemra therapy should be interrupted until the infection is controlled. Individuals should be closely monitored for the development of signs and symptoms of infection during and after treatment with Actemra, including the possible development of tuberculosis in individuals who tested negative for latent tuberculosis infection prior to initiating therapy.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. Actemra [Product Information], Genentech, Inc., Roche USA, South San Francisco, CA; May 11, 2018. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed on June 8, 2018.
2. Centers for Disease Control (CDC) and Prevention. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection - United States, 2010; 59(No. RR 5):1-28. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf. Accessed on June 8, 2018.
3. National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium® (electronic version). For additional information visit the NCCN website: http://www.nccn.org. Accessed on June 8, 2018.
4. NCCN Clinical Practice Guidelines in Oncology®. © 2018 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on June 8, 2018.
   - B-cell Lymphomas (V4.20187). Revised May 15, 2018.
   - Management of Immunotherapy-Related Toxicities (Immune-Checkpoint Inhibitor-Related Toxicities) (V1.2018). Revised February 14, 2018.
5. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013; 65(10):2499-2512.
6. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 2016; 68(1):1-26.
7. Tocilizumab. In: DrugPoints System (electronic). Truven Health Analytics, Greenwood Village, CO. Updated May 15, 2018. Available at: http://www.micromedexsolutions.com. Accessed on June 8, 2018.

Anthem Cimzia (certolizumab pegol)

CG-DRUG-65

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Strength	Quantity Limit
Cimzia (certolizumab pegol)	1 pack or kit = 2 x 200mg vials	1 pack or kit (2 x 200mg vials) per 28 days
	1 syringe kit = 2 x 200mg/ml syringes	1 syringe kit (2 x 200mg/ml syringes) per 28 days
	Starter kit = 6 x 200mg/ml	May approve 1 starter kit OR up to three packs (2 X 200mg vials) or syringe kits (2 x 200mg/ml syringes) **one time only** for the first month for initial dosing. **Note:** Pack content = 2 vials or syringes each containing 200mg

APPROVAL CRITERIA

Cimzia (certolizumab pegol) may be approved when criteria are met for any of the following indications:

I. **Crohn's Disease** when the following criteria are met:
   A. Individual is 18 years of age or older; **AND**
   B. Individual has a diagnosis of moderately to severely active Crohn's Disease; **AND**
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapies (such as 5-Aminosalicylic acid products, systemic corticosteroids, or immunosuppressants) and Cimzia (certolizumab pegol) is used for one of the following:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **AND**
   D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include - Humira

(adalimumab), Inflectra (infliximab-dyyb), Renflexis (infliximab-abda)], unless the following criteria is met:

1. Individual has been receiving and is maintained on a stable dose of Cimzia (certolizumab pegol); **OR**
2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
    a. Pregnant or planning on becoming pregnant;

OR

II. **Rheumatoid Arthritis** when the following criteria are met:

A. Individual is 18 years of age or older; **AND**
B. Individual has a diagnosis of moderately to severely active Rheumatoid Arthritis; **AND**
C. Agent is used for **any** of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **OR**
    3. To improve physical function; **AND**
D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more nonbiologic DMARDs (disease-modifying antirheumatic drugs); **AND**
E. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
    1. Individual has been receiving and is maintained on a stable dose of Cimzia (certolizumab pegol); **OR**
    2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with Cimzia (certolizumab pegol); **OR**
        b. Individual's age; **OR**
        c. Pregnant or planning on becoming pregnant; **OR**
        d. Serious infections or concurrent sepsis; **OR**
    3. The preferred agent(s) do not have activity against a concomitant clinical condition and Cimzia (certolizumab pegol) does. An example includes but may not be limited to the following:
        a. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred;

OR

III. **Ankylosing Spondylitis (AS)** when the following are met:

A. Individual is 18 years of age or older with active ankylosing spondylitis; **AND**
B. Agent is being used to reduce signs or symptoms of the disease; **AND**
C. Individual has failed to respond to, is intolerant of, or has medical contraindication to conventional therapy (such as NSAIDs or nonbiologic DMARDs); **AND**

D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include –Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
    1. Individual has been receiving and is maintained on a stable dose of Cimzia (certolizumab pegol); **OR**
    2. The preferred agents are not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Cimzia (certolizumab pegol) does; **OR**
    3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with Cimzia (certolizumab pegol); **OR**
        b. Individual's age; **OR**
        c. Pregnant or planning on becoming pregnant; **OR**
        d. Serious infections or concurrent sepsis;

OR

IV. **Psoriatic Arthritis** when the following are met:
A. Individual is 18 years of age or older with active psoriatic arthritis; **AND**
B. Agent is being used for **any** of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **OR**
    3. To improve physical function; **AND**
C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as nonbiologic DMARDs); **AND**
D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
    1. Individual has been receiving and is maintained on a stable dose of Cimzia (certolizumab pegol); **OR**
    2. The preferred agents are not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Cimzia (certolizumab pegol) does; **OR**
    3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with Cimzia (certolizumab pegol); **OR**
        b. Individual's age; **OR**
        c. Pregnant or planning on becoming pregnant; **OR**
        d. Serious infections or concurrent sepsis; **OR**
    4. The preferred agent(s) do not have activity against a concomitant clinical condition and Cimzia (certolizumab pegol) does. Examples include but may not be limited to the following:
        a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both

indications) or Stelara are preferred; **OR**

b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Cimzia (certolizumab pegol) may **not** be approved for individuals with any of the following:

A. Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **or**
B. Individuals who have not had a tuberculin skin (TST), or a CDC-recommended equivalent, to evaluate for latent tuberculosis; **or**
C. Using in combination with other TNF antagonists; **or**
D. Using in combination with tofacitinib citrate; **or**
E. Using in combination with the following non-TNF immunomodulatory drugs: abatacept (Orencia), anakinra (Kineret), natalizumab (Tysabri), or rituximab (Rituxan).

Note: Cimzia (certolizumab pegol) has a black box warning related to the increased risk of developing serious infections that could result in hospitalization or death. Individuals should be closely monitored for the development of infection during and after treatment with discontinuation of therapy if the individual develops a serious infection or sepsis. Reported infections include: Tuberculosis, invasive fungal infections (including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis), and infections (bacterial, viral, or other) due to opportunistic pathogens (including Legionella and Listeria). The risks and benefits of treatment with Cimzia should be considered prior to initiating in individuals with chronic or recurrent infection. Cimzia is not indicated for the use in pediatric individuals due to reports of lymphoma and other malignancies developing in children and adolescents treated with tumor necrosis factor (TNF) blockers.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2018. URL: http://www.clinicalpharmacology.com. Updated periodically.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed January 5, 2018.

DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.

Anthem Cosentyx (secukinumab)

DRUG.00077

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit*
Cosentyx 150 mg/mL Sensoready pen^*	2 pens per 28 days
Cosentyx 150 mg/mL Sensoready Pen 2-Pack^*	1 pack (2 x 150 mg/mL pens)
Cosentyx 150 mg/mL prefilled syringe^*	2 syringes per 28 days
Cosentyx 150 mg/mL prefilled Syringe 2-Pack^*	1 pack (2 x 150 mg/mL syringes)

^Initiation of therapy for Psoriatic Arthritis without coexistent Plaque Psoriasis (Psoriasis Vulgaris) or Ankylosing Spondylitis: May approve up to an additional 3 (three) single pens (150 mg/mL) or 3 (three) single syringes (150 mg/mL) in the first month (28 days) of treatment.

* Initiation of therapy for Plaque Psoriasis (Psoriasis Vulgaris) or Psoriatic Arthritis with coexistent Plaque Psoriasis (Psoriasis Vulgaris): May approve up to an additional 4 (four) 2-pack pens (2 x 150 mg/mL), 4 (four) 2-pack syringes (2 x 150 mg/mL), 8 (eight) single additional pens (150 mg/mL), or 8 (eight) single syringes (150 mg/mL) in the first month (28 days) of treatment.

APPROVAL CRITERIA

I. **Ankylosing spondylitis**
   A. Individual is 18 years of age or older with active ankylosing spondylitis ; **AND**
   B. The agent is used for any of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response;

   AND
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional drug therapy including a tumor necrosis factor (TNF) antagonist;

   AND
   D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO preferred biologic agents. [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met;
      1. Individual has been receiving and is maintained on a stable dose of Cosentyx (secukinumab); **OR**
      2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Cosentyx (secukinumab) does; **OR**
      3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:

a. Known hypersensitivity to any active or inactive component which is not also associated with Cosentyx (secukinumab); **OR**
b. Individual's age; **OR**
c. Pregnant or planning on becoming pregnant; **OR**
d. Serious infections or concurrent sepsis; **OR**

4. The individual has either concomitant clinical condition:
   a. Demyelinating disease; **OR**
   b. Heart failure with documented left ventricular dysfunction;

OR

II. **Psoriatic Arthritis**

A. Individual is 18 years of age or older with active psoriatic arthritis; **AND**
B. Agent is used for any of the following reasons:
   1. To reduce signs or symptoms; **OR**
   2. To induce or maintain clinical response;

AND

C. Individual has failed to respond to, is intolerant of, **or** has a medical contraindication to conventional drug therapy including disease-modifying anti-rheumatic drugs (DMARDs) or TNF antagonists;

AND

D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to <u>TWO</u> preferred biologic agents. [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met;
   1. Individual has been receiving and is maintained on a stable dose of Cosentyx (secukinumab); **OR**
   2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Cosentyx (secukinumab) does; **OR**
   3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
      a. Known hypersensitivity to any active or inactive component which is not also associated with Cosentyx (secukinumab); **OR**
      b. Individual's age; **OR**
      c. Pregnant or planning on becoming pregnant; **OR**
      d. Serious infections or concurrent sepsis; **OR**
   4. The individual has either concomitant clinical condition:
      a. Demyelinating disease; **OR**
      b. Heart failure with documented left ventricular dysfunction; **OR**
   5. The preferred agent(s) do not have activity against a concomitant clinical condition and Cosentyx (secukinumab) does. Examples include but may not be limited to the following:
      a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
      b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred;

OR

III. **Plaque Psoriasis (Psoriasis Vulgaris)**

A. Individual is 18 years of age or older with chronic moderate to severe plaque psoriasis with either of the following;
    1. Plaque psoriasis (psoriasis vulgaris) involving greater than 5% body surface area; **OR**
    2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to 5% body surface area involving sensitive areas or areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia);

AND

B. Agent is used for either of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response;

AND

C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to phototherapy or other systemic therapy (such as acitretin, cyclosporine, or methotrexate)

AND

D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO preferred biologic agents. [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met;
    1. Individual has been receiving and is maintained on a stable dose of Cosentyx (secukinumab); **OR**
    2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Cosentyx (secukinumab) does; **OR**
    3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with Cosentyx (secukinumab); **OR**
        b. Individual's age; **OR**
        c. Pregnant or planning on becoming pregnant; **OR**
        d. Serious infections or concurrent sepsis; **OR**
    4. The individual has either concomitant clinical condition:
        a. Demyelinating disease; **OR**
        b. Heart failure with documented left ventricular dysfunction; **OR**
    5. The preferred agent(s) do not have activity against a concomitant clinical condition and Cosentyx (secukinumab) does. Examples include but may not be limited to the following:
        a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
        b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Cosentyx (secukinumab) may **not** be approved for any of the following:

I. Use in combination with other immunosuppressive therapy or phototherapy; **OR**
II. Use in combination with other biologic drugs [such as Cimzia (certolizumab), Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab), Siliq (brodalumab), Stelara (ustekinumab), or Taltz (ixekizumab)]; **OR**
III. Individuals with Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**
IV. Individual has not had a tuberculin skin test (TST) or a Centers for Disease Control (CDC)-recommended equivalent test to evaluate for latent tuberculosis prior to initiating Cosentyx (secukinumab).

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2018. URL: http://www.clinicalpharmacology.com. Updated periodically.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.

DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.

Anthem Enbrel (etanercept)

CG-DRUG-65

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year unless otherwise specified*

Medications	Quantity Limit
Enbrel (etanercept) 25 mg/mL vial*	8 vials
Enbrel (etanercept) 25 mg/0.5 mL (0.51 mL) prefilled syringe*	8 syringes
Enbrel (etanercept) 50 mg/mL (0.98 mL) prefilled syringe*, SureClick® autoinjector*	4 syringes/autoinjectors
Enbrel (etanercept) 50 mg/mL Mini prefilled cartridge with AutoTouch*	4 cartridges

*Initiation of therapy for adult Plaque Psoriasis (Ps): May approve up to 2 (two) additional 25 mg vials (25 mg/mL) or syringes [(25 mg/0.5 mL (0.51 mL)] OR 1 (one) additional 50 mg syringe [50 mg/mL (0.98 mL)], pen (50 mg/0.5 mL), autoinjector [50 mg/mL (0.98 mL)], or cartridge (50 mg/mL) per week in the first 3 months (84 days) of treatment.

APPROVAL CRITERIA

I. **Individual has been on Enbrel (etanercept) in the past 180 days (medications samples/ coupons/ discount cards are excluded from consideration as a trial); OR**

II. Diagnosis of Rheumatoid Arthritis
   A. Individual is 18 years of age or older; **AND**
   B. Individual has a diagnosis of moderately to severely active rheumatoid arthritis; **AND**
   C. Agent is used for any of the following reasons:
      1. To reduce signs for symptoms; **OR**
      2. To induce or maintain clinical response; **OR**
      3. To inhibit the progression of structural damage; **OR**
      4. To improve physical function; **AND**
   D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more non biologic disease modifying anti-rheumatic agents (DMARDs);

OR

III. Diagnosis of Active Ankylosing Spondylitis
   A. Individual is 18 years of age or older; **AND**
   B. Individual has diagnosis of active Ankylosing Spondylitis; **AND**
   C. Agent is used to reduce signs or symptoms of the disease; **AND**
   D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as NSAIDs or non biologic DMARDs);

OR

IV. Diagnosis of Juvenile Idiopathic Arthritis
   A. Individual is 2 years of age or older; **AND**

B. Individuals with a diagnosis of moderate to severely active juvenile idiopathic arthritis; **AND**
C. Agent is used for **any** of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **AND**
D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more non biologic disease modifying anti-rheumatic agents (DMARDs);

OR

V. Diagnosis of Psoriatic Arthritis Individual is 18 years of age or older; **AND**
A. Individual has active psoriatic arthritis; **AND**
B. Agent is used for **any** of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **OR**
    3. To inhibit the progression of structural damage; **OR**
    4. To improve physical function; **AND**
C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy. (such as non biologic DMARDs);

OR

VI. Diagnosis of Plaque Psoriasis
A. Individual is 4 years of age or older; **AND**
B. Individual has a diagnosis of chronic moderate to severe plaque psoriasis (that is, extensive or disabling) with EITHER of the following:
    1. Plaque psoriasis involving greater than 5% of body surface area; **OR**
    2. Plaque psoriasis involving less than or equal to 5% of body surface area involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia); **AND**
C. Agent is used for **any** of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **AND**
D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to the use of phototherapy or other systemic therapies (such as methotrexate, acitretin, or cyclosporine).

Enbrel (etanercept) may **not** be approved for an individual with any of the following:

I. In combination with other TNF antagonists; **OR**
II. In combination with tofacitinib citrate; **OR**
III. In combination with the following non-TNF immunomodulatory drugs: abatacept, anakinra, cyclophosphamides, or vedolizumab; **OR**
IV. Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**
V. Individual has not had a tuberculin skin test, or a CDC-recommended equivalent, to evaluate for latent tuberculosis; **OR**
VI. If the above approval criteria are not met and for all other indications, including but not limited to treatment of asthma, disc-herniation-induced radiculopathy or sciatica, graft-versus-host disease, inclusion-body myositis, inflammatory bowel disease, hidradenitis suppurativa, sarcoidosis, septic shock, Sjogren's syndrome, and Wegener's granulomatosis.

Note: Enbrel (etanercept) has a black box warning related to the increased risk of developing serious infections that could result in hospitalization or death. Individuals should be closely monitored for the development of infection during and after treatment with discontinuation of therapy if the individual develops a serious infection or sepsis. Reported infections include: Tuberculosis, invasive fungal infections (including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis), and infections (bacterial, viral, or other) due to opportunistic pathogens (including Legionella and Listeria). The risks and benefits of treatment with Enbrel should be considered prior to initiating in individuals with chronic or recurrent infection. Enbrel is not indicated for the use in pediatric individuals due to reports of lymphoma and other malignancies developing in children and adolescents treated with tumor necrosis factor (TNF) blockers.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. American Academy of Dermatology (AAD). American Academy of Dermatology Association (AADA). Guidelines of care for the management of psoriasis and psoriatic arthritis. May 2008. Available at: http://www.aad.org/. Accessed on June 1, 2018.
2. American College of Rheumatology (ACR). Recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum. 2008; 59(6):762-784.
3. Brahmer JR, Lacchetti C, Schneider BJ, et al; National Comprehensive Cancer Network. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2018; 36(17):1714-1768.
4. Centers for Disease Control (CDC) and Prevention. MMWR™. Guidelines for using the QuantiFERON™ TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. 2005; 54(No. RR-15):49-55. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a4.htm. Accessed on June 1, 2018.
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7. Enbrel [Product Information], Thousand Oaks, CA. Immunex Corporation; May 25, 2018. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed on June 1, 2018.
8. Etanercept. In: DrugPoints System (electronic). Truven Health Analytics. Greenwood Village, CO. Updated March 29, 2018. Available at: https://www.micromedexsolutions.com. Accessed on June 1, 2018.
9. Etanercept Monograph. Lexicomp® Online, American Hospital Formulary Service® (AHFS®) Online, Hudson, Ohio, Lexi-Comp., Inc. Last revised December 11, 2015. Accessed on June 1, 2018.
10. Jessop S, Whitelaw DA, Delamere FM. Drugs for discoid lupus erythematosus. Cochrane Database Syst Rev. 2009;(4):CD002954.
11. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010; 105(3):501-523. Erratum in: Am J Gastroenterol. 2010; 105(3):500.
12. Lichtenstein GR, Hanauer SB, Sandborn WJ. Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009; 104(2):465-483.
13. Lu D, Song H, Shi G. Anti-TNF-alpha treatment for pelvic pain associated with endometriosis. Cochrane Database Syst Rev. 2010;(3):CD008088.
14. National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium® (electronic version). For additional information visit the NCCN website: http://www.nccn.org. Accessed on June 28, 2018.
15. NCCN Clinical Practice Guidelines in Oncology®. © 2018 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on June 28, 2018.
    - Management of Immunotherapy-Related Toxicities (Immune-Checkpoint Inhibitor-Related Toxicities) (V1.2018). Revised February 14, 2018.
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16. Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013; 65(10):2499-2512.
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Anthem Humira (adalimumab)

CG-DRUG-65

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Humira 10 mg/0.2 mL prefilled syringe	2 syringes per 28 days
Humira 10 mg/0.1 mL prefilled syringe	2 syringes per 28 days
Humira pediatric Crohn's Disease starter pack 40 mg/0.8 mL prefilled syringe†	1 pack (28 day supply, one time fill)
Humira pediatric Crohn's Disease starter pack 80 mg/0.8 mL + 40 mg/0.4 mL prefilled syringe†	1 pack (28 day supply, one time fill)
Humira 20 mg/0.2 mL prefilled syringe	2 syringes per 28 days
Humira 20 mg/0.4 mL prefilled syringe	2 syringes per 28 days
Humira 40 mg/0.4 mL prefilled pen/syringe#*¥^§†‡	2 pens/syringes per 28 days
Humira pediatric Crohn's Disease starter pack 80 mg/0.8 mL prefilled syringe†	1 pack (28 day supply, one time fill)
Humira 40 mg/0.8 mL prefilled pen#*¥^§†‡	2 pens per 28 days
Humira 40 mg/0.8 mL prefilled syringe#*¥^§†‡	2 syringes per 28 days
Humira Crohn's Disease/Ulcerative Colitis/ Hidradenitis Suppurativa starter pack 40 mg/0.4 mL prefilled pen†*	1 pack (28 day supply, one time fill)
Humira Crohn's Disease/Ulcerative Colitis/Hidradenitis Suppurativa starter pack 40 mg/0.8 mL prefilled pen†*	1 pack (28 day supply, one time fill)
Humira Crohn's Disease/Ulcerative Colitis/ Hidradenitis Suppurativa starter pack 80 mg/0.8 mL prefilled pen†*	1 pack (28 day supply, one time fill)
Humira Psoriasis/Uveitis starter pack 80 mg/0.8 mL + 40 mg/0.4 mL prefilled pen^‡	1 pack (28 day supply, one time fill)
Humira Psoriasis/Uveitis starter pack 40 mg/0.4 mL prefilled pen^‡	1 pack (28 day supply, one time fill)
Humira Psoriasis/Uveitis starter pack 40 mg/0.8 mL^‡	1 pack (28 day supply, one time fill)
Override Criteria	
†Initiation of therapy for pediatric Crohn's Disease (CD): Depending on individual's weight, may approve one (1) pediatric or adult Crohn's Disease starter pack **OR** up to four (4) additional pens or syringes (40 mg) in the first month (28 days) of treatment.	

*Initiation of therapy for adult Crohn's Disease (CD)or Ulcerative Colitis (UC): May approve one (1) Crohn's Disease/Ulcerative Colitis starter pack **OR** up to four (4) additional pens, autoinjectors or syringes (40 mg) in the first month (28 days) of treatment.

¥In the treatment of Crohn's Disease (CD) or Ulcerative Colitis (UC): May approve up to an additional 2 (two) syringes, autoinjectors, or pens (40 mg) every 28 days if the individual has an inadequate response to standard maintenance dosing.

#In the treatment of Rheumatoid Arthritis (RA): May approve up to four (4) syringes autoinjectors or pens (40mg) (up to an additional two (2) syringes, autoinjectors or pens) every 28 days if the individual is unable to take concomitant methotrexate.

§ Initiation of therapy for adult Hidradenitis Suppurativa (HS): May approve 1 (one) Crohn's Disease/Ulcerative Colitis/Hidradenitis Suppurativa starter pack **OR** up to 4 (four) additional pens or syringes (40 mg) in the first month (28 days) of treatment. Maintenance therapy: May approve up to 2 (two) additional pens or syringes (40 mg) per each 28 days.

ǂInitiation of therapy for Uveitis (UV): May approve up to 2 (two) additional pens or syringes (40 mg) in the first month (28 days) of treatment.

^Initiation of therapy for Plaque Psoriasis (Ps): May approve one (1) Psoriasis starter pack **OR** up to two (2) additional pens, autoinjectors or syringes (40 mg) in the first month (28 days) of treatment.

APPROVAL CRITERIA

I. **Individual has been on Humira (adalimumab) in the past 180 days (medication samples/ coupons/ discount cards are excluded from consideration as a trial); OR**

II. Diagnosis of Crohn's Disease:
   A. Individual is 6 years of age or older; **AND**
   B. Individual has a diagnosis of moderately to severely active Crohn's disease; **AND**
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy [such as 5-ASA products, sulfasalazine, systemic corticosteroids, or immunosuppressants] or has lost response to or is intolerant to infliximab or infliximab-dyyb, and Humira (adalimumab) is used for one of the following:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical remission;

OR

III. Diagnosis of Ulcerative Colitis:
   A. Individual is 18 years of age or older; **AND**
   B. Individual has a diagnosis of moderately to severely active ulcerative colitis; **AND**
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as 5-Aminosalicylic acid products, sulfasalazine, systemic corticosteroids, or immunosuppressive drugs), and Humira (adalimumab) is used for one of the following:
      1. To reduce signs or symptoms; **OR**

2. To induce or maintain clinical remission;

OR

IV. Diagnosis of Rheumatoid Arthritis:
   A. Individual must be 18 years of age or older; **AND**
   B. Individual must have moderately to severely active rheumatoid arthritis; **AND**
   C. Agent is used for **any** of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **OR**
      3. To inhibit the progression of structural damage; **OR**
      4. To improve physical function; **AND**
   D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more non-biologic disease-modifying anti-rheumatic agents (DMARDs);

OR

V. Diagnosis of Ankylosing Spondylitis:
   A. Individual is 18 years of age or older; **AND**
   B. Individual has active ankylosing spondylitis; **AND**
   C. Agent is used to reduce signs or symptoms of the disease; **AND**
   D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as NSAIDs or non-biologic; DMARDs);

OR

VI. Diagnosis of Juvenile Idiopathic Arthritis:
   A. Individual has a diagnosis of moderate to severely active juvenile idiopathic arthritis; **AND**
   B. Individual is 2 years of age or older; **AND**
   C. Agent is used for **any** of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **AND**
   D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more non-biologic DMARDs.

OR

VII. Diagnosis of Psoriatic Arthritis:
   A. Individual must be 18 years of age or older; **AND**
   B. Individual has active psoriatic arthritis; **AND**
   C. Agent is used for **any** of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **OR**
      3. To inhibit the progression of structural damage; **OR**
      4. To improve physical function; **AND**
   D. Individual has failed to respond to, is intolerant of, or has had a medical contraindication to conventional therapy (such as non biologic DMARDs);

OR

VIII. Diagnosis of Plaque Psoriasis (Psoriasis Vulgaris):
   A. Individual is 18 years of age or older; **AND**

B. Individual has a diagnosis of chronic moderate to severe (that is, extensive or disabling) plaque psoriasis (psoriasis vulgaris) with either of the following:
   1. Plaque psoriasis (psoriasis vulgaris) involving greater than 5% of body surface area (BSA); **OR**
   2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to 5% of BSA involving sensitive areas or areas that would significantly impact daily function (such as fingernails, palms, soles of feet, head/neck, or genitalia);

AND

C. Agent is used for **any** of the following reasons:
   1. To reduce signs or symptoms; **or**
   2. To induce or maintain clinical response; **AND**

D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to phototherapy or other systemic therapies (such as methotrexate, acitretin, or cyclosporine);

OR

IX. Diagnosis of Non-infectious Uveitis:
   A. Individual has chronic, recurrent, treatment-refractory or vision-threatening disease; **AND**
   B. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as corticosteroids or immunosuppressive drugs [for example, azathioprine, cyclosporine, or methotrexate]).

OR

X. Diagnosis of Hidradenitis Suppurativa:
   A. Individual is 18 years of age or older; **AND**
   B. Individual has moderate to severe HS (Hurley stage II or Hurley stage III disease); **AND**
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as oral antibiotics).

Humira (adalimumab) may **not** be approved for an individual with any of the following:

I. In combination with other TNF antagonists; **OR**
II. In combination with tofacitinib citrate; **OR**
III. In combination with the following non-TNF immunomodulatory drugs: abatacept, anakinra, or vedolizumab; **OR**
IV. Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**
V. Individual has not had a tuberculin skin test, or a CDC-recommended equivalent, to evaluate for latent tuberculosis prior to initiating adalimumab; **OR**
VI. When the above approval criteria are not met and for all other indications.

Note: Humira (adalimumab) has a black box warning related to the increased risk of developing serious infections that could result in hospitalization or death. Individuals should be closely monitored for the development of infection during and after treatment with discontinuation of therapy if the individual develops a serious infection or sepsis. Reported infections include: Tuberculosis, invasive fungal infections (including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis), and infections (bacterial, viral, or other) due to opportunistic pathogens (including Legionella and Listeria). The risks and benefits of treatment with Humira should be considered prior to initiating in individuals with chronic or recurrent infection. Lymphoma and other malignancies, some fatal, have been reported in children and adolescents treated with tumor necrosis factor (TNF) blockers.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. American Academy of Dermatology (AAD). American Academy of Dermatology Association (AADA). Guidelines of care for the management of psoriasis and psoriatic arthritis. May 2008. Available at: http://www.aad.org/. Accessed on June 1, 2018.
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    - Management of Immunotherapy-Related Toxicities (Immune-Checkpoint Inhibitor-Related Toxicities) (V1.2018). Revised February 14, 2018.
    - Melanoma (V2.2018). Revised January 19, 2018.

14. Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013; 65(10):2499-2512.
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16. Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti-TNF-α biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. Gastroenterology. 2013; 145(6):1459-1463.
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Anthem Ilaris (canakinumab)

CG-DRUG-74

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Ilaris (canakinumab)	May be subject to quantity limit

APPROVAL CRITERIA

I. Ilaris (canakinumab) may be approved for the treatment of any of the following periodic fever syndromes when the following criteria are met:
   A. Cryopyrin-associated periodic syndromes (CAPS) in an individual 4 years of age or older with **either** of the following:
      1. Familial cold auto inflammatory syndrome (FCAS); **OR**
      2. Muckle-Wells syndrome (MWS);

   OR

   B. Familial Mediterranean fever (FMF) in an individual who meets the following criteria:
      1. Has active type 1 FMF disease with genetic confirmation of the diagnosis (*MEFV* gene exon 10 mutation); **AND**
      2. Has documented recurrent, active disease (that is, at least one flare per month); **AND**
      3. Has failed to respond to, or is intolerant of colchicine therapy;

   OR

   C. Hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD) in an individual who meets the following criteria:
      1. Has HIDS with genetic confirmation of the diagnosis by deoxyribonucleic acid (DNA) analysis **or** enzymatic studies (that is, mutations in the *MVK* gene **or** markedly reduced mevalonate kinase activity); **AND**
      2. Has documented prior history of greater than or equal to three febrile acute flares within a 6-month period when not receiving prophylactic treatment;

   OR

   D. Tumor necrosis factor receptor associated periodic syndrome (TRAPS) in an individual who meets the following criteria:
      1. Has TRAPS with genetic confirmation of the diagnosis (*TNFRSF1A* gene mutation); **AND**
      2. Has chronic or recurrent disease activity defined as six flares in a 12-month period.

OR

II. Ilaris (canakinumab) may be approved for the treatment of active systemic juvenile idiopathic arthritis (SJIA) when **all** of the following criteria are met:
   A. Individual is 2 years of age or older; **AND**
   B. Agent is used for any of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response;

   AND
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs); **AND**
   D. May be used alone or in combination with corticosteroids, methotrexate (MTX), or NSAIDs.

Ilaris (canakinumab) may **not** be approved for an individual with **any** of the following:

1. Use of canakinumab in combination other biologic disease-modifying antirheumatic drugs (DMARDs) such as IL-1R antagonists, IL-6 receptor antagonists, Janus kinase inhibitors (for example, Xeljanz [tofacitinib citrate]), or tumor necrosis factor (TNF) antagonists; **or**
2. Tuberculosis, invasive fungal infection, or other active serious infections or a history of recurrent infections; **or**
3. Individual has not had a tuberculin skin test (TST) or Centers for Disease Control and Prevention (CDC)-recommended equivalent to evaluate for latent tuberculosis prior to initiating canakinumab.

Ilaris (canakinumab) may **not** be approved when the criteria are not met and for all other indications, including but not limited to the treatment of:

1. Adult onset Still's disease (AOSD)
2. Behçet's disease
3. Cardiovascular risk reduction and disorder prevention
4. Chronic obstructive pulmonary disease (COPD)
5. Diabetes, Type 1 and Type 2
6. Gout
7. Gouty arthritis
8. Heart failure
9. Majeed syndrome
10. Neonatal-onset multisystem inflammatory disease (NOMID)
11. Polyarticular juvenile idiopathic arthritis (PJIA)
12. Rheumatoid arthritis (RA)
13. Schnitzler syndrome

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. Canakinumab. In: DrugPoints System (electronic version). Truven Health Analytics, CO. Updated September 8, 2017. Available at: http://www.micromedexsolutions.com. Accessed on September 8, 2017.
2. Canakinumab Monograph. Lexicomp® Online, American Hospital Formulary Service® (AHFS®) Online, Hudson, Ohio, Lexi-Comp., Inc. Last revised December 9, 2011. Accessed on September 8, 2017.
3. Centers for Disease Control (CDC) and Prevention. Updated guidelines for using interferon gamma release assays to detect Mycobacterium tuberculosis infection - United States, 2010; 59(No. RR 5):1-28. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf. Accessed on September 8, 2017.
4. Dewitt EM, Kimura Y, Beukelman T, et al. Juvenile Idiopathic Arthritis Disease-specific Research Committee of Childhood Arthritis Rheumatology and Research Alliance. Consensus treatment plans for new-onset systemic juvenile idiopathic arthritis. Arthritis Care Res. 2012; 64(7):1001-1010.
5. Ilaris [Product Information], Novartis Pharma Stein AG, East Hanover, NJ; December 2016. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125319s088lbl.pdf. Accessed on September 8, 2017.
6. Khanna D, Khanna PP, Fitzgerald JD, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 2: therapy and antiinflammatory prophylaxis of acute gouty arthritis. Arthritis Care Res (Hoboken). 2012; 64(10):1447-1461.
7. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013; 65(10):2499-2512.
8. Sivera F, Wechalekar MD, Andres M, et al. Interleukin inhibitors for acute gout. Cochrane Database Syst Rev. 2014;(9):CD009993.

Anthem Kineret (anakinra)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Kineret (anakinra)	May be subject to quantity limit

APPROVAL CRITERIA

Requests for Kineret (anakinra) may be approved if the following criteria are met:

I. Individual has a diagnosis of Rheumatoid Arthritis (RA) when each of the following criteria are met:
   A. Individual is 18 years of age or older with moderately to severely active RA; **AND**
   B. Agent is used for any of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **OR**
      3. To inhibit the progression of structural damage; **OR**
      4. To improve physical function;

   AND
   C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to one or more disease modifying anti-rheumatic agents (DMARDs); **AND**
   D. Individual has had trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
      1. Individual has been receiving and is maintained on a stable dose of Kineret (anakinra); **OR**
      2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         a. Known hypersensitivity to any active or inactive component which is not also associated with Kineret (anakinra); **OR**
         b. Individual's age; **OR**
         c. Pregnant or planning on becoming pregnant; **OR**
         d. Serious infections or concurrent sepsis;
      3. The preferred agent(s) do not have activity against a concomitant clinical condition and Kineret (anakinra) does. An example includes but may not be limited to the following:
         a. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred;

OR

II. Individual has a diagnosis of treatment-naïve or refractory (DrugPoints B II a) neonatal-onset multisystem inflammatory disease (NOMID), also known as chronic infantile neurological cutaneous and articular (CINCA syndrome;

OR

III. Individual has a diagnosis of relapsed/refractory or progressive multicentric Castleman's Disease (MCD) (NCCN 2A);

OR

IV. Systemic Juvenile Idiopathic Arthritis (SJIA) when each of the following criteria is met (Quartier et al, 2011; ACR 2013):

A. Individual is 2 years of age or older with active SJIA; **AND**

B. Agent is used for any of the following reasons:

1. To reduce signs or symptoms; **OR**
2. To induce or maintain clinical response;

AND

C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to one or more corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs).

Kineret (anakinra) may **not** be approved for the following:

I. In combination with tumor necrosis factor (TNF) antagonists; **OR**
II. In combination with tofacitinib (Xeljanz); **OR**
III. In combination with non-TNF immunomodulatory drugs [such as but not limited to, Actemra (tocilizumab) or Orencia (abatacept)]; **OR**
IV. Tuberculosis or other active serious infections or a history of recurrent infections; **OR**
V. Individual has not had a tuberculin skin test (TST) or Centers for Disease Control (CDC) and Prevention - recommended equivalent to evaluate for latent tuberculosis prior to initiating Kineret.

State Specific Mandates		
State name	Date effective	Mandate details (including specific bill if applicable)
N/A	N/A	N/A

Key References:

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2016. URL: http://www.clinicalpharmacology.com. Updated periodically.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.

DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2016; Updated periodically.

Anthem Otezla (apremilast)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Otezla (apremilast)	14 Day Starter Pack – 1 pack (14 day supply, one time fill) 28 Day Starter Pack – 1 pack (28 day supply, one time fill) 30 mg – 2 tablets per day

APPROVAL CRITERIA

Requests for Otezla (apremilast) may be approved if the following criteria are met: Plaque

I. Psoriasis (Psoriasis Vulgaris)

A. Individual is 18 years of age or older with chronic moderate to severe (that is, extensive or disabling) plaque psoriasis (psoriasis vulgaris) with either of the following (AAD 2009, 2011):
   1. Plaque psoriasis (psoriasis vulgaris) involving greater than five percent (5%) body surface area (BSA); **OR**
   2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to five percent (5%) BSA involving sensitive areas or areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia); **AND**

B. Agent is used for any of the following reasons:
   1. To reduce signs or symptoms; **OR**
   2. To induce or maintain clinical response; **AND**

C. Individual has had an inadequate response to, is intolerant of or has a contraindication to phototherapy or other systemic therapy (such as acitretin, cyclosporine or methotrexate);

AND

D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance of TWO (2) preferred biologic agents [Current preferred biologics include - Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
   1. Individual has been receiving and is maintained on a stable dose of Otezla (apremilast); **OR**
   2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Otezla (apremilast) does; **OR**
   3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
      a. Known hypersensitivity to any active or inactive component which is not also associated with Otezla (apremilast); **OR**

b. Individual's age; **OR**
c. Pregnant or planning on becoming pregnant; **OR**
d. Serious infections or concurrent sepsis; **OR**

4. Individual is unable to take biologic agent due to product warning contraindication for any of the following:
    a. Serious infection or sepsis; **OR**
    b. Chronic or recurrent infection; **OR**
    c. Tuberculosis infection; **OR**
    d. Malignancy; **OR**
5. The preferred agent(s) do not have activity against a concomitant clinical condition and Otezla (apremilast) does. Examples include but may not be limited to the following:
    a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
    b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred;

OR

II. Psoriatic Arthritis (PsA)

A. Individual is 18 years of age or older with active PsA; **AND**
B. Agent is used for any of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **OR**
    3. To improve physical function; **AND**
C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as methotrexate, sulfasalazine, leflunomide);

AND

D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance of TWO (2) preferred biologic agents [Current preferred biologics include - (Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
    1. Individual has been receiving and is maintained on a stable dose of Otezla (apremilast); **OR**
    2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Otezla (apremilast) does; **OR**
    3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with Otezla (apremilast); **OR**
        b. Individual's age; **OR**
        c. Pregnant or planning on becoming pregnant; **OR**
        d. Serious infections or concurrent sepsis; **OR**
    4. Individual is unable to take biologic agent due to product warning or contraindication for any of the following:
        a. Serious infection or sepsis; **OR**
        b. Chronic or recurrent infection; **OR**

c. Tuberculosis infection; **OR**
d. Malignancy; **OR**

5. The preferred agent(s) do not have activity against a concomitant clinical condition and Otezla (apremilast) does. Examples include but may not be limited to the following:
    a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; OR
    b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Otezla (apremilast) may **not** be approved for the following:

I. In combination with a biologic DMARD [such as Enbrel (etanercept), Humira (adalimumab), Simponi (golimumab), Cimzia (certolizumab pegol), Remicade (infliximab), Stelara (ustekinumab)].

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2016. URL: http://www.clinicalpharmacology.com. Updated periodically.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.

DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2016; Updated periodically.

Anthem Inflectra (infliximab-dyyb), Remicade (infliximab), Renflexis (infliximab-abda),

CG-DRUG-64, CG-DRUG-65

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Inflectra (infliximab-dyyb) Remicade (infliximab) Renflexis (infliximab-abda)

APPROVAL CRITERIA

Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) may be approved the following criteria are met:

I. Diagnosis of Crohn's Disease:
   A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to a ONE (1) preferred biologic agent [Current preferred biologics include – Humira (adalimumab), Inflectra (infliximab-dyyb) or Renflexis (infliximab-abda)] unless the following criteria is met:
      1. Individual has been receiving and is maintained on a stable dose of Remicade (infliximab); **OR**
      2. The preferred agents are not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Remicade (infliximab) does; **OR**
      3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         a. Known hypersensitivity to any active or inactive component which is not also associated with Remicade (infliximab); **OR**
         b. Individual's age; **OR**
         c. Pregnant or planning on becoming pregnant; **OR**
         d. Serious infections or concurrent sepsis; **OR**
      4. The preferred agent(s) do not have activity against a concomitant clinical condition and Remicade (infliximab) does. Examples include but may not be limited to the following:
         a. Concomitant Psoriasis: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**

b. Concomitant Rheumatoid Arthritis: TNFi agents are preferred;

AND

B. Individual is 6 year of age or older; **AND**

C. Individual has fistulizing or moderately to severely active Crohn's Disease which has previously responded to therapy with Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**

D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as 5-Aminosalicylic acid [5-ASA] products, sulfasalazine, systemic corticosteroid, or immunosuppressive drugs) and infliximab, infliximab-dyyb, or infliximab-abda is used for one of the following:

1. To reduce signs or symptoms in an individual with moderately to severely active Crohn's Disease; **OR**
2. To induce or maintain clinical remission in an individual with moderately to severely active Crohn's Disease; **OR**
3. To reduce the number of draining enterocutaneous or rectovaginal fistulas in an individual with fistulizing Crohn's Disease of at least 3 months duration.

OR

II. Diagnosis of Ulcerative Colitis:

A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to ONE (1) preferred biologic agent [Current preferred biologic include – Humira (adalimumab) , Inflectra (infliximab-dyyb) or Renflexis (infliximab-abda)] unless the following criteria is met:

1. Individual has been receiving and is maintained on a stable dose of Remicade (infliximab); **OR**
2. The preferred agents are not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Remicade (infliximab) does ; **OR**
3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
   a. Known hypersensitivity to any active or inactive component which is not also associated with the requested agent Remicade (infliximab); **OR**
   b. Individual's age; **OR**
   c. Pregnant or planning on becoming pregnant; **OR**
   d. Serious infections or concurrent sepsis; **OR**
4. The preferred agent(s) do not have activity against a concomitant clinical condition Remicade (infliximab) does. Examples include but may not be limited to the following:
   a. Concomitant Psoriasis: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
   b. Concomitant Rheumatoid Arthritis: TNFi agents are preferred;

AND

B. Individual is 6 years of age or older; **AND**

C. Individual has moderately to severely active ulcerative colitis; **AND**

D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as 5-ASA products, sulfasalazine, systemic corticosteroids, or immunosuppressive drugs) and infliximab, infliximab-dyyb, or infliximab-abda is used for one of the following:

1. To reduce signs or symptoms; **OR**

2. To induce or maintain clinical remission and mucosal healing;

OR

III. Diagnosis of Rheumatoid Arthritis:

A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met:

1. Individual has been receiving and is maintained on a stable dose of Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
   a. Known hypersensitivity to any active or inactive component which is not also associated with Inflectra (infliximab- dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
   b. Individual's age; **OR**
   c. Pregnant or planning on becoming pregnant; **OR**
   d. Serious infections or concurrent sepsis; **OR**
3. The preferred agent(s) do not have activity against a concomitant clinical condition and Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) does. An example includes but may not be limited to the following:
   a. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred; **AND**

B. Individual is 18 years of age or older;

AND

C. Individual has moderately to severely active Rheumatoid Arthritis; **AND**

D. Agent is used for **any** of the following reasons:

1. To reduce signs or symptoms; **OR**
2. To induce or maintain clinical response; **OR**
3. To inhibit the progression of structural damage; **OR**
4. To improve physical function;

AND

E. Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) is given in combination with methotrexate or with another immunosuppressive agent if the individual is intolerant to methotrexate; **AND**

F. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more non-biologic disease modifying anti-rheumatic drugs (DMARDs);

OR

IV. Diagnosis of Ankylosing spondylitis:

A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met:

1. Individual has been receiving and is maintained on a stable dose of Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
2. The preferred agents are not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Inflectra

(infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) does; **OR**

3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
   a. Known hypersensitivity to any active or inactive component which is not also associated with Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
   b. Individual's age; **OR**
   c. Pregnant or planning on becoming pregnant; **OR**
   d. Serious infections or concurrent sepsis;

AND

B. Individual is 18 years of age or older; **AND**
C. Individual has active ankylosing spondylitis; **AND**
D. Is used to reduce signs or symptoms of the disease; **AND**
E. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as nonsteroidal anti-inflammatory drugs or non- biologic DMARDs);

OR

V. Diagnosis of Psoriatic arthritis:
   A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met:
      1. Individual has been receiving and is maintained on a stable dose of Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
      2. The preferred agents are not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) does; **OR**
      3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         a. Known hypersensitivity to any active or inactive component which is not also associated with Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
         b. Individual's age; **OR**
         c. Pregnant or planning on becoming pregnant; **OR**
         d. Serious infections or concurrent sepsis; **OR**
      4. The preferred agent(s) do not have activity against a concomitant clinical condition and Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) does. Examples include but may not be limited to the following:
         a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
         b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred;

AND

B. Individual is 18 years of age or older; **AND**
C. Individual has active psoriatic arthritis; **AND**
D. Agent is used for **any** of the following reasons:

1. To reduce signs or symptoms; **OR**
2. To induce or maintain clinical response; **OR**
3. To inhibit the progression of structural damage; **OR**
4. To improve physical function;

AND

E. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as non-biologic DMARDs);

OR

VI. Diagnosis of Plaque psoriasis (Psoriasis vulgaris):

A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met:

1. Individual has been receiving and is maintained on a stable dose of Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
2. The preferred agents are not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) does; **OR**
3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
   a. Known hypersensitivity to any active or inactive component which is not also associated with the requested agent [Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda)]; **OR**
   b. Individual's age; **OR**
   c. Pregnant or planning on becoming pregnant; **OR**
   d. Serious infections or concurrent sepsis; **OR**
4. The preferred agent(s) do not have activity against a concomitant clinical condition and the requested non-preferred agent does. Examples include but may not be limited to the following:
   a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
   b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred;

AND

B. Individual is 18 years of age or older; **AND**

C. Diagnosis of chronic moderate to severe plaque psoriasis (psoriasis vulgaris) with EITHER of the following:

1. Plaque psoriasis (psoriasis vulgaris) involving greater than 5% of body surface area ; **OR**
2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to 5% body surface area involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia)

AND

D. Agent is used for **any** of the following reasons:

1. To reduce signs or symptoms; **OR**
2. To induce or maintain clinical response;

AND

E. Individual has failed to respond to, is intolerant of, or has a medical contraindication

to the use of phototherapy or other systemic therapies (such as methotrexate, acitretin, or cyclosporine);

OR

VII. Diagnosis of Juvenile Idiopathic Arthritis:
- A. Individual is 2 years of age or older with moderately to severely active juvenile idiopathic arthritis; **AND**
- B. Agent is used for **any** of the following reasons:
  1. To reduce signs or symptoms; **OR**
  2. To induce or maintain clinical response;

AND

- C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more nonbiologic DMARDs;

OR

VIII. Diagnosis of Non-infectious Uveitis:
- A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to the preferred biologic agent, Humira (adalimumab), unless the following criteria is met:
  1. Individual has been receiving and is maintained on a stable dose of Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
  2. The preferred agent is not FDA approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) does; **OR**
  3. The preferred agent is not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
     a. Known hypersensitivity to any active or inactive component which is not also associated with Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda); **OR**
     b. Individual's age; **OR**
     c. Pregnant or planning on becoming pregnant; **OR**
     d. Serious infections or concurrent sepsis;

AND

- B. Individual has chronic, recurrent, treatment-refractory or vision-threatening disease;

AND

- C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as corticosteroids or immunosuppressive drugs [for example, azathioprine, cyclosporine, or methotrexate]);

OR

IX. Immune checkpoint inhibitor therapy-related toxicities (grade 3 or grade 4 adverse events)* in an individual with any of the following conditions:
- A. Severe or life-threatening diarrhea or colitis unresponsive to high-dose systemic corticosteroids; **OR**
- B. Severe or life-threatening pneumonitis if no improvement after 48 hours of high-dose systemic corticosteroids; **OR**
- C. Severe or life-threatening renal failure or elevated serum creatinine (that is, greater than 3 times baseline or greater than 4.0 mg/dL) if toxicity remains greater than grade 2 after 1 week of corticosteroids; **OR**

D. Severe or life-threatening cardiovascular adverse events (such as, arrhythmias, impaired ventricular function, myocarditis, or pericarditis); **OR**
E. Severe or life-threatening inflammatory arthritis unresponsive to corticosteroids or anti-inflammatory agents.

*Note: See Definitions for grade 3 and grade 4 adverse events

Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) may **not** be approved for an individual with the following:

I. In combination with other TNF antagonists; **OR**
II. In combination with tofacitinib citrate (Xeljanz); **OR**
III. In combination with the following non-TNF immunomodulator drugs: abatacept (Orencia), anakinra (Kineret), tocilizumab (Actemra), or vedolizumab (Entyvio); **OR**
IV. Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**
V. Individual has not had a tuberculin skin test or a Centers for Disease Control and Prevention (CDC)-recommended equivalent, to evaluate for latent tuberculosis prior to initiating therapy; **OR**
VI. When the above criteria are not met and for all other indications, including, but not limited to treatment of asthma, chronic obstructive pulmonary disease, disc-herniation-induced sciatica, hairy cell leukemia, graft-versus-host disease (GVHD), hidradenitis suppurativa, acute Kawasaki disease, neurosarcoidosis, sarcoidosis, Still's disease, Sjörgren's syndrome, Takayasu arteritis, and Wegener's granulomatosis.

Note: The clinician should consider the status of an individual with moderate or severe heart failure – New York Heart Association (NYHA) Functional Class III-IV before initiating treatment with infliximab, infliximab-dyyb, or infliximab-abda at doses >5mg/kg.

*Grading systems for immune checkpoint inhibitor-related adverse events (severe: grade 3 [G3]; life-threatening: grade 4 [G4]):

- Gastrointestinal (diarrhea and colitis): The Common Terminology Criteria for Adverse Events (v5.0) grading system is most often used to clinically define grades of diarrhea/colitis as follows:
  - Grade 3: Increase of 7 or more stools per day over baseline, incontinence, hospitalization indicated, severe increase in ostomy output compared with baseline, limiting self-care ADLs;
  - Grade 4: Life-threatening consequences; urgent intervention indicated.
- Lung (pneumonitis) (Brahmer, 2018):
  - Grade 3: Severe symptoms, hospitalization required, involves all lung lobes or greater than 50% of lung parenchyma, limiting self-care ADL, oxygen indicated;
  - Grade 4: Life-threatening respiratory compromise, urgent intervention indicated (intubation).
- Renal (renal failure or elevated serum creatinine) (Brahmer, 2018; NCCN CPG, V1.2018):
  - Grade 3: Creatinine greater than 3 times baseline or greater than 4.0 mg/dL, hospitalization indicated;
  - Grade 4: Life-threatening consequences, creatinine greater than 6 times baseline, dialysis indicated.

- Cardiovascular (arrhythmias, impaired ventricular function, myocarditis, or pericarditis) (Brahmer, 2018; NCCN CPG V1.2018):
  - Grade 3: Moderate to severely abnormal testing or symptoms with mild activity, including arrhythmia, significant echocardiogram findings without hypotension, abnormal cardiac markers (greater than upper limit of normal [ULN]);
  - Grade 4: Moderate to severe decompensation, arrhythmia, hemodynamic (hypotension/cardiomyopathy) greater than 3 times ULN, IV medication or intervention required, life-threatening symptoms.
- Musculoskeletal (inflammatory arthritis) (Brahmer, 2018; NCCN CPG V1.2018):
  - Grade 3-4: Severe pain associated with signs of inflammation, erythema, or joint swelling, with or without irreversible joint damage, disabling, limiting self-care ADLs.

Note: Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) have a black box warning related to the increased risk of developing serious infections that could result in hospitalization or death. Individuals should be closely monitored for the development of infection during and after treatment with discontinuation of therapy if the individual develops a serious infection or sepsis. Reported infections include: Tuberculosis, invasive fungal infections (including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis), and infections (bacterial, viral, or other) due to opportunistic pathogens (including Legionella and Listeria). The risks and benefits of treatment with Inflectra, Remicade, or Renflexis should be considered prior to initiating in individuals with chronic or recurrent infection. Inflectra, Remicade, and Renflexis are not indicated for the use in pediatric individuals due to reports of lymphoma and other malignancies developing in children and adolescents treated with tumor necrosis factor (TNF) blockers.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. American Academy of Dermatology (AAD). American Academy of Dermatology Association (AADA). Guidelines of care for the management of psoriasis and psoriatic arthritis. May 2008. Available at: http://www.aad.org/. Accessed on June 1, 2018.
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Anthem Rituxan (rituximab)

CG-DRUG-94

Override(s)	Approval Duration
Prior Authorization	1 year; unless state regulations require otherwise

Medications
Rituxan (rituximab)

APPROVAL CRITERIA

I. **Rheumatoid Arthritis**
Rituximab **may be approved** when all of the following are met:
A. Individual is 18 years of age or older with moderately to severely active rheumatoid arthritis; **AND**
B. Rituximab is given in combination with methotrexate unless intolerant of or has a medical contraindication; **AND**
C. Individual had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies, or has a medical contraindication to TNF antagonist therapy.

II. **Wegener's Granulomatosis and Microscopic Polyangiitis**
Rituximab in combination with glucocorticoids, **may be approved** for the treatment of individuals with Wegener's granulomatosis and microscopic polyangiitis.

III. **Other Indications**
Rituximab **may be approved** for the treatment of **any** of the following conditions:
A. Acquired inhibitors in individuals with hemophilia who fail cyclophosphamide and prednisone therapy; **OR**
B. Autoimmune hemolytic anemia, refractory; **OR**
C. Cryoglobulinemia, primary Sjogren Syndrome , or systemic lupus erythematosus refractory to standard therapy (that is, lack of response to corticosteroids **and** at least two (2) immunosuppressive agents); **OR**
D. Graft-Versus-Host Disease as third line of therapy or greater; **OR**
E. Hepatitis C virus infection-related cryoglobulinemic vasculitis in conjunction with intravenous methylprednisolone, and concomitant antiviral therapy for individuals with any of the following:
    1. Nephrotic proteinuria; **OR**
    2. Evidence of rapidly progressive kidney disease; **OR**
    3. Uncontrolled nephrotic syndrome; **OR**
    4. Acute flare of cryoglobulinemia; **OR**
F. Immunoglobulin G4-related disease when **any** of the following are met:
    1. Failure to respond to prednisone or other corticosteroid agents; **OR**
    2. Unable to tolerate tapering of prednisone or other corticosteroid agents; **OR**

3. Has a medical contraindication to prednisone or other corticosteroid agents; **OR**

G. Multiple sclerosis when **both** of the following are met:
   1. Individual has a relapsing-remitting form of multiple sclerosis; **AND**
   2. Has had an inadequate response to, **or** is unable to tolerate, **or** has a medical contraindication to at least two alternative drug therapies indicated for the treatment of multiple sclerosis; **OR**

H. Neuromyelitis optica ; **OR**

I. Pediatric nephrotic syndrome when **all** of the following are met:
   1. Individual 18 years of age or younger; **AND**
   2. Has steroid-dependent, relapsing disease; **AND**
   3. Has an inadequate response to, is intolerant of, or has a medical contraindication to corticosteroid or immunosuppressive drug therapy (such as, cyclosporine, cyclophosphamide, or mycophenolate mofetil); **OR**

J. Pemphigus vulgaris and other autoimmune blistering skin diseases (for example, Pemphigus foliaceus, bullous pemphiboid, cicatricial pemphigoid, epidermolysis bullosa acquisita and paraneoplastic pemphigus) when refractory; **OR**

K. Renal transplant setting for either of the following indications:
   1. Pre-transplant to suppress panel reactive anti-human leukocyte antigens (HLA) antibodies in individuals with high panel reactive antibody (PRA) levels to HLAs; **OR**
   2. Post-transplant in individuals with acute rejection who had received rituximab treatment pre-transplant; **OR**

L. Thrombocytopenic purpura, immune or idiopathic; **OR**

M. Thrombotic thrombocytopenic purpura (TTP), refractory or relapsing disease (that is, lack of response to plasma exchange therapy and glucocorticoids) in an individual who meets the diagnostic criteria for TTP [that is, TTP is confirmed by severely reduced baseline activity of ADAMTS 13 (less than 5%), with or without the presence of an ADAMTS 13 inhibitor in the appropriate clinical setting].

Rituximab may <u>NOT</u> be approved for the following:

A. Criteria above are not met: **OR**

B. All other non-oncologic indications, including but ***<u>not</u>*** limited to:
   1. Chronic inflammatory demyelinating polyradiculoneuropathy; **OR**
   2. Graft-Versus-Host Disease as first or second-line therapy; **OR**
   3. Membranous glomerulonephropathy; **OR**
   4. Multiple sclerosis, other than relapsing forms (such as, primary progressive or secondary progressive); **OR**
   5. Renal transplant rejection, except as specified above (Section III. K.); **OR**
   6. Stiff person syndrome.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

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Anthem Simponi (golimumab)

CG-DRUG-65

Override(s)	Medications	Line of business
Prior Authorization Quantity Limit	Simponi (golimumab)	All MCD
	Simponi Aria (golimumab)	AGP, VA MCD ONLY

Medication	Quantity Limit
Simponi 50mg/0.5 mL SmartJect autoinjector	1 autoinjector per 28 days
Simponi 50mg/0.5 mL prefilled syringe	1 syringe per 28 days
Simponi 100mg/1 mL SmartJect autoinjector	1 autoinjector* per 28 days
Simponi 100mg/1 mL prefilled syringe	1 syringe* per 28 days

*Initiation of therapy for Ulcerative Colitis: May approve up to 2 (two) additional syringes or autoinjectors (100mg/1 mL) in the first month (28 days) of treatment.

APPROVAL CRITERIA

Requests for Simponi (golimumab) may be approved when the following criteria are met:

I. Diagnosis of Ulcerative Colitis:
   A. Individual is 18 years of age or older; **AND**
   B. Individual has a diagnosis of moderately to severely active ulcerative colitis; **AND**
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as 6-mercaptopurine, azathioprine, oral aminosalicylates, or oral corticosteroids), or has demonstrated dependence on corticosteroids, and Simponi (golimumab) is used for one of the following:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical remission and mucosal healing; **AND**
   D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to ONE (1) preferred biologic agent [Current preferred biologic include Humira (adalimumab), Inflectra (infliximab-dyyb), or Renflexis (infliximab-abda)] unless the following criteria is met:
      1. Individual has been receiving and is maintained on a stable dose Simponi (golimumab); **OR**
      2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Simponi (golimumab) does; **OR**
      3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         a. Known hypersensitivity to any active or inactive component which is not also associated with Simponi (golimumab); **OR**

b. Individual's age; **OR**
c. Pregnant or planning on becoming pregnant; **OR**
d. Serious infections or concurrent sepsis; **OR**

4. The preferred agent(s) do not have activity against a concomitant clinical condition and Simponi (golimumab) does. Examples include but may not be limited to the following:
    a. Concomitant Psoriasis: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
    b. Concomitant Rheumatoid Arthritis: TNFi agents are preferred.

Requests for Simponi (golimumab) and Simponi Aria (golimumab) may be approved when following criteria are met:

I. Diagnosis of Ankylosing Spondylitis:
- A. Individual is 18 years of age or older; **AND**
- B. Individual has a diagnosis of active ankylosing spondylitis; **AND**
- C. Is being used to reduce signs or symptoms of the disease; **AND**
- D. Individual failed to respond to, is intolerant of, or has a medical contraindication to, conventional therapy (such as NSAIDs or non-biologic DMARDs); **AND**
- E. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
    1. Individual has been receiving and is maintained on a stable dose Simponi (golimumab); **OR**
    2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Simponi (golimumab) does; **OR**
    3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with Simponi (golimumab); **OR**
        b. Individual's age; **OR**
        c. Pregnant or planning on becoming pregnant; **OR**
        d. Serious infections or concurrent sepsis.

II. Diagnosis of Psoriatic Arthritis:
- A. Individual is 18 years of age or older; **AND**
- B. Individual has a diagnosis of active psoriatic arthritis; **AND**
- C. Agent is used for **any** of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **OR**
    3. To improve physical function; **AND**
- D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as non-biologic DMARDs); **AND**
- E. Individual has had a trial (medication samples/coupons/discount cards are excluded

from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:

1. Individual has been receiving and is maintained on a stable dose Simponi (golimumab); **OR**
2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Simponi (golimumab) does; **OR**
3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
    a. Known hypersensitivity to any active or inactive component which is not also associated with Simponi (golimumab); **OR**
    b. Individual's age; **OR**
    c. Pregnant or planning on becoming pregnant; **OR**
    d. Serious infections or concurrent sepsis; **OR**
4. The preferred agent(s) do not have activity against a concomitant clinical condition and Simponi (golimumab) does. Examples include but may not be limited to the following:
    a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
    b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

III. Diagnosis of Rheumatoid Arthritis:

A. Individual is 18 years of age or older with moderately to severely active rheumatoid arthritis; **AND**
B. Agent is used for **any** of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response; **OR**
    3. To improve physical function; **AND**
C. Golimumab is given in combination with methotrexate or with another immunosuppressive agent if the individual is intolerant to methotrexate; **AND**
D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to one or more nonbiologic DMARDs. **AND**
E. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
    1. Individual has been receiving and is maintained on a stable dose Simponi (golimumab); **OR**
    2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
        a. Known hypersensitivity to any active or inactive component which is not also associated with the prescribed non-preferred; **OR**
        b. Individual's age; **OR**
        c. Pregnant or planning on becoming pregnant; **OR**

d. Serious infections or concurrent sepsis; **OR**

3. The preferred agent(s) do not have activity against a concomitant clinical condition and Simponi (golimumab) does. An example includes but may not be limited to the following:
    a. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred.

Requests for Simponi (golimumab) and Simponi Aria (golimumab) may **not** be approved for individuals with any of the following:

I. In combination with TNF antagonists; **OR**
II. In combination with tofacitinib citrate; **OR**
III. In combination with the following non-TNF immunomodulatory drugs: abatacept, anakinra, or vedolizumab; **OR**
IV. Tuberculosis, invasive fungal infections, other active serious infections, or a history of recurrent infections; **OR**
V. Individual has not had a tuberculin skin test or a CDC-recommended equivalent to evaluate for latent tuberculosis prior to initiating golimumab; **OR**
VI. When the above approval criteria are not met and for all other indications.

Note: Simponi/Simponi Aria (golimumab) has black box warnings related to serious infection and malignancy. The increased risk of developing serious infections can result in hospitalization or death. Most individuals that developed serious infections were taking concomitant immunosuppressants. Individuals should be closely monitored for the development of an infection during and after treatment with discontinuation of therapy if the individual develops a serious infection or sepsis. Reported infections include: Tuberculosis, invasive fungal infections (including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis), and infections (bacterial, viral, or other) due to opportunistic pathogens (including Legionella and Listeria). The risks and benefits of treatment with Simponi/Simponi Aria should be considered prior to initiating in individuals with chronic or recurrent infection. Simponi/Simponi Aria is not indicated for the use in pediatric individuals due to reports of lymphoma and other malignancies developing in children and adolescents treated with tumor necrosis factor (TNF) blockers.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

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Anthem Stelara (ustekinumab)

CG-DRUG-69

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Stelara (ustekinumab) 130mg/26 mL (5 mg/mL) vial	4 vials (8 week supply, one time fill)
Stelara (ustekinumab) 45 mg/0.5 mL vial*	1 vial per 84 days (12 weeks)
Stelara (ustekinumab) 45 mg/0.5 mL single-use prefilled syringe*†	1 syringe per 84 days (12 weeks)
Stelara (ustekinumab) 90 mg/1 mL single-use prefilled syringe*#^	1 syringe per 84 days (12 weeks)

*Initiation of therapy for Plaque Psoriasis (psoriasis vulgaris) or Psoriatic Arthritis in individuals less than or equal to 100 kg (220 lbs.): May approve 1 (one) additional syringe (45mg/0.5mL) in the first 84 days (12 weeks) of treatment.

†Initiation of therapy for Psoriatic Arthritis in individuals greater than or equal to 100 kg (220 lbs.): May approve 1 (one) additional syringe or vial (45 mg/0.5 mL) in the first 84 days (12 weeks) of treatment.

#Initiation of therapy for moderate to severe Plaque Psoriasis (psoriasis vulgaris) or concomitant Psoriatic Arthritis in individuals greater than 100 kg (220 lbs.): May approve 1 (one) additional syringe (90 mg/1 mL) in the first 84 days (12 weeks) of treatment.

^Maintenance therapy for adult Crohn's Disease: May approve 1 (one) syringe (90 mg/1 mL) every 8 weeks (56 days).

Requests for Stelara (ustekinumab) 90 mg/1mL may only be approved if the individual weighs greater than 100 kilograms (220 pounds) for diagnosis of concomitant Psoriatic Arthritis OR Plaque Psoriasis (psoriasis vulgaris), in addition to meeting the approval criteria below.

Requests for Stelara (ustekinumab) 90 mg/1mL are not subject to weight limits for diagnosis of Crohn's Disease.

APPROVAL CRITERIA

Stelara (ustekinumab) may be approved when the following criteria are met:

I. Crohn's disease when the following criteria are met:
   A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to ONE (1) preferred biologic agent [Current preferred biologics include - Humira (adalimumab), Inflectra (infliximab-dyyb), Renflexis (infliximab-abda)] unless the following criteria is met**:**
      1. Individual has been receiving and is maintained on a stable dose of Stelara (ustekinumab); **OR**
      2. The preferred agent is not FDA-approved and does not have an accepted off-label use per the off-label policy for the prescribed indication and Stelara (ustekinumab) does; **OR**
      3. The preferred agent is not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         a. Known hypersensitivity to any active or inactive component which is not also associated with Stelara (ustekinumab); **OR**
         b. Individual's age; **OR**
         c. Pregnant or planning on becoming pregnant; **OR**
         d. Serious infections or concurrent sepsis; **OR**
      4. The individual has either concomitant clinical condition:
         a. Demyelinating disease; **OR**
         b. Heart failure with documented left ventricular dysfunction; **OR**
         c. Malignancy [such as but not limited to, solid or hematologic cancers and excluding superficial skin cancers (such as basal and squamous cell)]; **OR**
      5. The preferred agent(s) do not have activity against a concomitant clinical condition and Stelara (ustekinumab) does. Examples include but may not be limited to the following:
         a. Concomitant Psoriasis: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
         b. Concomitant Rheumatoid Arthritis: TNFi agents are preferred;

   AND
   B. Individual is 18 years of age or older with moderately to severely active Crohn's disease; **AND**
   C. Individual has failed to respond to, lost response to, is intolerant of, or has a medical contraindication to either of the following:
      1. A tumor necrosis factor antagonist drug; **OR**
      2. Conventional drug therapy, such as aminosalicylate products (for example, mesalamine, sulfasalazine) or an immunomodulatory drug (for example, azathioprine , 6-mercaptopurine , or methotrexate ; **OR**
   D. Individual has failed to respond to, is intolerant of, or has demonstrated dependence on systemic corticosteroids; **AND**
   E. Individual is using Stelara (ustekinumab) for one of the following:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response or remission;

OR

II. Psoriatic arthritis when the following criteria are met:

A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents. [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met**;**

1. Individual has been receiving and is maintained on a stable dose of Stelara (ustekinumab); **OR**
2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Stelara (ustekinumab) does; **OR**
3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
    a. Known hypersensitivity to any active or inactive component which is not also associated with Stelara (ustekinumab); **OR**
    b. Individual's age; **OR**
    c. Pregnant or planning on becoming pregnant; **OR**
    d. Serious infections or concurrent sepsis; **OR**
4. The individual has either concomitant clinical condition:
    a. Demyelinating disease; **OR**
    b. Heart failure with documented left ventricular dysfunction; **OR**
5. The preferred agent(s) do not have activity against a concomitant clinical condition and Stelara (ustekinumab) does. Examples include but may not be limited to the following:
    a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
    b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred;

AND

B. Individual is 18 years of age or older with active psoriatic arthritis ; **AND**

C. Individual is using Stelara (ustekinumab) for any of the following reasons:

1. To reduce signs or symptoms; **OR**
2. To induce or maintain clinical response; **OR**
3. To inhibit the progression of structural damage; **OR**
4. To improve physical function;

AND

D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional therapy (such as nonbiologic disease-modifying antirheumatic drugs);

OR

III. Plaque psoriasis (psoriasis vulgaris) when the following criteria are met:

A. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents. [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met**;**

1. Individual has been receiving and is maintained on a stable dose of Stelara (ustekinumab); **OR**
2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Stelara (ustekinumab) does; **OR**
3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
    a. Known hypersensitivity to any active or inactive component which is not also associated with Stelara (ustekinumab); **OR**
    b. Individual's age; **OR**
    c. Pregnant or planning on becoming pregnant; **OR**
    d. Serious infections or concurrent sepsis; **OR**
4. The individual has either concomitant clinical condition:
    a. Demyelinating disease; **OR**
    b. Heart failure with documented left ventricular dysfunction; **OR**
5. The preferred agent(s) do not have activity against a concomitant clinical condition and Stelara (ustekinumab) does. Examples include but may not be limited to the following:
    a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
    b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred;

AND

B. Individual is 12 years of age or older with chronic moderate to severe plaque psoriasis (psoriasis vulgaris) with either of the following:
    1. Plaque psoriasis (psoriasis vulgaris) involving greater than 5% body surface area ; **OR**
    2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to 5% body surface area involving sensitive areas or areas that significantly impact daily function (such as palms, soles of the feet, head/neck, or genitalia);

AND

C. Individual is using Stelara (ustekinumab) for any of the following reasons:
    1. To reduce signs or symptoms; **OR**
    2. To induce or maintain clinical response;

AND

D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to phototherapy or other systemic therapy (such as acitretin, cyclosporine, or methotrexate).

Stelara (ustekinumab) may **not** be approved for an individual with any of the following:

A. When used in combination with other immunosuppressive therapy or phototherapy for the treatment of plaque psoriasis (psoriasis vulgaris); **OR**
B. History of Reversible Posterior Leukoencephalopathy Syndrome ; **OR**
C. Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**
D. Individual has not had a tuberculin skin test or a Centers for Disease Control and Prevention-recommended equivalent test to evaluate for latent tuberculosis prior to initiating Stelara (ustekinumab).

Requests for Stelara (ustekinumab) may **not** be approved for the treatment of all other indications, including, but not limited to treatment of Ankylosing spondylitis, and relapsing-remitting multiple sclerosis, Sarcoidosis, and Rheumatoid arthritis .

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

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Anthem Taltz (ixekizumab)

DRUG.00077

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Taltz 80 mg/mL prefilled autoinjector*	1 autoinjector per 28 days
Taltz 80 mg/mL prefilled syringe*	1 syringe per 28 days

*Initiation of therapy for Plaque Psoriasis (Psoriasis Vulgaris): May approve up to 3 (three) additional prefilled autoinjectors or syringes (80 mg/mL) in the first 28 days (4 weeks) of treatment and up to 2 (two) additional prefilled autoinjectors or syringes (80 mg/mL) during days 29-84 (4-12 weeks) of treatment.

*Initiation of therapy for Psoriatic Arthritis without concomitant Plaque Psoriasis: May approve up to 1 (one) additional prefilled autoinjector or syringe (80 mg/mL) in the first 28 days (4 weeks) of treatment.

APPROVAL CRITERIA

Requests for Taltz (ixekizumab) may be approved if the following criteria are met:

I. Plaque Psoriasis (Psoriasis Vulgaris) when the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe plaque psoriasis (psoriasis vulgaris) with either of the following:
      1. Plaque psoriasis (psoriasis vulgaris) involving greater than 5% body surface area (BSA);
         OR
      2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to 5% BSA involving sensitive areas or areas that significantly impact daily function (such as, palms, soles of feet, head, neck, or genitalia);

      AND

      3. Agent is used for any of the following reasons:
         a. To reduce signs or symptoms; **OR**
         b. To induce or maintain clinical response;

      AND

      4. Individual has failed to respond to, is intolerant of, or has a medical contraindication to phototherapy or other systemic therapy (such as acitretin, cyclosporine, or methotrexate);

OR

II. Psoriatic Arthritis when the following are met:
   A. Individual is 18 years of age or older with active psoriatic arthritis; **AND**
      1. Agent is used for any of the following reasons:

a. To reduce signs or symptoms; **OR**
b. To induce or maintain clinical response;

AND

2. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional drug therapy including disease-modifying antirheumatic drugs or a tumor necrosis factor antagonist;

AND

III. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab), unless the following criteria is met:
   A. Individual has been receiving and is maintained on a stable dose of Taltz (ixekizumab); **OR**
   B. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Taltz (ixekizumab) does; **OR**
   C. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
      1. Known hypersensitivity to any active or inactive component which is not also associated with the Taltz (ixekizumab); **OR**
      2. Individual's age; **OR**
      3. Pregnant or planning on becoming pregnant; **OR**
      4. Serious infections or concurrent sepsis; **OR**
   D. The individual has either concomitant clinical condition:
      1. Demyelinating disease; **OR**
      2. Heart failure with documented left ventricular dysfunction; **OR**
   E. The preferred agent(s) do not have activity against a concomitant clinical condition and Taltz (ixekizumab) does. Examples include but may not be limited to the following:
      1. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
      2. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Taltz (ixekizumab) may **not** be approved for any of the following:

I. In combination with other immunosuppressive therapy or phototherapy; **OR**
II. In combination with a biologic DMARD [such as Cimzia (certolizumab pegol), Cosentyx (secukinumab), Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab), Siliq (brodalumab), or Stelara (ustekinumab)]; **OR**
III. Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**

IV. Individual has not had a tuberculin skin test (TST) or a Centers for Disease Control (CDC)-recommended equivalent test to evaluate for latent tuberculosis prior to initiating Taltz (ixekizumab).

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

American Academy of Dermatology (AAD). American Academy of Dermatology Association (AADA). Guidelines of care for management of psoriasis and psoriatic arthritis. May 2008. Available at: http://www.aad.org/education-and-quality-care/clinical-guidelines. Accessed on December 7, 2017.

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Anthem Tremfya (guselkumab)

DRUG.00111

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Tremfya (guselkumab)	1 injection per 56 days (8 weeks)*

*Initiation of therapy for Plaque Psoriasis (Psoriasis Vulgaris): May approve up to 1 additional injection (100 mg) in the first 28 days (4 weeks) of treatment.

APPROVAL CRITERIA

I. Diagnosis of Plaque Psoriasis (Psoriasis Vulgaris)

A. Individual is 18 years of age or older with chronic moderate to severe plaque psoriasis (psoriasis vulgaris) with either of the following;
   1. Plaque psoriasis (psoriasis vulgaris) involving greater than 5% body surface area; **OR**
   2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to 5% body surface area involving sensitive areas or areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia);

AND

B. Agent is used for either of the following reasons:
   1. To reduce signs or symptoms; **OR**
   2. To induce or maintain clinical response;

AND

C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to phototherapy or other systemic therapy (such as acitretin, cyclosporine, or methotrexate);

AND

D. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents. [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab] unless the following criteria is met:
   1. Individual has been receiving and is maintained on a stable dose of Tremfya (guselkumab); **OR**
   2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Tremfya (guselkumab) does; **OR**
   3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
      a. Known hypersensitivity to any active or inactive component which is not also associated with the Tremfya (guselkumab); **OR**
      b. Individual's age; **OR**
      c. Pregnant or planning on becoming pregnant; **OR**

d. Serious infections or concurrent sepsis; **OR**

4. The individual has either concomitant clinical condition:
   a. Demyelinating disease; **OR**
   b. Heart failure with documented left ventricular dysfunction; **OR**
5. The preferred agent(s) do not have activity against a concomitant clinical condition and Tremfya (guselkumab) does. Examples include but may not be limited to the following:
   a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; OR
   b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Tremfya (guselkumab) may **not** be approved for any of the following:

I. When used in combination with other immunosuppressive therapy (such as other biologic drugs or phototherapy); **OR**
II. Individuals with tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**
III. Individual has not had a tuberculin skin test or a Centers for Disease Control and Prevention-recommended equivalent test to evaluate for latent tuberculosis prior to initiating Tremfya (guselkumab).

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

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Anthem Xeljanz (tofacitinib), Xeljanz XR (tofacitinib extended-release)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Xeljanz (tofacitinib) 5mg, 10mg Xeljanz XR (tofacitinib extended-release) 11mg	May be subject to quantity limit

APPROVAL CRITERIA

Requests for Xeljanz (tofacitinib), Xeljanz XR (tofacitinib extended-release) may be approved based on the following criteria:

I. Individual is 18 years of age or older with moderately to severely active rheumatoid arthritis; **AND**
   A. Agent is used for any of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **OR**
      3. To improve physical function;

   AND
   B. Individual has had an inadequate response to, is intolerant of or has a contraindication to methotrexate;

   AND
   C. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria are met:
      1. Individual has been receiving and is maintained on a stable dose of Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release); **OR**
      2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         a. Known hypersensitivity to any active or inactive component which is not also associated with Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release); **OR**
         b. Individual's age; **OR**
         c. Pregnant or planning on becoming pregnant; **OR**
         d. Serious infections or concurrent sepsis; **OR**
      3. The individual has either concomitant clinical condition:
         a. Demyelinating disease; **OR**
         b. Heart failure with documented left ventricular dysfunction; **OR**
      4. The preferred agent(s) do not have activity against a concomitant clinical condition and Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release) does. An example includes but may not be limited to the following:

a. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred;

OR

II. Individual is 18 years of age or older with active Psoriatic Arthritis (PsA); **AND**

A. Agent is used for any of the following reasons:
   1. To reduce signs or symptoms; **OR**
   2. To induce or maintain clinical response; **OR**
   3. To improve physical function;

AND

B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as methotrexate, sulfasalazine, leflunomide);

AND

C. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria are met:
   1. Individual has been receiving and is maintained on a stable dose of Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release); **OR**
   2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release) does; **OR**
   3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
      a. Known hypersensitivity to any active or inactive component which is not also associated with Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release); **OR**
      b. Individual's age; **OR**
      c. Pregnant or planning on becoming pregnant; **OR**
      d. Serious infections or concurrent sepsis; **OR**
   4. The individual has either concomitant clinical condition:
      a. Demyelinating disease; **OR**
      b. Heart failure with documented left ventricular dysfunction; **OR**
   5. The preferred agent(s) do not have activity against a concomitant clinical condition and Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release) does. Examples include but may not be limited to the following:
      a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; OR
      b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Xeljanz XR (tofacitinib extended-release) may **not** be approved for the following:

I. Individual has a diagnosis of moderate [30-59 mL/min/1.73 m2 (NKF 2002, KDIGO 2012)] or severe [less than 30 mL/min/1.73 m2 (NKF 2002, KDIGO 2012)] renal impairment; **OR**
II. Individual has a diagnosis of moderate hepatic impairment (Child Pugh Class B).

Xeljanz (tofacitinib) or Xeljanz XR (tofacitinib extended-release) may **not** be approved for the following:

I. In combination with biologic disease-modifying antirheumatic drugs (DMARDs) or potent immunosuppressants such as azathioprine and cyclosporine; **OR**
II. At initiation of therapy, absolute neutrophil count (ANC) less than 1000 cells/mm3, lymphocyte count less than 500 cells/mm3, or hemoglobin less than 9 g/dL; **OR**
III. Tuberculosis or other active serious infections or a history of recurrent infections; **OR**
IV. Individual has not had a tuberculin skin test (TST) or a Centers for Disease Control (CDC)-recommended equivalent to evaluate for latent tuberculosis prior to initiating Xeljanz; **OR**
V. Individual has severe hepatic impairment (Child Pugh class C).

Note: Xeljanz (tofacitinib), Xeljanz XR (tofacitinib extended-release) has black box warnings for serious infections and malignancy. The increased risk of developing serious infections can result in hospitalization or death. Most individuals that developed serious infections were taking concomitant immunosuppressants. Individuals should be closely monitored for the development of an infection during and after treatment with discontinuation of therapy if the individual develops a serious infection. Reported infections include: Active tuberculosis (pulmonary or extrapulmonary disease), invasive fungal infections (including cryptococcosis and pneumocystosis), and infections (bacterial, viral, or other) due to opportunistic pathogens. Individuals should be tested for latent tuberculosis prior to and during therapy. Latent tuberculosis should be treated prior to initiation of therapy. The risks and benefits of treatment with Xeljanz should be considered prior to initiating in individuals with chronic or recurrent infection. Lymphoma and other malignancies have occurred with therapy. Epstein Barr virus-associated post-transplant lymphoproliferative disorder has been observed in renal transplant individuals taking concomitant immunosuppressants.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2018. URL: http://www.clinicalpharmacology.com. Updated periodically.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.

DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.

Anthem Siliq (brodalumab)

DRUG.00077

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Siliq (brodalumab) 210 mg/1.5 mL*	2 prefilled syringes per 28 days

*Initiation of therapy for Plaque Psoriasis (Psoriasis Vulgaris): May approve up to 2 (two) additional syringes (210 mg) in the first 28 days (4 weeks) of treatment.

APPROVAL CRITERIA

I. Siliq (brodalumab) may be approved for the treatment of plaque psoriasis (psoriasis vulgaris) when each of the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe plaque psoriasis (psoriasis vulgaris) with either of the following:
      1. Plaque psoriasis (psoriasis vulgaris) involving greater than 5% body surface area (BSA); **OR**
      2. Plaque psoriasis (psoriasis vulgaris) involving less than or equal to 5% BSA involving sensitive areas or areas that significantly impact daily function (such as, palms, soles of feet, head, neck, or genitalia); **AND**
   B. Agent is used for any of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **AND**
   C. Individual has failed to respond to, is intolerant of, or has a medical contraindication to phototherapy or other systemic therapy (such as acitretin, cyclosporine, or methotrexate);

AND

II. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance of TWO (2) preferred biologic agents [Current preferred biologics include - (Enbrel (etanercept), Humira (adalimumab)] unless the following criteria is met:
   A. Individual has been receiving and is maintained on a stable dose of Siliq (brodalumab); **OR**
   B. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Siliq (brodalumab) does; **OR**
   C. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to the following:
      1. Known hypersensitivity to any active or inactive component which is not also associated with Siliq (brodalumab); **OR**
      2. Individual's age; **OR**
      3. Pregnant or planning on becoming pregnant; **OR**

4. Serious infections or concurrent sepsis; **OR**

D. The individual has either concomitant clinical condition:
   1. Demyelinating disease; **OR**
   2. Heart failure with documented left ventricular dysfunction; **OR**

E. The preferred agent(s) do not have activity against a concomitant clinical condition and Siliq (brodalumab) does. Examples include but may not be limited to the following:
   1. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
   2. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Siliq (brodalumab) may **not** be approved for an individual with any of the following:

A. Use of Siliq (brodalumab) in combination with other immunosuppressive therapy or phototherapy; **OR**
B. Use of Siliq (brodalumab) in combination with other biologic drugs [such as, Cimzia (certolizumab pegol), Cosentyx (secukinumab), Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab), Stelara (ustekinumab), or Taltz (ixekizumab)]; **OR**
C. Tuberculosis, invasive fungal infection, other active serious infections, or a history of recurrent infections; **OR**
D. Individual has not had a tuberculin skin test (TST) or a Centers for Disease Control and Prevention (CDC)-recommended equivalent test to evaluate for latent tuberculosis prior to initiating brodalumab.

Siliq (brodalumab) may not be approved for all other conditions including, but not limited to:
A. Asthma; **OR**
B. Crohn's disease; **OR**
C. Psoriatic arthritis; **OR**
D. Rheumatoid arthritis.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. American Academy of Dermatology (AAD). American Academy of Dermatology Association (AADA). Guidelines of care for management of psoriasis and psoriatic arthritis. May 2008. Available at: http://www.aad.org/education-and-quality-care/clinical-guidelines. Accessed on February 16, 2017.
2. Centers for Disease Control (CDC) and Prevention. Updated guidelines for using interferon gamma release assays to detect Mycobacterium tuberculosis infection - United States, 2010; 59(No. RR 5):1-28. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf. Accessed on February 16, 2017.
3. Siliq [Product Infomration]. Bridgewater, NJ. Valeant Pharmaceuticals North America, LLC, Inc.; February 15, 2017. Available at: http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=761032. Accessed on February 16, 2017.
4. U.S. Food and Drug Administration (FDA). FDA approves new psoriasis drug (Siliq). February 15, 2017. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm541981.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery. Accessed on February 16, 2017.

5. Siliq [Package insert]. Bridgewater, NJ. Valeant Pharmaceuticals North America LLC; 2017. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761032lbl.pdf. Accessed on: March 3, 2017.

Anthem Entyvio (vedolizumab)

DRUG.00068

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 Year

Medications	Quantity Limit
Entyvio (vedolizumab)	1 vial per 56 days Initiation of therapy for both Crohn's Disease and Ulcerative Colitis: May allow up to 2 addition single use vials in the first 6 weeks (42 days) of treatment

APPROVAL CRITERIA

Requests for Entyvio (vedolizumab) may be approved if the following criteria are met:

I. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to ONE (1) preferred biologic agent [Current preferred biologic includes – Humira (adalimumab), Inflectra (infliximab-dyyb), Renflexis (infliximab-abda)] unless the following is met:

   A. Individual has been receiving and is maintained on a stable dose of the Entyvio (vedolizumab); **OR**
   B. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Entyvio (vedolizumab) does; **OR**
   C. The preferred agent(s) are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
      1. Known hypersensitivity to any active or inactive component which is not also associated with Entyvio (vedolizumab); OR
      2. Individual's age; OR
      3. Pregnant or planning on becoming pregnant; OR
      4. Serious infections or concurrent sepsis; OR
   D. The preferred agent(s) do not have activity against a concomitant clinical condition and Entyvio (vedolizumab) does. Examples include but may not be limited to the following:
      1. Concomitant Psoriasis: TNFi (agents FDA-approved for both indications) or Stelara are preferred; OR
      2. Concomitant Rheumatoid Arthritis: TNFi agents are preferred;
   E. Individual has any of the following concomitant clinical conditions:
      1. Demyelinating disease; **OR**
      2. Heart failure with documented left ventricular dysfunction; **OR**
      3. Malignancy [such as but not limited to, solid or hematologic cancers and excluding superficial skin cancers (such as basal and squamous cell)]; **OR**
      4. Tuberculosis infection;

AND

II. Crohn's Disease when each of the following are met:
   A. Individual is 6 years of age or older with moderately to severely active Crohn's disease; **AND**
   B. Individual has failed to respond to, is intolerant of, or has a medical contraindication to either of the following:
      1. A tumor necrosis factor (TNF) antagonist drug; **OR**
      2. Conventional drug therapy, such as aminosalicylates/5-ASA products (for example, mesalamine, sulfasalazine), an immunomodulator (for example, 6-mercaptopurine, azathioprine or an immunosuppressive drug; **OR**
   C. Individual has failed to respond to, is intolerant of or has demonstrated dependence on systemic corticosteroids; **AND**
   D. Individual is using for one of the following:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response or remission;

OR

III. Ulcerative colitis when each of the following are met:
   A. Individual is 6 years of age or older with moderately to severely active ulcerative colitis; **AND**
   B. Individual has failed to respond to, lost response to, is intolerant of, or has a medical contraindication to either of the following:
      1. A TNF antagonist drug; **OR**
      2. Conventional drug therapy such as aminosalicylates/5-ASA products (for example, mesalamine, sulfasalazine) an immunomodulator (for example, 6-mercaptopurine, azathioprine, or an immunosuppressive drug ; **OR**
   C. Individual has failed to respond to, is intolerant of, or has demonstrated dependence on systemic corticosteroids; **AND**
   D. Individual is using for one of the following:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical remission or response and mucosal healing.

Entyvio (vedolizumab) may not be approved for an individual with any of the following:

I. In combination with TNF antagonist; **OR**
II. In combination with a non-TNF antagonist immunomodulator drug, such as natalizumab (Tysabri); **OR**
III. Active, serious infection or a history of recurrent infections; **OR**
IV. New or worsening neurological signs or symptoms of John Cunningham virus (JCV) infection or risk of progressive multifocal leukoencephalopathy (PML).

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

1. Bickston SJ, Behm BW, Tsoulis DJ, et al. Vedolizumab for induction and maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev. 2014;(8):CD007571.
2. Danese S, Fiorino G, Peyrin-Biroulet L, et al. Biological agents for moderately to severely active ulcerative colitis: a systematic review and network meta-analysis. Ann Intern Med. 2014; 160(10):704-711.
3. Entyvio. In: DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated November 16, 2016. Available at: http://www.micromedexsolutions.com. Accessed on December 29, 2016.
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6. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010; 105(3):501-523. Erratum in: Am J Gastroenterol. 2010; 105(3):500.
7. Lichtenstein GR, Hanauer SB, Sandborn WJ. Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009; 104(2):465-483.

Anthem Orencia (abatacept)

CG-DRUG-105

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Comments	Quantity Limit
Orencia (abatacept) - Intravenous	AGP, VA MCD only	4 vials per 28 days*
Orencia (abatacept) - Subcutaneous	ALL MCD	4 syringes/autojectors per 28 days

*Initiation of intravenous therapy: May approve 4 (four) additional vials (250 mg/vial) in the first 28 days (4 weeks) of treatment.

APPROVAL CRITERIA

I. Rheumatoid Arthritis:
   A. Individual is 18 years of age or older; **AND**
   B. Individual has a diagnosis of moderately to severely active rheumatoid arthritis; **AND**
   C. Agent is being used to reduce signs and symptoms, induce major clinical response, inhibit the progression of structural damage, and improve physical function; **AND**
   D. Individual has had an inadequate response to a trial of one or more non-biologic or biologic disease-modifying anti-rheumatic drugs (DMARDs), such as, methotrexate or a tumor necrosis factor (TNF) antagonist; **AND**
   E. Individual is not using in combination with a biologic DMARD (for example, TNF antagonist); **AND**
   F. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met:
      1. Individual has been receiving and is maintained on a stable dose of Orencia (abatacept); **OR**
      2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         a. Known hypersensitivity to any active or inactive component which is not also associated with Orencia (abatacept); **OR**
         b. Individual's age; **OR**
         c. Pregnant or planning on becoming pregnant; **OR**
         d. Serious infections or concurrent sepsis; **OR**
      3. The individual has either concomitant clinical condition:
         a. Demyelinating disease; **OR**
         b. Heart failure with documented left ventricular dysfunction; **OR**
      4. The preferred agent(s) do not have activity against a concomitant clinical

condition and Orencia (abatacept) does. An example includes but may not be limited to the following:
a. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred;

OR

II. Polyarticular Juvenile Idiopathic Arthritis:
A. Individual is 6 years of age or older;
AND
B. Request is for intravenous infusion;

OR
C. Individual is 2 years of age and older;
AND
D. Request is for subcutaneous injection;

AND
E. Agent is being used to reduce signs and symptoms of the disease; **AND**
F. Individual has a diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis; **AND**
G. Individual has had an inadequate response to a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) of one or more non-biologic or biologic disease-modifying antirheumatic drugs (DMARDs), such as, methotrexate or a tumor necrosis factor (TNF) antagonist;
AND
H. Individual is not using in combination with a biologic DMARD (for example, TNF antagonist); **AND**
I. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met;
1. Individual has been receiving and is maintained on a stable dose of Orencia (abatacept); **OR**
2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Orencia (abatacept) does; **OR**
3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
    a. Known hypersensitivity to any active or inactive component which is not also associated with Orencia (abatacept); **OR**
    b. Individual's age; **OR**
    c. Pregnant or planning on becoming pregnant; **OR**
    d. Serious infections or concurrent sepsis; **OR**
4. The individual has either concomitant clinical condition:
    a. Demyelinating disease; **OR**
    b. Heart failure with documented left ventricular dysfunction.

OR

III. Psoriatic Arthritis:
- A. Individual is 18 years of age or older; **AND**
- B. Individual has a diagnosis of active psoriatic arthritis; **AND**
- C. Agent is used for any of the following reasons:
  1. To reduce signs or symptoms; **OR**
  2. To induce or maintain clinical response; **AND**
- D. Individual has failed to respond to, is intolerant of, or has a medical contraindication to conventional drug therapy including disease-modifying anti-rheumatic drugs or a tumor necrosis factor antagonist; **AND**
- E. Is not used in combination with a biologic DMARD (for example, TNF antagonist) or other biologic rheumatoid arthritis therapy, such as anakinra (Kineret);

AND
- F. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept) and Humira (adalimumab)] unless the following criteria is met:
  1. Individual has been receiving and is maintained on a stable dose of Orencia (abatacept); **OR**
  2. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label policy for the prescribed indication and Orencia (abatacept) does; **OR**
  3. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
     a. Known hypersensitivity to any active or inactive component which is not also associated with Orencia (abatacept); **OR**
     b. Individual's age; **OR**
     c. Pregnant or planning on becoming pregnant; **OR**
     d. Serious infections or concurrent sepsis; **OR**
  4. The preferred agent(s) do not have activity against a concomitant clinical condition and the requested non-preferred agent does. Examples include but may not be limited to the following:
     a. Concomitant Crohn's Disease: TNFi (agents FDA-approved for both indications) or Stelara are preferred; **OR**
     b. Concomitant Ulcerative Colitis: TNFi (agents FDA-approved for both indications) are preferred.

Note: May be used as monotherapy or concomitantly with methotrexate

Orencia (abatacept) may **not** be approved for an individual with any of the following:

- A. Use in combination with TNF antagonists or other biologic rheumatoid arthritis therapy, such as anakinra; **OR**
- B. Tuberculosis or other active serious infections or a history of recurrent infections;
- C. Individual has not had a tuberculin skin test or Centers for Disease Control - recommended equivalent test to evaluate for latent tuberculosis; **OR**

D. All other indications, including, but not limited to the treatment of: ankylosing spondylitis, Crohn's disease, giant cell arteritis and Takayasu's arteritis, graft versus host disease (GVHD), lupus nephritis, multiple sclerosis, psoriasis vulgaris, scleroderma, systemic lupus erythematosus, type 1 diabetes, ulcerative colitis, and uveitis.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. Centers for Disease Control (CDC) and Prevention. Updated guidelines for using interferon gamma release assays to detect Mycobacterium tuberculosis infection - United States, 2010; 59(No. RR 5):1-28. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf. Accessed on May 14, 2018.
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4. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016; 68(1):1-26. Available at: http://www.rheumatology.org/Portals/0/Files/ACR%202015%20RA%20Guideline.pdf. Accessed on May 14, 2018.
5. United States FDA. Clinical review of Orencia (Abatacept). Reviewed May 2, 2016. Available at: https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM552559.pdf. Accessed on May 14, 2018.

Anthem Kevzara (sarilumab)

CG-DRUG-93

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Kevzara (sarilumab)	May be subject to quantity limit

APPROVAL CRITERIA

I. Kevzara (sarilumab) may be approved for the treatment of an individual with moderately to severely active Rheumatoid Arthritis when **ALL** of the following criteria are met:
   A. Individual is 18 years of age or older; **AND**
   B. Agent is used for any of the following reasons:
      1. To reduce signs or symptoms; **OR**
      2. To induce or maintain clinical response; **OR**
      3. To inhibit the progression of structural damage; **OR**
      4. To improve physical function;

   AND
   C. Individual has had an inadequate response to a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) of one or more disease modifying anti-rheumatic drugs (such as, methotrexate) or a tumor necrosis factor antagonist drug; **AND**
   D. May be used alone or in combination with methotrexate **or** with other nonbiologic disease modifying anti-rheumatic drugs;

   AND
   E. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to TWO (2) preferred biologic agents [Current preferred biologics include – Enbrel (etanercept), Humira (adalimumab)] unless the following criteria are met:
      1. Individual has been receiving and is maintained on a stable dose of Kevzara (sarilumab); **OR**
      2. The preferred agents are not acceptable due to concomitant clinical conditions, such as but not limited to any of the following:
         A. Known hypersensitivity to any active or inactive component which is not also associated with the Kevzara (sarilumab); **OR**
         B. Individual's age; **OR**
         C. Pregnant or planning on becoming pregnant; **OR**
         D. Serious infections or concurrent sepsis;

OR

3. The individual has either concomitant clinical condition:
    A. Demyelinating disease; **OR**
    B. Heart failure with documented left ventricular dysfunction;

OR

4. The preferred agent(s) do not have activity against a concomitant clinical condition and the requested non-preferred agent does. An example includes but may not be limited to the following:
    A. Concomitant Crohn's disease: TNFi (agents FDA-approved for both indications) are preferred.

Kevzara (sarilumab) may **NOT** be approved for an individual with **any** of the following:

A. In combination with other biologic disease modifying anti-rheumatic drugs such as anti-CD20 monoclonal antibodies, IL-1R antagonists, , selective co-stimulation modulators, or tumor necrosis factor antagonists; **OR**
B. At initiation of therapy, absolute neutrophil count less than 2000/mm^3, platelet count less than 150,000/mm^3, or alanine aminotransferase or aspartate aminotransferase greater than 1.5 times the upper limit of normal ; **OR**
C. Tuberculosis, invasive fungal infection, or other active serious infections or a history of recurrent infections; **OR**
D. Individual has not had a tuberculin skin test or Centers for Disease Control and Prevention-recommended equivalent to evaluate for latent tuberculosis prior to initiating Kevzara (sarilumab).

Kevzara (sarilumab) may **not** be approved when the criteria above are not met and for all other indications, including but not limited to the treatment of:

A. Ankylosing spondylitis; **OR**
B. Non-infectious uveitis; **OR**
C. Polyarticular juvenile idiopathic arthritis; **OR**
D. Systemic juvenile idiopathic arthritis.

Note:
Kevzara (sarilumab) has a black box warning for risk of serious infections. Individuals treated with Kevzara are at increased risk for developing serious infections that may lead to hospitalization or death. Opportunistic infections have also been reported in patients receiving sarilumab. Most patients who developed infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Avoid use of Kevzara (sarilumab) in patients with an active infection. Reported infections include: Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before sarilumab use and during therapy. Treatment for latent infection should be initiated prior to sarilumab use; Invasive fungal infections, such as candidiasis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease; Bacterial, viral and other infections due to opportunistic pathogens. Closely monitor patients for signs and symptoms of infection during treatment with sarilumab. If a serious infection develops, interrupt sarilumab until the infection is controlled. Consider the

risks and benefits of treatment with sarilumab prior to initiating therapy in patients with chronic or recurrent infection.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

1. Centers for Disease Control (CDC) and Prevention. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection - United States, 2010; 59(No. RR 5):1-28. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf. Accessed on January 23, 2018.
2. Kevzara [Product Information], sanofi-aventis U.S., Bridgewater, NJ and Regeneron Pharmaceuticals, Inc., Tarrytown, NY; May 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761037s000lbl.pdf. Accessed on January 23, 2018.
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 2016; 68(1):1-26.
4. U.S. National Institutes of Health (NIH). ClinicalTrials.gov. Search: sarilumab. Available at: https://clinicaltrials.gov/ct2/results?term=sarilumab&Search=Search. Accessed on January 23, 2018.

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Actemra

Program	Prior Authorization
Medication	Actemra (tocilizumab) subcutaneous
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Jersey, New Mexico, New York, Pennsylvania, Ohio, Rhode Island
Issue Date	2/2015
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Actemra is indicated for the treatment of adult patients with moderately-to severely-active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).

Actemra is also indicated in adult patients with giant cell arteritis.

Actemra IV is not a pharmacy benefit for the UnitedHealthcare Community Plan

2. Coverage Criteria:

A. Rheumatoid Arthritis (RA)

1. **Initial Authorization**

a. Diagnosis of moderately to severely active RA (e.g., swollen, tender joints with limited range of motion)

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one non-biologic disease modifying anti-rheumatic drug (DMARD) [eg, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine]

-AND-

d. Patient is not receiving Actemra in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

e. **One** of the following:

(1) **Both** of the following:

(a) History of failure, contraindication, or intolerance to **two** of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-AND-

(b) History of failure, contraindication, or intolerance to Kevzara (sarilumab)

-OR-

(2) For continuation of prior Actemra therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Actemra therapy

-AND-

b. Patient is not receiving Actemra in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Giant Cell Arteritis

1. **Initial Authorization**

a. Diagnosis of giant cell arteritis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one glucocorticoid (e.g., prednisone)

-AND-

d. Patient is not receiving Actemra in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Actemra therapy

-AND-

b. Patient is not receiving Actemra in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

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2. American College of Rheumatology 2008 Recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum.2008;59(6):762-784.
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14. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011;63(4):465-82.

Program	Program type – Prior Authorization
Change Control	
Date	Change
2/2015	New policy
3/2016	Initial therapy section: Added Enbrel to list of preferred drugs that require history of failure, contraindication, or intolerance Added technician note indicating Actemra as a non-preferred drug and listing the preferred alternatives Annual Review- Updated policy template
10/2016	Annual Review – no change
3/2017	Updated "Community & State" to "Community Plan" in background. Added Otezla to list of medications not to be used with Actemra. Updated policy template.
4/2017	Added hydroxychloroquine to example list of non-biologic DMARDs
10/2017	Added review criteria for giant cell arteritis. Updated background and references.
2/2018	Updated step therapy medications in the rheumatoid arthritis section to a trial of two TNF inhibitors and Kevzara due to PDL changes effective 4/1/18.

ACTEMRA® (TOCILIZUMAB) INJECTION FOR INTRAVENOUS INFUSION

Policy Number: CS2018D0043I **Effective Date**: March 1, 2018

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Commercial Policy

- Actemra® (Tocilizumab) Injection for Intravenous Infusion

INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

Please refer to the Oncology Medication Clinical Coverage Policy for updated information based upon the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium® (NCCN Compendium®) for oncology indications.

This policy refers only to Actemra (tocilizumab) injection for intravenous infusion for the treatment of polyarticular juvenile idiopathic arthritis, rheumatoid arthritis, systemic juvenile idiopathic arthritis, and cytokine release syndrome. Actemra, for self-administered subcutaneous injection, is obtained under the pharmacy benefit and is indicated in the treatment of rheumatoid arthritis and giant cell arteritis.

Actemra is proven and medically necessary for the treatment of:

I. **Polyarticular juvenile idiopathic arthritis when ALL of the following criteria are met**:[1]
   A. Diagnosis of polyarticular juvenile idiopathic arthritis (PJIA); **and**
   B. Actemra is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for polyarticular juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule):

1. 10mg/kg every 4 weeks for patients weighing < 30kg
2. 8mg/kg every 4 weeks for patients weighing ≥ 30kg;

and

C. Patient is not receiving Actemra in combination with either of the following:
   1. Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
   2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)].[6]

II. **Rheumatoid arthritis when ALL of the following criteria are met**: [1]
   A. Diagnosis of moderately to severely active rheumatoid arthritis (RA); **and**
   B. History of failure, contraindication, or intolerance to at least one non-biologic DMARD [e.g., methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, minocycline, etc.];[1] **and**
   C. Actemra is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for rheumatoid arthritis up to a maximum of 800mg every 4 weeks (or equivalent dose and interval schedule); **and**
   D. Patient is not receiving Actemra in combination with either of the following: [1]
      1. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)].[6]

III. **Systemic juvenile idiopathic arthritis when ALL of the following criteria are met**:
   A. Diagnosis of systemic juvenile idiopathic arthritis (SJIA); **and**
   B. Actemra is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for systemic juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule):
      1. 12mg/kg every 2 weeks for patients weighing < 30kg
      2. 8mg/kg every 2 weeks for patients weighing ≥ 30kg;

      and
   C. Patient is not receiving Actemra in combination with either of the following:[1]
      1. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)].[6]

IV. **Cytokine release syndrome when ALL of the following criteria are met**:
   A. Diagnosis of chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS); **and**
   B. Actemra is prescribed according to U.S. Food and Drug Administration labeled dosing for CRS:
      1. 12mg/kg for patients weighing < 30kg
      2. 8mg/kg for patients weighing ≥ 30kg; up to a maximum of 800mg per infusion;

      and
   C. Actemra is prescribed for a maximum of 4 doses.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Actemra is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). For this indication, Actemra may be used alone or in combination with methotrexate or other DMARDs.[1]

Actemra is also indicated for the treatment of active polyarticular juvenile idiopathic arthritis and active systemic juvenile idiopathic arthritis in patients 2 years of age and older. For these indications, Actemra may be used alone or in combination with methotrexate.[1]

Actemra is also indicated for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older. Actemra may be used alone or in combination with corticosteroids.[1]

BACKGROUND

Actemra (tocilizumab) is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody. It binds specifically to both soluble and membrane-bound IL-6 receptors, and has been shown to inhibit IL-6-mediated signaling through these receptors. IL-6 is a pro-inflammatory cytokine and has been shown to be involved in diverse physiological processes such as T-cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis, and stimulation of hematopoietic precursor cell proliferation and differentiation. IL-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis.[1]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J3262	Injection, tocilizumab, 1 mg

ICD-10 Diagnosis Code	Description
M05.00	Felty's syndrome, unspecified site
M05.011	Felty's syndrome, right shoulder
M05.012	Felty's syndrome, left shoulder
M05.019	Felty's syndrome, unspecified shoulder
M05.021	Felty's syndrome, right elbow
M05.022	Felty's syndrome, left elbow
M05.029	Felty's syndrome, unspecified elbow
M05.031	Felty's syndrome, right wrist
M05.032	Felty's syndrome, left wrist
M05.039	Felty's syndrome, unspecified wrist
M05.041	Felty's syndrome, right hand
M05.042	Felty's syndrome, left hand
M05.049	Felty's syndrome, unspecified hand
M05.051	Felty's syndrome, right hip
M05.052	Felty's syndrome, left hip
M05.059	Felty's syndrome, unspecified hip
M05.061	Felty's syndrome, right knee
M05.062	Felty's syndrome, left knee
M05.069	Felty's syndrome, unspecified knee
M05.071	Felty's syndrome, right ankle and foot
M05.072	Felty's syndrome, left ankle and foot
M05.079	Felty's syndrome, unspecified ankle and foot
M05.09	Felty's syndrome, multiple sites
M05.20	Rheumatoid vasculitis with rheumatoid arthritis of unspecified site
M05.211	Rheumatoid vasculitis with rheumatoid arthritis of right shoulder
M05.212	Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.219	Rheumatoid vasculitis with rheumatoid arthritis of unspecified shoulder
M05.221	Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222	Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.229	Rheumatoid vasculitis with rheumatoid arthritis of unspecified elbow
M05.231	Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232	Rheumatoid vasculitis with rheumatoid arthritis of left wrist
M05.239	Rheumatoid vasculitis with rheumatoid arthritis of unspecified wrist
M05.241	Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242	Rheumatoid vasculitis with rheumatoid arthritis of left hand
M05.249	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hand
M05.251	Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252	Rheumatoid vasculitis with rheumatoid arthritis of left hip

ICD-10 Diagnosis Code	Description
M05.259	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hip
M05.261	Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262	Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.269	Rheumatoid vasculitis with rheumatoid arthritis of unspecified knee
M05.271	Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272	Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot
M05.279	Rheumatoid vasculitis with rheumatoid arthritis of unspecified ankle and foot
M05.29	Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.30	Rheumatoid heart disease with rheumatoid arthritis of unspecified site
M05.311	Rheumatoid heart disease with rheumatoid arthritis of right shoulder
M05.312	Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.319	Rheumatoid heart disease with rheumatoid arthritis of unspecified shoulder
M05.321	Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322	Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.329	Rheumatoid heart disease with rheumatoid arthritis of unspecified elbow
M05.331	Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332	Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.339	Rheumatoid heart disease with rheumatoid arthritis of unspecified wrist
M05.341	Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342	Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.349	Rheumatoid heart disease with rheumatoid arthritis of unspecified hand
M05.351	Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352	Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.359	Rheumatoid heart disease with rheumatoid arthritis of unspecified hip
M05.361	Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362	Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.369	Rheumatoid heart disease with rheumatoid arthritis of unspecified knee
M05.371	Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372	Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.379	Rheumatoid heart disease with rheumatoid arthritis of unspecified ankle and foot
M05.39	Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.40	Rheumatoid myopathy with rheumatoid arthritis of unspecified site
M05.411	Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412	Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.419	Rheumatoid myopathy with rheumatoid arthritis of unspecified shoulder
M05.421	Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422	Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.429	Rheumatoid myopathy with rheumatoid arthritis of unspecified elbow
M05.431	Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432	Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.439	Rheumatoid myopathy with rheumatoid arthritis of unspecified wrist
M05.441	Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442	Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.449	Rheumatoid myopathy with rheumatoid arthritis of unspecified hand
M05.451	Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452	Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.459	Rheumatoid myopathy with rheumatoid arthritis of unspecified hip

ICD-10 Diagnosis Code	Description
M05.461	Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462	Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.469	Rheumatoid myopathy with rheumatoid arthritis of unspecified knee
M05.471	Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472	Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.479	Rheumatoid myopathy with rheumatoid arthritis of unspecified ankle and foot
M05.49	Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.50	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site
M05.511	Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512	Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder
M05.519	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified shoulder
M05.521	Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522	Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow
M05.529	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified elbow
M05.531	Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532	Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.539	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.549	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.559	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.569	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot
M05.579	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.60	Rheumatoid arthritis of unspecified site with involvement of other organs and systems
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.619	Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.629	Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.639	Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.649	Rheumatoid arthritis of unspecified hand with involvement of other organs and systems

ICD-10 Diagnosis Code	Description
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.659	Rheumatoid arthritis of unspecified hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems
M05.669	Rheumatoid arthritis of unspecified knee with involvement of other organs and systems
M05.671	Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672	Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems
M05.679	Rheumatoid arthritis of unspecified ankle and foot with involvement of other organs and systems
M05.69	Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.70	Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement
M05.711	Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712	Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.719	Rheumatoid arthritis with rheumatoid factor of unspecified shoulder without organ or systems involvement
M05.721	Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722	Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.729	Rheumatoid arthritis with rheumatoid factor of unspecified elbow without organ or systems involvement
M05.731	Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732	Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement
M05.739	Rheumatoid arthritis with rheumatoid factor of unspecified wrist without organ or systems involvement
M05.741	Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742	Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.749	Rheumatoid arthritis with rheumatoid factor of unspecified hand without organ or systems involvement
M05.751	Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752	Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.759	Rheumatoid arthritis with rheumatoid factor of unspecified hip without organ or systems involvement
M05.761	Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762	Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement
M05.769	Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement

ICD-10 Diagnosis Code	Description
M05.771	Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement
M05.772	Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement
M05.779	Rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot without organ or systems involvement
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M05.80	Other rheumatoid arthritis with rheumatoid factor of unspecified site
M05.811	Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812	Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.819	Other rheumatoid arthritis with rheumatoid factor of unspecified shoulder
M05.821	Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822	Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.829	Other rheumatoid arthritis with rheumatoid factor of unspecified elbow
M05.831	Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832	Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.839	Other rheumatoid arthritis with rheumatoid factor of unspecified wrist
M05.841	Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842	Other rheumatoid arthritis with rheumatoid factor of left hand
M05.849	Other rheumatoid arthritis with rheumatoid factor of unspecified hand
M05.851	Other rheumatoid arthritis with rheumatoid factor of right hip
M05.852	Other rheumatoid arthritis with rheumatoid factor of left hip
M05.859	Other rheumatoid arthritis with rheumatoid factor of unspecified hip
M05.861	Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862	Other rheumatoid arthritis with rheumatoid factor of left knee
M05.869	Other rheumatoid arthritis with rheumatoid factor of unspecified knee
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.879	Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00	Rheumatoid arthritis without rheumatoid factor, unspecified site
M06.011	Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012	Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.019	Rheumatoid arthritis without rheumatoid factor, unspecified shoulder
M06.021	Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022	Rheumatoid arthritis without rheumatoid factor, left elbow
M06.029	Rheumatoid arthritis without rheumatoid factor, unspecified elbow
M06.031	Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032	Rheumatoid arthritis without rheumatoid factor, left wrist
M06.039	Rheumatoid arthritis without rheumatoid factor, unspecified wrist
M06.041	Rheumatoid arthritis without rheumatoid factor, right hand
M06.042	Rheumatoid arthritis without rheumatoid factor, left hand
M06.049	Rheumatoid arthritis without rheumatoid factor, unspecified hand
M06.051	Rheumatoid arthritis without rheumatoid factor, right hip
M06.052	Rheumatoid arthritis without rheumatoid factor, left hip
M06.059	Rheumatoid arthritis without rheumatoid factor, unspecified hip

ICD-10 Diagnosis Code	Description
M06.061	Rheumatoid arthritis without rheumatoid factor, right knee
M06.062	Rheumatoid arthritis without rheumatoid factor, left knee
M06.069	Rheumatoid arthritis without rheumatoid factor, unspecified knee
M06.071	Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072	Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.079	Rheumatoid arthritis without rheumatoid factor, unspecified ankle and foot
M06.08	Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.1	Adult-onset Still's disease
M06.20	Rheumatoid bursitis, unspecified site
M06.211	Rheumatoid bursitis, right shoulder
M06.212	Rheumatoid bursitis, left shoulder
M06.219	Rheumatoid bursitis, unspecified shoulder
M06.221	Rheumatoid bursitis, right elbow
M06.222	Rheumatoid bursitis, left elbow
M06.229	Rheumatoid bursitis, unspecified elbow
M06.231	Rheumatoid bursitis, right wrist
M06.232	Rheumatoid bursitis, left wrist
M06.239	Rheumatoid bursitis, unspecified wrist
M06.241	Rheumatoid bursitis, right hand
M06.242	Rheumatoid bursitis, left hand
M06.249	Rheumatoid bursitis, unspecified hand
M06.251	Rheumatoid bursitis, right hip
M06.252	Rheumatoid bursitis, left hip
M06.259	Rheumatoid bursitis, unspecified hip
M06.261	Rheumatoid bursitis, right knee
M06.262	Rheumatoid bursitis, left knee
M06.269	Rheumatoid bursitis, unspecified knee
M06.271	Rheumatoid bursitis, right ankle and foot
M06.272	Rheumatoid bursitis, left ankle and foot
M06.279	Rheumatoid bursitis, unspecified ankle and foot
M06.28	Rheumatoid bursitis, vertebrae
M06.29	Rheumatoid bursitis, multiple sites
M06.30	Rheumatoid nodule, unspecified site
M06.311	Rheumatoid nodule, right shoulder
M06.312	Rheumatoid nodule, left shoulder
M06.319	Rheumatoid nodule, unspecified shoulder
M06.321	Rheumatoid nodule, right elbow
M06.322	Rheumatoid nodule, left elbow
M06.329	Rheumatoid nodule, unspecified elbow
M06.331	Rheumatoid nodule, right wrist
M06.332	Rheumatoid nodule, left wrist
M06.339	Rheumatoid nodule, unspecified wrist
M06.341	Rheumatoid nodule, right hand
M06.342	Rheumatoid nodule, left hand
M06.349	Rheumatoid nodule, unspecified hand
M06.351	Rheumatoid nodule, right hip

ICD-10 Diagnosis Code	Description
M06.352	Rheumatoid nodule, left hip
M06.359	Rheumatoid nodule, unspecified hip
M06.361	Rheumatoid nodule, right knee
M06.362	Rheumatoid nodule, left knee
M06.369	Rheumatoid nodule, unspecified knee
M06.371	Rheumatoid nodule, right ankle and foot
M06.372	Rheumatoid nodule, left ankle and foot
M06.379	Rheumatoid nodule, unspecified ankle and foot
M06.38	Rheumatoid nodule, vertebrae
M06.39	Rheumatoid nodule, multiple sites
M06.80	Other specified rheumatoid arthritis, unspecified site
M06.811	Other specified rheumatoid arthritis, right shoulder
M06.812	Other specified rheumatoid arthritis, left shoulder
M06.819	Other specified rheumatoid arthritis, unspecified shoulder
M06.821	Other specified rheumatoid arthritis, right elbow
M06.822	Other specified rheumatoid arthritis, left elbow
M06.829	Other specified rheumatoid arthritis, unspecified elbow
M06.831	Other specified rheumatoid arthritis, right wrist
M06.832	Other specified rheumatoid arthritis, left wrist
M06.839	Other specified rheumatoid arthritis, unspecified wrist
M06.841	Other specified rheumatoid arthritis, right hand
M06.842	Other specified rheumatoid arthritis, left hand
M06.849	Other specified rheumatoid arthritis, unspecified hand
M06.851	Other specified rheumatoid arthritis, right hip
M06.852	Other specified rheumatoid arthritis, left hip
M06.859	Other specified rheumatoid arthritis, unspecified hip
M06.861	Other specified rheumatoid arthritis, right knee
M06.862	Other specified rheumatoid arthritis, left knee
M06.869	Other specified rheumatoid arthritis, unspecified knee
M06.871	Other specified rheumatoid arthritis, right ankle and foot
M06.872	Other specified rheumatoid arthritis, left ankle and foot
M06.879	Other specified rheumatoid arthritis, unspecified ankle and foot
M06.88	Other specified rheumatoid arthritis, vertebrae
M06.89	Other specified rheumatoid arthritis, multiple sites
M06.9	Rheumatoid arthritis, unspecified
M08.00	Unspecified juvenile rheumatoid arthritis of unspecified site
M08.011	Unspecified juvenile rheumatoid arthritis, right shoulder
M08.012	Unspecified juvenile rheumatoid arthritis, left shoulder
M08.019	Unspecified juvenile rheumatoid arthritis, unspecified shoulder
M08.021	Unspecified juvenile rheumatoid arthritis, right elbow
M08.022	Unspecified juvenile rheumatoid arthritis, left elbow
M08.029	Unspecified juvenile rheumatoid arthritis, unspecified elbow
M08.031	Unspecified juvenile rheumatoid arthritis, right wrist
M08.032	Unspecified juvenile rheumatoid arthritis, left wrist
M08.039	Unspecified juvenile rheumatoid arthritis, unspecified wrist
M08.041	Unspecified juvenile rheumatoid arthritis, right hand
M08.042	Unspecified juvenile rheumatoid arthritis, left hand

ICD-10 Diagnosis Code	Description
M08.049	Unspecified juvenile rheumatoid arthritis, unspecified hand
M08.051	Unspecified juvenile rheumatoid arthritis, right hip
M08.052	Unspecified juvenile rheumatoid arthritis, left hip
M08.059	Unspecified juvenile rheumatoid arthritis, unspecified hip
M08.061	Unspecified juvenile rheumatoid arthritis, right knee
M08.062	Unspecified juvenile rheumatoid arthritis, left knee
M08.069	Unspecified juvenile rheumatoid arthritis, unspecified knee
M08.071	Unspecified juvenile rheumatoid arthritis, right ankle and foot
M08.072	Unspecified juvenile rheumatoid arthritis, left ankle and foot
M08.079	Unspecified juvenile rheumatoid arthritis, unspecified ankle and foot
M08.08	Unspecified juvenile rheumatoid arthritis, vertebrae
M08.09	Unspecified juvenile rheumatoid arthritis, multiple sites
M08.20	Juvenile rheumatoid arthritis with systemic onset, unspecified site
M08.211	Juvenile rheumatoid arthritis with systemic onset, right shoulder
M08.212	Juvenile rheumatoid arthritis with systemic onset, left shoulder
M08.219	Juvenile rheumatoid arthritis with systemic onset, unspecified shoulder
M08.221	Juvenile rheumatoid arthritis with systemic onset, right elbow
M08.222	Juvenile rheumatoid arthritis with systemic onset, left elbow
M08.229	Juvenile rheumatoid arthritis with systemic onset, unspecified elbow
M08.231	Juvenile rheumatoid arthritis with systemic onset, right wrist
M08.232	Juvenile rheumatoid arthritis with systemic onset, left wrist
M08.239	Juvenile rheumatoid arthritis with systemic onset, unspecified wrist
M08.241	Juvenile rheumatoid arthritis with systemic onset, right hand
M08.242	Juvenile rheumatoid arthritis with systemic onset, left hand
M08.249	Juvenile rheumatoid arthritis with systemic onset, unspecified hand
M08.251	Juvenile rheumatoid arthritis with systemic onset, right hip
M08.252	Juvenile rheumatoid arthritis with systemic onset, left hip
M08.259	Juvenile rheumatoid arthritis with systemic onset, unspecified hip
M08.261	Juvenile rheumatoid arthritis with systemic onset, right knee
M08.262	Juvenile rheumatoid arthritis with systemic onset, left knee
M08.269	Juvenile rheumatoid arthritis with systemic onset, unspecified knee
M08.271	Juvenile rheumatoid arthritis with systemic onset, right ankle and foot
M08.272	Juvenile rheumatoid arthritis with systemic onset, left ankle and foot
M08.279	Juvenile rheumatoid arthritis with systemic onset, unspecified ankle and foot
M08.28	Juvenile rheumatoid arthritis with systemic onset, vertebrae
M08.29	Juvenile rheumatoid arthritis with systemic onset, multiple sites
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.80	Other juvenile arthritis, unspecified site
M08.811	Other juvenile arthritis, right shoulder
M08.812	Other juvenile arthritis, left shoulder
M08.819	Other juvenile arthritis, unspecified shoulder
M08.821	Other juvenile arthritis, right elbow
M08.822	Other juvenile arthritis, left elbow
M08.829	Other juvenile arthritis, unspecified elbow
M08.831	Other juvenile arthritis, right wrist
M08.832	Other juvenile arthritis, left wrist
M08.839	Other juvenile arthritis, unspecified wrist

ICD-10 Diagnosis Code	Description
M08.841	Other juvenile arthritis, right hand
M08.842	Other juvenile arthritis, left hand
M08.849	Other juvenile arthritis, unspecified hand
M08.851	Other juvenile arthritis, right hip
M08.852	Other juvenile arthritis, left hip
M08.859	Other juvenile arthritis, unspecified hip
M08.861	Other juvenile arthritis, right knee
M08.862	Other juvenile arthritis, left knee
M08.869	Other juvenile arthritis, unspecified knee
M08.871	Other juvenile arthritis, right ankle and foot
M08.872	Other juvenile arthritis, left ankle and foot
M08.879	Other juvenile arthritis, unspecified ankle and foot
M08.88	Other juvenile arthritis, vertebrae
M08.89	Other juvenile arthritis, multiple sites
M08.90	Juvenile arthritis, unspecified, unspecified site
M08.911	Juvenile arthritis, unspecified, right shoulder
M08.912	Juvenile arthritis, unspecified, left shoulder
M08.919	Juvenile arthritis, unspecified, unspecified shoulder
M08.921	Juvenile arthritis, unspecified, right elbow
M08.922	Juvenile arthritis, unspecified, left elbow
M08.929	Juvenile arthritis, unspecified, unspecified elbow
M08.931	Juvenile arthritis, unspecified, right wrist
M08.932	Juvenile arthritis, unspecified, left wrist
M08.939	Juvenile arthritis, unspecified, unspecified wrist
M08.941	Juvenile arthritis, unspecified, right hand
M08.942	Juvenile arthritis, unspecified, left hand
M08.949	Juvenile arthritis, unspecified, unspecified hand
M08.951	Juvenile arthritis, unspecified, right hip
M08.952	Juvenile arthritis, unspecified, left hip
M08.959	Juvenile arthritis, unspecified, unspecified hip
M08.961	Juvenile arthritis, unspecified, right knee
M08.962	Juvenile arthritis, unspecified, left knee
M08.969	Juvenile arthritis, unspecified, unspecified knee
M08.971	Juvenile arthritis, unspecified, right ankle and foot
M08.972	Juvenile arthritis, unspecified, left ankle and foot
M08.979	Juvenile arthritis, unspecified, unspecified ankle and foot
M08.98	Juvenile arthritis, unspecified, vertebrae
M08.99	Juvenile arthritis, unspecified, multiple sites
T86.5	Complications of stem cell transplant
T80.89XA	Other complications following infusion, transfusion and therapeutic injection, initial encounter
T80.89XD	Other complications following infusion, transfusion and therapeutic injection, subsequent encounter
T80.89XS	Other complications following infusion, transfusion and therapeutic injection, sequela
T80.90XA	Unspecified complication following infusion and therapeutic injection, initial encounter
T80.90XD	Unspecified complication following infusion and therapeutic injection, subsequent encounter
T80.90XS	Unspecified complication following infusion and therapeutic injection, sequela

ICD-10 Diagnosis Code	Description
T81.89XA	Other complications of procedures, not elsewhere classified, initial encounter
T81.89XD	Other complications of procedures, not elsewhere classified, subsequent encounter
T81.89XS	Other complications of procedures, not elsewhere classified, sequela
T81.9XXA	Unspecified complication of procedure, initial encounter
T81.9XXD	Unspecified complication of procedure, subsequent encounter
T81.9XXS	Unspecified complication of procedure, sequela

CLINICAL EVIDENCE

Rheumatoid Arthritis

Huizinga et al, published the analysis for the 2-year and 3-year results of the double-blind, placebo-controlled, parallel-group ACT-RAY trial that assessed the efficacy and safety of tocilizumab (TCZ) plus methotrexate/placebo (MTX/PBO) and the course of disease activity in patients who discontinued TCZ due to sustained remission.[8] During the first 24 weeks, all patients (N=556) were randomized either to continue oral MTX with the addition of open-label TCZ 8 mg/kg intravenously every 4 weeks (add-on strategy) or switch to TCZ alone with PBO (switch strategy). Between weeks 24 and 52, treatment with TCZ plus blinded MTX/PBO continued unchanged; however, if Disease Activity Score in 28 joints based on erythrocyte sedimentation rate (DAS28-ESR) was >3.2 at week 24, an open-label conventional synthetic disease-modifying antirheumatic drug (csDMARD) (sulfasalazine, leflunomide, hydroxychloroquine or azathioprine; choice and dose at investigator's discretion) was added. If DAS28-ESR was >3.2 at week 36 with an added csDMARD, the patient was moved to the maintenance arm (TCZ+blinded MTX/PBO + open-label csDMARD) for the remainder of the study, with the option to receive an additional open-label csDMARD per the investigator's discretion. Between weeks 52 and 104, open-label treatment was adapted based on response every 12 weeks, and patients continued the study in one of four treat-to-target strategies. The primary endpoint has previously been published.[9] Secondary endpoints included rate and time to TCZ-free and drug-free remission, time to flare after TCZ-free remission, and time to restart of treatment after TCZ-free remission. Radiographic endpoints included progression of joint destruction based on the Genant-modified Sharp Score (GSS) at weeks 24, 52, and 104 among others. Of the randomized patients, 76% (472) completed year 2, where 50.4% discontinued TCZ by week 104, with no significant difference between treatment groups [129 (53.1%) add-on vs. 109 (47.6%) switch patients; p = 0.170)]. Twenty-eight (11.8%) of 238 patients achieved total drug-free remission due to sustained achievement of DAS28-ESR <2.6. A significantly higher proportion of patients in the add-on arm achieved drug-free remission compared with patients in the switch arm [21/243 (8.6%) vs 7/229 (3.1%); p=0.010]. A total of 200 patients subsequently flared following TCZ-free remission, with 82.5% (95% CI 75.4% to 88.5%) and 88.5% (95% CI 81.5% to 93.7%) of patients in the add-on and switch arms, respectively, experiencing flare within 52 weeks after achieving TCZ-free remission. At week 104, the majority of patients demonstrated minimal progression of radiographic structural damage. The adjusted mean change in total GSS was 0.35 for add-on and 0.95 for switch (p=0.034). The overall safety profile was similar for both treatment groups. The frequencies of adverse events (AE), serious AE (SAE), and discontinuations due to AEs were similar between the two treatment groups. The investigators concluded that treat-to-target strategies could be successful with TCZ to achieve a sustained free remission after discontinuation. TCZ free remission was maintained on average of three months prior to flaring, which then was controlled with resumption of TCZ.

Professional Societies

American College of Rheumatology (ACR)

Rheumatoid Arthritis

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDS, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (≥ 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs.[10] The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions. Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

Supplementary Appendix 5, of the 2015 ACR RA guideline, summarizes recommendations for patients with early RA, established RA, and high-risk comorbidities:[10]

Recommendations for Early RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, another target may be chosen because risk tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with early, symptomatic RA, the panel strongly recommends DMARD monotherapy over double or triple DMARD therapy in patients with low disease activity and conditionally recommends DMARD monotherapy over double or triple DMARD therapy in patients with moderate or high disease activity. Methotrexate should be the preferred initial therapy for most patients with early RA with active disease.
- For patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids), the panel strongly recommends treatment with a combination of DMARDs *or* a TNFi *or* a non-TNF biologic, with or without methotrexate (MTX) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to superior efficacy.
- For patients with moderate or high disease activity despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids (defined as ≤10 mg/day of prednisone or equivalent). Low-dose glucocorticoids may also be used in patients who need a bridge until realizing the benefits of DMARD therapy. The risk/benefit ratio of glucocorticoid therapy is favorable as long as the dose is low and the duration of therapy is short.
- For patients experiencing a flare of RA, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose for the shortest possible duration, to provide a favorable benefit-risk ratio for the patient.

Recommendations for Established RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, however, another target may be chosen because tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with low disease activity, the panel strongly recommends using DMARD monotherapy over a TNFi. For DMARD-naïve patients with moderate or high disease activity, the panel conditionally recommends DMARD monotherapy over double or triple DMARD therapy and DMARD monotherapy over tofacitinib. In general, MTX should be the preferred initial therapy for most patients with established RA with active disease.
- For patients with moderate or high disease activity despite DMARD monotherapy including methotrexate, the panel strongly recommends using combination DMARDs or adding a TNFi or a non-TNF biologic or tofacitinib (all choices with or without methotrexate) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to its superior efficacy.

For all scenarios for established RA below, treatment may be with or without MTX:

- For moderate or high disease activity despite TNFi therapy in patients currently not on a DMARD, the panel strongly recommends that one or two DMARDs be added to TNFi therapy rather than continuing TNFi therapy alone.
- If disease activity is moderate or high despite single TNFi biologic therapy, the panel conditionally recommends using a non-TNF biologic.
- If disease activity is moderate or high despite non-TNF biologic therapy, the panel conditionally recommends using another non-TNF biologic. However, if a patient has failed multiple non-TNF biologics and they are TNFi-naïve with moderate or high disease activity, the panel conditionally recommends treatment with a TNFi.
- For patients with moderate or high disease activity despite prior treatment with at least one TNFi and at least one non-TNF-biologic (sequentially, not combined), the panel conditionally recommends first treating with another non-TNF biologic. However, when a non-TNF biologic is not an option (e.g., patient declines non-TNF biologic therapy due to inefficacy or side effects), the panel conditionally recommends treatment with tofacitinib.
- If disease activity is moderate or high despite the use of multiple (2+) TNFi therapies (in sequence, not concurrently), the panel conditionally recommends non-TNF biologic therapy and then conditionally treating with tofacitinib when a non-TNF biologic is not an option.
- If disease activity is moderate or high despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids.
- If patients with established RA experience an RA flare while on DMARD, TNFi, or non-TNF biologic therapy, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose and for shortest possible duration to provide the best benefit-risk ratio for the patient.

- In patients with established RA and low disease activity but not remission, the panel strongly recommends continuing DMARD therapy, TNFi, non-TNF biologic or tofacitinib rather than discontinuing respective medication.
- In patients with established RA currently in remission, the panel conditionally recommends tapering DMARD therapy, TNFi, non-TNF biologic, or tofacitinib.
- The panel strongly recommends not discontinuing all therapies in patients with established RA in disease remission.

Recommendations for RA patients with High-Risk Comorbidities

- Congestive Heart Failure:
  - In patients with established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF), the panel conditionally recommends using combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a TNFi.
  - If patients in this population are treated with a TNFi and their CHF worsens while on the TNFi, the panel conditionally recommends switching to combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a different TNFi.
- Hepatitis B:
  - In patients with established RA with moderate or high disease activity and evidence of active hepatitis B infection (hepatitis surface antigen positive > 6 months), who are receiving or have received effective antiviral treatment, the panel strongly recommends treating them the same as patients without this condition.
  - For a patient with natural immunity from prior exposure to hepatitis B (i.e., HB core antibody and HBS antibody positive and normal liver function tests), the panel recommends the same therapies as those without such findings as long as the patient's viral load is monitored.
  - For patients with chronic hepatitis B who are untreated, referral for antiviral therapy is appropriate prior to immunosuppressive therapy.
- Hepatitis C:
  - In patients with established RA with moderate or high disease activity and evidence of chronic hepatitis C virus (HCV) infection, who are receiving or have received effective antiviral treatment, the panel conditionally recommends treating them the same as the patients without this condition.
  - The panel recommends that rheumatologists work with gastroenterologists and/or hepatologists who would monitor patients and reassess the appropriateness of antiviral therapy. This is important considering the recent availability of highly effective therapy for HCV, which may lead to a greater number of HCV patients being treated successfully.
  - If the same patient is not requiring or receiving antiviral treatment for their hepatitis C, the panel conditionally recommends using DMARD therapy rather than TNFi.
- Malignancy:
  - Previous Melanoma and Non-Melanoma Skin Cancer:
    - In patients with established RA and moderate or high disease activity and a history of previously treated or untreated skin cancer (melanoma or non-melanoma), the panel conditionally recommends the use of DMARD therapy over biologics or tofacitinib.
  - Previous Lymphoproliferative Disorders:
    - In patients with established RA with moderate or high disease activity and a history of a previously treated lymphoproliferative disorder, the panel strongly recommends using rituximab rather than a TNFi and conditionally recommends using combination DMARD therapy, abatacept or tocilizumab rather than TNFi.
  - Previous Solid Organ Cancer:
    - In patients with established RA with moderate or high disease activity and previously treated solid organ cancer, the panel conditionally recommends that they be treated for RA just as one would treat an RA patient without a history of solid organ cancer.
- Serious Infections:
  - In patients with established RA with moderate or high disease activity and previous serious infection(s), the panel conditionally recommends using combination DMARD therapy or abatacept rather than TNFi.

Juvenile Idiopathic Arthritis

The 2013 update to the 2011 ACR recommendations includes the use of tocilizumab in those patients with systemic JIA with continued disease activity and synovitis.[7]

- For patients with systemic JIA with active systemic features and varying degrees of synovitis:
  - Tocilizumab was recommended as a therapeutic option for patients with continued disease activity following systemic glucocorticoid (GC) monotherapy (level A), MTX or leflunomide (level B), or anakinra (level B) irrespective of the physician global assessment (MD global) and active joint count (AJC). Tocilizumab was also recommended for patients with an MD global ≥5 irrespective of the AJC despite prior NSAID monotherapy (level C).
- For patients with systemic JIA without active systemic features and varying degrees of active synovitis:
  - Initiation of tocilizumab was recommended for an AJC >0 following treatment with anakinra (level B) or MTX or leflunomide (level B).

- For patients with systemic JIA with features concerning for Macrophage Activation Syndrome (MAS)
  - Use of tocilizumab was uncertain.

Level of evidence "A" was assigned when the recommendation was supported by randomized controlled trials.

Level of evidence "B" was assigned when the recommendation was supported by nonrandomized controlled studies (e.g., cohort and case–control studies) or extrapolations from randomized clinical trials.

Level of evidence "C" was assigned when the recommendation was supported by uncontrolled studies (case series), extrapolations from nonrandomized controlled studies, or marked extrapolations from randomized clinical trials (e.g., studies of adult arthritis patients applied to juvenile arthritis or studies of polyarthritis phenotype applied to oligoarthritis).

Level of evidence "D" was assigned when the recommendation was based upon expert opinion.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for Actemra® (tocilizumab). Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, Section 50 Drugs and Biologicals at https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c15.pdf.
(Accessed January 5, 2018)

STATE EXCEPTIONS

State	Note
Kansas	Drug policy not approved for use in this market

REFERENCES

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2. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis. Arthritis Care & Research. Arthritis Rheum. 2008;59(6):762-84.
3. Singh JA, Furst DE, Bharat A, et al. 2012 Update of the 2008 American College of Rheumatology Recommendations for the Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. 2012 May;64(5):625–639. DOI 10.1002/acr.21641.
4. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Initiation and Safety Monitoring of Therapeutic Agents for the Treatment of Arthritis and Systemic Features. Arthritis Care & Research. 2011 April;63(4):465-82.
5. MCG™ Care Guidelines, Ambulatory Care, 21st edition. Tocilizumab. Accessed January 4, 2018.
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7. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013 Oct;65(10):2499-512.
8. Huizinga TW, Conaghan PG, Martin-Mola E, et al. Clinical and radiographic outcomes at 2 years and the effect of tocilizumab discontinuation following sustained remission in the second and third year of the ACT-RAY study. Ann Rheum Dis 2015;74:35–43.
9. Dougados M, Kissel K, Sheeran T, et al. Adding tocilizumab or switching to tocilizumab monotherapy in methotrexate inadequate responders: 24-week symptomatic and structural results of a 2-year randomised controlled strategy trial in rheumatoid arthritis (ACT-RAY). Ann Rheum Dis 2013;72:43–50.
10. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. Arthritis Rheum. 2016;68(1):1-26.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
03/01/2018	• Updated coverage rationale; replaced language indicating "this policy refers to Actemra (tocilizumab) injection for intravenous infusion" with "this policy refers *only* to Actemra (tocilizumab) injection for intravenous infusion *for the treatment of polyarticular juvenile idiopathic arthritis, rheumatoid arthritis, systemic juvenile idiopathic arthritis, and cytokine release syndrome; Actemra for self-administered subcutaneous injection, is obtained under the pharmacy benefit and is indicated in the treatment of rheumatoid arthritis and giant cell arteritis*" • Archived previous policy version CS2018D0043H

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Arcalyst

Program	Prior Authorization
Medication	Arcalyst (rilonacept injection)
Markets in Scope	Arizona, California, Florida- CHIP, Hawaii, Maryland, New Mexico, Nevada, New York, New York EPP, New Jersey, Ohio, Pennsylvania, Rhode Island
Issue Date	12/20019
Pharmacy and Therapeutics Approval Date	4/2018
Effective Date	6/2018

1. Background:

Arcalyst is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.

CAPS refer to rare genetic syndromes generally caused by mutations in the NLRP-3 [Nucleotide-binding domain, leucine rich family (NLR), pyrin domain containing 3] gene (also known as Cold-Induced Auto-inflammatory Syndrome-1 [CIAS1]). CAPS disorders are inherited in an autosomal dominant pattern with male and female offspring equally affected. Features common to all disorders include fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis. In most cases, inflammation in CAPS is associated with mutations in the NLRP-3 gene which encodes the protein cryopyrin, an important component of the inflammasome. Mutations in NLRP-3 result in an overactive inflammasome resulting in excessive release of activated IL-1 that drives inflammation.

In clinical studies, Arcalyst has not been administered concomitantly with tumor necrosis factor (TNF) inhibitors. An increased incidence of serious infections has been associated with administration of an IL-1 blocker in combination with TNF inhibitors. Taking Arcalyst with TNF inhibitors is not recommended because this may increase the risk of serious infections. Treatment with Arcalyst should be discontinued if a patient develops a serious infection. Patients should be counseled not to take any IL-1 blocking drug, including Arcalyst, if they are also taking a drug that blocks TNF such as etanercept, infliximab, or adalimumab. Use of Arcalyst with other IL-1 blocking agents, such as anakinra, is not recommended.

Note: This criteria does not apply to Washington

2. Coverage Criteria:

A. Initial Authorization

1. Patient is 12 years of age or older

-AND-

2. Diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and/or Muckle-Wells Syndrome (MWS)

-AND-

3. Prescribed by or in consultation with an immunologist, allergist, dermatologist, rheumatologist, neurologist or other medical specialist

-AND-

4. The medication will not be used in combination with another biologic

Authorization will be issued for 12 months.

B. Reauthorization

1. Patient has experienced disease stability or improvement in clinical symptoms while on therapy as evidenced by one of the following:

- Improvement in rash, fever, joint pain, headache, or conjunctivitis
- Decreased number of disease flare days
- Normalization of inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], serum amyloid A [SAA])

Authorization will be issued for 12 months.

3. References:

1. Arcalyst (rilonacept) for Subcutaneous Injection Prescribing Information. Regeneron Pharmaceuticals, September, 2016.
2. Hoffman HM et al. Durability of response to rilonacept (IL-1 Trap) in a phase 3 study of patients with cryopyrin-associated periodic syndromes (CAPS): familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome. Journal of Allergy and Clinical Immunology. 2008; 121(2):S175.
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Program	Prior Authorization - Arcalyst (rilonacept injection)
Change Control	
Date	Change
12/2009	New drug policy.
3/2010	Addition of Ilaris to this policy
12/2010	Annual Review
6/2011	Added new logo and replaced all AmeriChoice references with UnitedHealthcare Community & State.
6/2012	Annual Review
6/2013	Separated Ilaris and Arcalyst into individual guidelines. Converted policy to new UHC enterprise wide formatting. Added requirement of confirmation of CAPS diagnosis.
9/2013	Requirements 2.2, 3, and 4 were added to policy. Removed requirement of overproduction of interleukin-1 and the age requirement. Split criteria into initial and reauthorization sections. Added evidence of clinical inflammation, including clinical symptoms and elevated acute phase reactants, as an additional option to satisfy the confirmation of CAPS diagnosis requirement.
9/2014	Annual Review
12/2015	Annual Review
8/2016	Updated clinical criteria to align with ORx policy. Updated policy

	to new template.
10/2017	Updated references and policy template
4/2018	Annual review. No changes to criteria.

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Cimzia

Program	Prior Authorization
Medication	Cimzia (certolizumab pegol)
Issue Date	9/2009
Pharmacy and Therapeutics Approval Date	4/2017
Effective Date	6/2017

1. Background:

Cimzia (certolizumab) is a tumor necrosis factor (TNF) blocker indicated for reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy. Examples of conventional therapy include anti-inflammatory drugs, corticosteroids, and oral immunosuppressive agents. Cimzia is also indicated for the treatment of adults with moderately to severely active rheumatoid arthritis. Cimzia is indicated for the treatment of adult patients with active psoriatic arthritis. It is also indicated for the treatment of adults with active ankylosing spondylitis.

NOTE: This policy does not apply to Washington

2. Coverage Criteria:

A. Crohn's disease

1. Initial Authorization

a. Diagnosis of moderately to severely active Crohn's disease

-AND-

b. History of failure, contraindication, or intolerance to one or more of the following conventional therapies:

(1) Corticosteroids (eg, prednisone, methylprednisolone, budesonide)
(2) 6-mercaptopurine (Purinethol)
(3) Azathioprine (Imuran)
(4) Methotrexate (Rheumatrex, Trexall)

-AND-

c. Prescribed or recommended by a gastroenterologist

-AND-

d. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Cimzia therapy

-AND-

b. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Rheumatoid Arthritis (RA)

1. Initial Authorization

a. Diagnosis of moderately to severely active RA

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one non-biologic disease modifying anti-rheumatic drug (DMARD) [eg, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine]

-AND-

d. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Cimzia therapy

-AND-

b. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Psoriatic Arthritis

1. Initial Authorization

a. Diagnosis of active psoriatic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist or dermatologist

-AND-

c. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Cimzia therapy

-AND-

b. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

D. Ankylosing Spondylitis

1. Initial Authorization

a. Diagnosis of ankylosing spondylitis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to two or more NSAIDs

-AND-

d. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab),

Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Cimzia therapy

-AND-

b. Patient is not receiving Cimzia in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

1. Cimzia Prescribing Information, UCB. January 2017.
2. Schreiber S, Rutgeerts P, Fedorak RN, et al. A randomized, placebo-controlled trial of certolizumab pegol (CDP870) for treatment of Crohn's disease. Gastroenterology. 2005; 129(3): 807-18.
3. Sandborn WJ, Feagan BG, Stoinov S, et al. Certolizumab pegol for the treatment of Crohn's disease. N Engl J Med. 2007 Jul 19; 357(3):228-38.
4. Schreiber WJ, Khaliq-Kareemi M, Lawrance IC, et al. Maintenance therapy with certolizumab pegol for Crohn's disease. N Engl J Med. 2007 Jul 19; 357(3):239-50
5. Lichtenstein GR, Abreu MT, Cohen R, Tremaine W. American Gastroenterological Association Institute medical position statement on corticosteroids, immunomodulators, and infliximab in inflammatory bowel disease. Gastroenterology 2006 Mar;130(3):935-9.
6. American College of Rheumatology 2008 Recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum.2008;59(6):762-784.
7. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases. Ann Rheum Dis. 2011;70(Suppl 1):i2-i36.

8. Keystone E, van der Heijde D, Mason Jr. D, et al. Certolizumab pegol plus methotrexate is significantly more effective than placebo plus methotrexate in active rheumatoid arthritis. Arthritis Rheum. 2008; 58(11): 3319-3329.
9. Fleischmann R, Vencovsky J, van Vollenhoven RF, et al. Efficacy and safety of certolizumab pegol monotherapy every 4 weeks in patients with rheumatoid arthritis failing previous disease-modifying antirheumatic therapy: the FAST4WARD study. Ann Rheum Dis. 2009; 68: 805-811.
10. Smolen J, Landewe RB, Mease P, et al. Efficacy and safety of certolizumab pegol plus methotrexate in active rheumatoid arthritis: the RAPID 2 study: A randomized controlled trial. Ann Rheum Dis. 2009; 68: 797-804.
11. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995;38:727-735.
12. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993; 36 (6): 729-740.
13. Per clinical consult with rheumatologist, June 30, 2011.
14. Lichtenstein GR, Hanauer SB, Sandborn WJ, and The Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009;104:465-483.
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16. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of Ankylosing spondylitis. Ann Rheum Dis. 2011;70:896-904.
17. van der Heijde, Sieper J, Maksymowych WP, et al. 2010 update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70:905-908.
18. Kyle S, Chandler D, Griffiths EM, et al. Guideline for anti-TNF-? therapy in psoriatic arthritis. Rheumatology. 2005;44:390-397.
19. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. Ann Rheum Dis. 2012;71(Supp II):i2–i45.

Program	Program type – Prior Authorization
Change Control	
Date	Change
September 2009	Guidelines taken from previously approved AmeriChoice and Unison policies and updated based upon evidence in the literature.
December 2009	Guidelines revised to remove criteria for Ulcerative Colitis.

December 2010	Annual Review
December 2011	Annual Review • Changed requirement of history of failure of 2 DMARDs to history of failure of 1 DMARD for rheumatoid arthritis and psoriatic arthritis • Created Humira once weekly dosing criteria for rheumatoid arthritis • Specified "moderate to severe" for the severity of disease required for polyarticular JIA • Changed prerequisite medication requirements for polyarticular JIA and psoriatic arthritis • Specified severity of disease for plaque psoriasis • Changed prerequisite therapy to one phototherapy and one systemic therapy • Specified severity of disease for Crohn's disease • Combined fistulizing and nonfistulizing Crohn's disease to have the same prerequisite requirements.
June 2012	Cimzia added to policy for rheumatoid arthritis (III.A.) and Crohn's disease (III.F.)
Sept 2012	Added option of additional alternative therapy failure of infliximab for initial therapy of Humira. No change to Cimzia for Crohn's disease.
Feb 2015	Converted existing multidrug policy to a Cimzia specific policy. Updated criteria to align with current UHC clinical criteria template. Removed age requirement for all indications. Removed prescriber requirement for all reauthorization criteria sections. Added "Janus kinase inhibitor" to all areas noting that the patient should not receive Cimzia in combination with other immunomodulator/biologic DMARDs.

March 2016	Updated criteria for psoriatic arthritis (PsA) to remove the requirement for history of one oral DMARD to be consistent with other biologic DMARD criteria Updated the list of conventional therapies required in the Crohn's disease (CD) criteria to remove aminosalicylates Removed all "notes to prescriber" Added formulary note in preface Annual Review- Updated policy template
October 2016	Annual Review – no change to criteria
March 2017	Added Otezla to list of medications not to be taken with Cimzia. Updated references and policy template.
April 2017	Added hydroxychloroquine to example list of non-biologic DMARDs

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Cosentyx

Program	Prior Authorization
Medication	Cosentyx (secukinumab)
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Mexico, New York, Ohio, Rhode Island
Issue Date	3/2015
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Cosentyx (secukinumab) is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. It is also indicated for the treatment of adult patients with active psoriatic arthritis or for treatment of adults with active ankylosing spondylitis.

2. Coverage Criteria:

A. <u>Plaque Psoriasis</u>

1. <u>Initial Authorization</u>

a. Diagnosis of moderate to severe plaque psoriasis

-AND-

b. Patient is not receiving Cosentyx in combination with any of the following:
- i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab), Orencia (abatacept)]
- ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
- iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

c. One of the following:

(1) History of failure, contraindication, or intolerance to one of the following:

(a) Humira (adalimumab)
(b) Enbrel (etanercept)

-OR-

(2) For continuation of prior Cosentyx therapy

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Cosentyx therapy

-AND-

b. Patient is not receiving Cosentyx in combination with any of the following:
   i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab), Orencia (abatacept)]
   ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
   iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Ankylosing Spondylitis

1. Initial Authorization

a. Diagnosis of active ankylosing spondylitis

-AND-

b. Patient is not receiving Cosentyx in combination with any of the following:
   i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab), Orencia (abatacept)]
   ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
   iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

c. One of the following:

(1) History of failure, contraindication, or intolerance to two of the following:

(a) Humira (adalimumab)

(b) Enbrel (etanercept)
(c) Cimzia (certolizumab pegol)

-OR-

(2) For continuation of prior Cosentyx therapy

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Cosentyx therapy

-AND-

b. Patient is not receiving Cosentyx in combination with any of the following:
i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab), Orencia (abatacept)]
ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Psoriatic Arthritis

1. Initial Authorization

a. Diagnosis of active psoriatic arthritis

-AND-

b. Patient is not receiving Cosentyx in combination with any of the following:
i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab), Orencia (abatacept)]
ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

c. One of the following:

(1) History of failure, contraindication, or intolerance to two of the following:

(a) Humira (adalimumab)
(b) Enbrel (etanercept)
(c) Cimzia (certolizumab pegol)

-OR-

(2) For continuation of prior Cosentyx therapy

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Cosentyx therapy

-AND-

b. Patient is not receiving Cosentyx in combination with any of the following:
   i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab), Orencia (abatacept)]
   ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
   iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

1. Cosentyx Prescribing Information. Novartis Pharmaceuticals Corp, January 2015.
2. Langley RG, Elewski BE, Lebwohl M, et al.; ERASURE Study Group; FIXTURE Study Group. Secukinumab in plaque psoriasis--results of two phase 3 trials. N Engl J Med. 2014;374:326-338.

Program	Prior Authorization - Cosentyx (secukinumab)
Change Control	
Date	Change
3/2015	New Guideline
3/2016	Initial therapy section: Added Enbrel to list of preferred drugs that require history of failure, contraindication, or intolerance Added technician note indicating Actemra as a non-preferred drug Annual Review- Updated policy template

5/2016	Added criteria sections for ankylosing spondylitis and psoriatic arthritis. Added Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] to Section C in Plaque Psoriasis.
7/2016	Added Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] to Ankylosing Spondylitis (initial and reauthorization) and Plaque Psoriasis (reauthorization).
9/2016	Updated background. Removed prescriber check from all sections. Removed trial and failure of NSAIDs from Ankylosing Spondylitis section. Changed trial and failure requirements from "all" to "two" biologics in Ankylosing Spondylitis and Psoriatic Arthritis sections and from "both" to "one" for Plaque Psoriasis.
3/2017	Updated template. No changes to clinical criteria.
9/2017	Updated preferred products for plaque psoriasis and psoriatic arthritis to include Otezla
2/2018	Removed Otezla as a step therapy medication and updated number of trial/fail medications in the psoriasis and psoriatic arthritis sections.

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Enbrel

Program	Prior Authorization
Medication	Enbrel (etanercept)
Issue Date	9/2009
Pharmacy and Therapeutics Approval Date	4/2017
Effective Date	6/2017

Enbrel (etanercept) is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis. It is also indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age or older. Enbrel is indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis. It is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis. Enbrel is also indicated for the treatment of patients 4 years of age and older with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

NOTE: This policy does not apply to Washington

1. Coverage Criteria:

A. <u>Rheumatoid Arthritis (RA)</u>

1. <u>Initial Authorization</u>

a. Diagnosis of moderately to severely active RA

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one non-biologic disease modifying anti-rheumatic drug (DMARD) [eg, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine]

-AND-

d. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Enbrel therapy

-AND-

b. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Juvenile Idiopathic Arthritis

1. Initial Authorization

a. Diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one of the following DMARDs:
(1) Leflunomide (Arava)
(2) Methotrexate (Rheumatrex/Trexall)

-AND-

d. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Enbrel therapy

-AND-

b. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Psoriatic Arthritis

1. Initial Authorization

a. Diagnosis of active psoriatic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist or dermatologist

-AND-

c. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Enbrel therapy

-AND-

b. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

D. Plaque Psoriasis

1. Initial Authorization

a. Diagnosis of moderate to severe chronic plaque psoriasis

-AND-

b. Prescribed or recommended by a dermatologist

-AND-

c. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Enbrel therapy

-AND-

b. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

E. Ankylosing Spondylitis

1. Initial Authorization

a. Diagnosis of ankylosing spondylitis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to two or more NSAIDs

-AND-

d. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Enbrel therapy

-AND-

b. Patient is not receiving Enbrel in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. References:

1. Enbrel Prescribing Information. Amgen and Wyeth Pharmaceuticals; November 2016.
2. Moreland, L, Schiff, M, Baumgartner, S, et al. Etanercept therapy in rheumatoid arthritis. Ann Intern Med 1999;130:478-486.
3. Weinblatt M, Kremer J, Bankhurst A, et al. A trial of etanercept, a recombinant tumor necrosis factor receptor: Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. NEJM 2005;340: 253-359.
4. Bathon J, Martin R, Fleischman R, et al. A comparison of etanercept and methotrexate in patients with early rheumatoid arthritis. NEJM 2000;343:1586-1593.
5. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-639.
6. Pavy S. Constantin A, Pham T, et al. Methotrexate therapy for rheumatoid arthritis: clinical practice guidelines based on published evidence and expert opinions. Joint Bone Spine 2006; [Epub ahead of print]:1-8.
7. Ledingham J, Deighton C, on behalf of the British Society of Rheumatology Standards, Guidelines and Audit Working Group (SGAWG). Update on the British Society for Rheumatology guidelines for prescribing TNF-alpha blockers in adults with rheumatoid arthritis (update of previous guidelines of April 2001). Rheumatol 2005; 44: 157-163.
8. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995; 38(6):727-735.
9. Bulletin on the Rheumatic Diseases for evidence-based management of rheumatic disease, a publication of the arthritis foundation: Use of etanercept in children. Bulletin on the Rheumatic Dis 2000; 49 (12):1-4.

10. Giannini H, Ruperto N, Ravelli A, et al. Preliminary definition of improvement in juvenile arthritis. Arthritis Rheum 1997; 40(7):1202-9.
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Program	Program type – Prior Authorization
Change Control	
Date	Change
September 2009	Guidelines taken from previously approved AmeriChoice and Unison policies and updated based upon evidence in the literature.
December 2009	Guidelines revised to remove criteria for Ulcerative Colitis.
December 2010	Annual Review
December 2011	Annual Review • Changed requirement of history of failure of 2 DMARDs to history of failure of 1 DMARD for rheumatoid arthritis and psoriatic arthritis • Created Humira once weekly dosing criteria for rheumatoid arthritis • Specified “moderate to severe” for the severity of disease required for polyarticular JIA • Changed prerequisite medication requirements for polyarticular JIA and psoriatic arthritis • Specified severity of disease for plaque psoriasis • Changed prerequisite therapy to one phototherapy and one systemic therapy • Specified severity of disease for Crohn’s disease • Combined fistulizing and nonfistulizing Crohn’s disease to have the same prerequisite requirements.
June 2012	Cimzia added to policy for rheumatoid arthritis (III.A.) and Crohn’s disease (III.F.)

Sept 2012	Added option of additional alternative therapy failure of infliximab for initial therapy of Humira. No change to Cimzia for Crohn's disease.
Feb 2015	Converted existing multidrug policy to an Enbrel specific policy. Updated criteria to align with current UHC clinical criteria template. Removed age requirement for all indications. Removed prescriber requirement for all reauthorization criteria sections. JIA, initial therapy: Removed the requirement of trial of NDAIDs or corticosteroids, now only requires trial of methotrexate. Added "Janus kinase inhibitor" to all areas noting that the patient should not receive Cimzia in combination with other immunomodulator/biologic DMARDs. Added new requirement requiring trials of preferred alternatives to all sections: history of failure, contraindication, or intolerance to both* of the following: Cimzia and Humira (where indicated for the specific diagnosis) or Continuation of prior Enbrel therapy. *Both Cimzia and Humira are required only when both drugs indicated for the diagnosis. If only one preferred drugs is indicated for a specific diagnosis, then only a trial of the one drug is required (eg, Humira for JIA).
March 2016	Removed prerequisite therapy requirements throughout policy that required other biologic DMARD trials before Enbrel. Updated Juvenile Idiopathic Arthritis (JIA) initial therapy to include leflunomide as a part of the DMARD requirement Annual Review- Updated policy template
October 2016	Updated background with expanded age for plaque psoriasis
March 2017	Added Otezla to list of medications not to be used with Enbrel. Updated policy template.
April 2017	Added hydroxychloroquine to example list of non-biologic DMARDs

ENTYVIO® (VEDOLIZUMAB)

Policy Number: CS2018D0053G **Effective Date**: July 1, 2018

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Commercial Policy

- Entyvio® (Vedolizumab)

INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

Entyvio (vedolizumab) is proven and medically necessary for the treatment of:

I. **Crohn's disease when ALL of the following criteria are met**: [1,2]
   A. For initial therapy, **all** of the following:
      1. Diagnosis of moderately to severely active Crohn's disease (CD); **and**
      2. **One** of the following:
         a. History of failure, contraindication, or intolerance to at least **one** of the following conventional therapies:
            i. Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Cimzia (certolizumab)]
            ii. Immunomodulator (e.g., azathioprine, 6-mercaptopurine)
            iii. Corticosteroid;
         b. Corticosteroid dependent (e.g., unable to successfully taper corticosteroids without a return of the symptoms of CD);

         and
      3. Entyvio is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for Crohn's disease up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
      4. Patient is not receiving Entyvio in combination with **either** of the following:

a. Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Cimzia (certolizumab)]
b. Tysabri (natalizumab);
and

5. Initial authorization will be for no more than 14 weeks.

B. For continuation therapy, **all** of the following:
1. Documentation of positive clinical response to Entyvio; **and**
2. Entyvio dosing for Crohn's disease is in accordance with the FDA labeled dosing up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
3. Reauthorization will be for no more than 12 months.

II. **Ulcerative colitis when ALL of the following criteria are met**: [1,2]

A. For initial therapy, **all** of the following:
1. Diagnosis of moderately to severely active ulcerative colitis (UC); **and**
2. **One** of the following:
a. History of failure, contraindication, or intolerance to at least **one** of the following conventional therapies:
i. Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Simponi (golimumab)]
ii. Immunomodulator (e.g., azathioprine, 6-mercaptopurine)
iii. Corticosteroid;
b. Corticosteroid dependent (e.g., unable to successfully taper corticosteroids without a return of the symptoms of UC);
and
3. Entyvio is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for ulcerative colitis up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
4. Patient is not receiving Entyvio in combination with **either** of the following:
a. Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Simponi (golimumab)]
b. Tysabri (natalizumab);
and
5. Initial authorization will be for no more than 14 weeks.

B. For continuation therapy, **all** of the following:
1. Documentation of positive clinical response to Entyvio; **and**
2. Entyvio dosing for ulcerative colitis is in accordance with the FDA labeled dosing up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
3. Reauthorization will be for no more than 12 months.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Entyvio is indicated for treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for the following: [1]

- Inducing and maintaining clinical response
- Inducing and maintaining clinical remission
- Improving endoscopic appearance of the mucosa
- Achieving corticosteroid-free remission

It is also indicated for treatment of adult patients with moderately to severely active Crohn's Disease (CD) who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for the following: [1]

- Achieving clinical response
- Achieving clinical remission
- Achieving corticosteroid-free remission

BACKGROUND

Entyvio is a monoclonal antibody that reduces chronically inflamed gastrointestinal parenchymal tissue associated with ulcerative colitis and Crohn's disease by binding specifically to the alpha-4-beta-7-integrin receptor and blocking its interaction with mucosal addressin cell adhesion molecule-1 which then inhibits the movement of memory T-lymphocytes across the endothelium into inflamed gastrointestinal tissue. [1,2]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J3380	Injection, vedolizumab, 1 mg

ICD-10 Diagnosis Code	Description
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction

ICD-10 Diagnosis Code	Description
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.40	Inflammatory polyps of colon without complications
K51.411	Inflammatory polyps of colon with rectal bleeding
K51.412	Inflammatory polyps of colon with intestinal obstruction
K51.413	Inflammatory polyps of colon with fistula
K51.414	Inflammatory polyps of colon with abscess
K51.418	Inflammatory polyps of colon with other complication
K51.419	Inflammatory polyps of colon with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications

Maximum Dosage Requirements

Maximum Allowed Quantities by HCPCS Units

This section provides information about the maximum dosage per administration for vedolizumab administered by a medical professional.

Medication Name		Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic			
Entyvio	vedolizumab	300 mg	J3380	300 HCPCS units (1 mg per unit)

HCPCS Code Based Maximum Dosage Information

Maximum Allowed Quantities by National Drug Code (NDC) Units

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDC's for each drug product and is subject to change.

Medication Name		How Supplied	National Drug Code	Maximum Allowed
Brand	Generic			
Entyvio	vedolizumab	300 mg powder for reconstitution	64764-0300-20	1 Vial

CLINICAL EVIDENCE

Technology Assessments

Ulcerative Colitis

A 2014 Cochrane review was published which evaluated efficacy and safety of vedolizumab used for induction and maintenance of remission in ulcerative colitis. [7] Authors concluded that:

- Moderate to high quality data from four studies shows that vedolizumab is superior to placebo for induction of clinical remission and response and endoscopic remission in patients with moderate to severely active ulcerative colitis and prevention of relapse in patients with quiescent ulcerative colitis.
- Moderate quality data from one study suggests that vedolizumab is superior to placebo for prevention of relapse in patients with quiescent ulcerative colitis.
- Adverse events appear to be similar to placebo.
- Future trials are needed to define the optimal dose, frequency of administration and long-term efficacy and safety of vedolizumab used for induction and maintenance therapy of ulcerative colitis.
- Vedolizumab should be compared to other currently approved therapies for ulcerative colitis in these trials.

A 2015 Cochrane review was published which examined the impact of biological interventions for ulcerative colitis on health-related quality of life (HRQL). [8] The authors concluded that:

- Biologics have the potential to improve HRQL in UC patients.
- High quality evidence suggests that infliximab provides a clinically meaningful improvement in HRQL in UC patients receiving induction therapy.
- Moderate quality evidence suggests that vedolizumab provides a clinically meaningful improvement in HRQL in UC patients receiving maintenance therapy.
- These findings are important since there is a paucity of effective drugs for the treatment of UC that have the potential to both decrease disease activity and improve HRQL.
- More research is needed to assess the long-term effect of biologic therapy on HRQL in patients with UC.
- More research is needed to assess the impact of golimumab and adalimumab on HRQL in UC patients.
- Trials involving direct head to head comparisons of biologics would help determine which biologics provide optimum benefit for HRQL.

Professional Societies

Crohn's Disease

According to the American College of Gastroenterology Practice Guidelines for the Management of Crohn's Disease in Adults (ACG Practice Guidelines) published in February 2009, patients with moderate-severe disease usually have a Crohn's Disease Activity Index (CDAI) of 220-450. [3] They have failed to respond to treatment for mild-moderate disease, or have more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia.

The CDAI is the sum of the following clinical or laboratory variables after multiplying by their weighting factor given in parentheses:

- Number of liquid or soft stools each day for seven days (2)
- Abdominal pain graded from 0-3 in severity each day for seven days (5)
- General well-being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days (7)
- Presence of complications where 1 point is added for each complication (20). Complications include:
  - The presence of joint pains (arthralgia) or frank arthritis
  - Inflammation of the iris or uveitis
  - Presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers
  - Anal fissures, fistulae or abscesses
  - Other fistulae (e.g. Enterocutaneous, vesicle, vaginal)

- Fever (>37.8° C) during the previous week
- Taking diphenoxylate/atropine [Lomotil®] or opiates for diarrhea (30)
- Presence of an abdominal mass where 0 = none, 2 = questionable, 5 = definite (10);
- Absolute deviation of hematocrit from 47% in males and 42% in females (6)
- Percentage deviation from standard body weight (1)

In 2013, the AGA released an updated guideline which describes their relative positioning of immunomodulators and anti-TNF-α biologic agents in inducing and maintaining clinical remission in patients with inflammatory (luminal) Crohn's disease. [4] A summary of the recommendations along with strength of evidence are described below.

Recommendations for the induction of remission:
- We suggest against using thiopurine monotherapy to induce remission in patients with moderately severe Crohn's disease (weak recommendation, moderate-quality evidence).
- We suggest against using methotrexate to induce remission in patients with moderately severe Crohn's disease (weak recommendation, low-quality evidence).
- We recommend using anti-TNF-α drugs to induce remission in patients with moderately severe Crohn's disease (strong recommendation, moderate-quality evidence).
- We recommend using anti-TNF-α monotherapy over thiopurine monotherapy to induce remission in patients who have moderately severe Crohn's disease (strong recommendation, moderate-quality evidence).
- We recommend using anti-TNF-α drugs in combination with thiopurines over thiopurine monotherapy to induce remission in patients who have moderately severe Crohn's disease (strong recommendation, high-quality evidence).
- We suggest using anti-TNF-α drugs in combination with thiopurines over anti-TNF-α drug monotherapy to induce remission in patients who have moderately severe Crohn's disease (weak recommendation, moderate-quality evidence).

Recommendations for maintenance of remission:
- We recommend using thiopurines over no immunomodulator therapy to maintain a steroid-induced remission in patients with Crohn's disease (strong recommendation, moderate-quality evidence).
- We suggest using methotrexate over no immunomodulator therapy to maintain a steroid-induced remission in patients with Crohn's disease (weak recommendation, low-quality evidence).
- We recommend using anti-TNF-α drugs over no anti-TNF-α drugs to maintain a steroid or anti-TNF-α drug-induced remission in patients with Crohn's disease (strong recommendation, high-quality evidence).
- We make no recommendation for or against the combination of an anti-TNF-α drug and a thiopurine versus an anti-TNF-α drug alone to maintain remission induced by a combination of these drugs in patients with Crohn's disease (no recommendation, low-quality evidence).

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for Entyvio® (vedolizumab). Local Coverage Determinations (LCDs) do not exist at this time.

Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals.
(Accessed March 7, 2018)

STATE EXCEPTIONS

State	Note
Kansas	Drug policy not approved for use in this market

REFERENCES

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
07/01/2018	• Added state exceptions language to indicate this policy is not approved for use in the Kansas market • Updated supporting information to reflect the most current references; no change to coverage rationale or lists of applicable codes • Archived previous policy version CS2017D0053F

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Humira

Program	Prior Authorization
Medication	Humira (adalimumab)
Issue Date	9/2009
Pharmacy and Therapeutics Approval Date	4/2017
Effective Date	6/2017

1. Background:

Humira (adalimumab) is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. It is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 2- 4 years of age and older. Humira is also indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis. It is indicated for reducing signs and symptoms in adult patients with active ankylosing spondylitis. Humira is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn′s disease who have had an inadequate response to conventional therapy. Humira is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate. It is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab. Examples of conventional therapy include anti-inflammatory drugs, corticosteroids, and oral immunosuppressive agents. Humira is also indicated for inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). Humira is indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. Humira is indicated for the treatment of moderate to severe hidradenitis suppurativa. Finally, Humira is indicated for the treatment of non-infectious intermediate, posterior and panuveitis in adult patients.

NOTE: This policy does not apply to Washington

UnitedHealthcare Community Plan

2. Coverage Criteria:

A. Rheumatoid Arthritis (RA)

1. Initial Authorization

a. Diagnosis of moderately to severely active rheumatoid arthritis

-AND-

b. Prescribed by or in consultation with a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one nonbiologic disease modifying anti-rheumatic drug (DMARD) [eg, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine]

-AND-

d. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Polyarticular Juvenile Idiopathic Arthritis

1. Initial Authorization

a. Diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis

-AND-

b. Prescribed or in consultation by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one of the following DMARDs:
(1) Leflunomide (Arava)
(2) Methotrexate (Rheumatrex/Trexall)

-AND-

d. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Psoriatic Arthritis

1. Initial Authorization

a. Diagnosis of active psoriatic arthritis

-AND-

b. Prescribed by or in consultation with a rheumatologist or dermatologist

-AND-

c. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

D. Plaque Psoriasis

1. Initial Authorization

a. Diagnosis of moderate to severe chronic plaque psoriasis

-AND-

b. Prescribed by or in consultation with a dermatologist

-AND-

c. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

E. Ankylosing Spondylitis

1. Initial Authorization

a. Diagnosis of ankylosing spondylitis

-AND-

b. Prescribed by or in consultation with a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to two or more NSAIDs

-AND-

d. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

F. Crohn's disease

1. Initial Authorization

a. Diagnosis of moderately to severely active Crohn's disease

-AND-

b. One of the following:

(1) History of failure, contraindication, or intolerance to one or more of the following conventional therapies:

- Corticosteroids (eg, prednisone, methylprednisone, budesonide)
- 6-mercaptopurine (Purinethol)
- Azathioprine (Imuran)
- Methotrexate (Rheumatrex, Trexall)

-OR-

(2) History of failure (ie, lost response) or intolerance to Remicade (infliximab)

-AND-

c. Prescribed by or in consultation with a gastroenterologist

-AND-

d. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. <u>Reauthorization</u>

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

G. Ulcerative Colitis

1. Initial Authorization

a. Diagnosis of moderately to severely active ulcerative colitis

-AND-

b. History of failure, contraindication, or intolerance to one of the following conventional therapies:

(1) Corticosteroids (eg, prednisone, methylprednisone, budesonide)
(2) 6-mercaptopurine (Purinethol)
(3) Azathioprine (Imuran)
(4) Methotrexate (Rheumatrex, Trexall)

-AND-

c. Prescribed by or in consultation with a gastroenterologist

-AND-

d. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. One of the following:

(1) For patients who initiated Humira therapy within the past 12 weeks: Documentation of clinical remission or significant clinical benefit by eight weeks (Day 57) of therapy

-OR-

(2) For patients who have been maintained on Humira therapy for longer than 12 weeks: Documentation of positive clinical response to Humira therapy.

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

H. Hidradenitis Suppurativa

1. Initial Authorization

a. Diagnosis of moderate to severe hidradenitis suppurativa (ie, Hurley Stage II or III)

-AND-

b. Prescribed by or in consultation with a dermatologist

-AND-

c. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

I. Uveitis (UV)

1. Humira will be approved based on **both** of the following criteria:

a. Diagnosis of non-infectious uveitis

-AND-

b. Uveitis is classified as one of the following:
(1) intermediate
(2) posterior
(3) panuveitis

-AND-

c. Prescribed by or in consultation with a rheumatologist or ophthalmologist

-AND-

d. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Humira therapy

-AND-

b. Patient is not receiving Humira in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

1. Humira Prescribing Information. Abbott Laboratories, July 2016.
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Program	Program type – Prior Authorization
Change Control	
Date	Change
September 2009	Guidelines taken from previously approved AmeriChoice and Unison policies and updated based upon evidence in the literature.
December 2009	Guidelines revised to remove criteria for Ulcerative Colitis.

December 2010	Annual Review
December 2011	Annual Review • Changed requirement of history of failure of 2 DMARDs to history of failure of 1 DMARD for rheumatoid arthritis and psoriatic arthritis • Created Humira once weekly dosing criteria for rheumatoid arthritis • Specified "moderate to severe" for the severity of disease required for polyarticular JIA • Changed prerequisite medication requirements for polyarticular JIA and psoriatic arthritis • Specified severity of disease for plaque psoriasis • Changed prerequisite therapy to one phototherapy and one systemic therapy • Specified severity of disease for Crohn's disease • Combined fistulizing and nonfistulizing Crohn's disease to have the same prerequisite requirements.
June 2012	Cimzia added to policy for rheumatoid arthritis (III.A.) and Crohn's disease (III.F.)
Sept 2012	Added option of additional alternative therapy failure of infliximab for initial therapy of Humira. No change to Cimzia for Crohn's disease.
Feb 2015	Converted existing multidrug policy to a Humira specific policy. Updated criteria to align with current UHC clinical criteria template. Removed age requirement for all indications. Removed prescriber requirement for all reauthorization criteria sections. Added "Janus kinase inhibitor" to all areas noting that the patient should not receive Cimzia in combination with other immunomodulator/biologic DMARDs.
Dec 2015	Policy updated with the new FDA-approved indication for hidradenitis suppurativa Prescriber requirement was modified to read, "Prescribed by or in consultation with a(n)…." for all indications Removed endnotes related to age restrictions since criteria no longer have age restrictions.
March 2016	Updated Juvenile Idiopathic Arthritis (JIA) initial therapy to include leflunomide as a part of the DMARD requirement Updated the list of conventional therapies required in the Crohn's disease (CD) criteria to remove aminosalicylates Updated the list of conventional therapies required for ulcerative colitis (UC)

	criteria to add aminosalicylates Removed all “notes to prescriber” Annual Review- Updated policy template
October 2016	Added not to use in combination with Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] to all sections Added prescriber requirement for Hidradenitis Suppurativa Added criteria for Uveitis
March 2017	Updated ulcerative colitis initial authorization duration to 12 months to match initial authorization durations for other indications. Updated policy template.
April 2017	Added hydroxychloroquine to example list of non-biologic DMARDs

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Ilaris

Program	Prior Authorization
Medication	Ilaris (canakinumab)
Issue Date	12/2009
Pharmacy and Therapeutics Approval Date	11/2017
Effective Date	1/2018

1. Background:

Indications

Cryopyrin-Associated Periodic Syndromes (CAPS)
Ilaris is an interleukein-1 beta blocker indicated for the treatment of the following autoinflammatory Periodic Fever Syndromes: Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children 4 years of age and older including, Familial Cold Autoinflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS); Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adult and pediatric patients; Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients; Familial Mediterranean Fever (FMF) in adult and pediatric patients.

Systemic Juvenile Idiopathic Arthritis (SJIA)
Ilaris is indicated for the treatment of active Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older.

NOTE: This policy does not apply to Washington

2. Coverage Criteria:

A. Periodic Fever Syndromes: Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), Familial Mediterranean Fever (FMF)

1. Initial Authorization

a. Diagnosis of one of the following periodic fever syndromes:

(1) Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)
(2) Tumor Necrosis Factor (TNF) Receptor Associated Periodic

Syndrome (TRAPS)
(3) Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
(4) Familial Mediterranean Fever (FMF)

-AND-

b. Prescribed by or in consultation with one of the following:

(1) Allergist
(2) Immunologist
(3) Dermatologist
(4) Rheumatologist
(5) Neurologist

-AND-

c. Patient is not receiving concomitant treatment with either of the following:

(1) Tumor necrosis factor (TNF) inhibitors [eg, Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab)]
(2) Interleukin-1 inhibitors [eg, Arcalyst (rilonacept), Kineret (anakinra)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Ilaris therapy

-AND-

b. Patient is not receiving concomitant treatment with either of the following:

(1) Tumor necrosis factor (TNF) inhibitors [eg, Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab)]
(2) Interleukin-1 inhibitors [eg, Arcalyst (rilonacept), Kineret (anakinra)]

Authorization will be issued for 12 months.

B. Systemic Juvenile Idiopathic Arthritis (SJIA)

1. Initial Authorization

a. Diagnosis of active systemic juvenile idiopathic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one of the following:

(1) Non-steroidal anti-inflammatory drugs (NSAIDs)
(2) Corticosteroids
(3) Methotrexate

-AND-

d. Patient is not receiving concomitant treatment with either of the following:

(1) Tumor necrosis factor (TNF) inhibitors [eg, Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab)]
(2) Interleukin-1 inhibitors [eg, Arcalyst (rilonacept), Kineret (anakinra)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Ilaris therapy

-AND-

b. Patient is not receiving concomitant treatment with either of the following:

(1) Tumor necrosis factor (TNF) inhibitors [eg, Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab)]
(2) Interleukin-1 inhibitors [eg, Arcalyst (rilonacept), Kineret (anakinra)]

Authorization will be issued for 12 months.

3. References:

1. Ilaris Prescribing Information. Novartis Pharmaceuticals Corporation, December 2016.
2. Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, et al. Use of canakinumab in the cryopyrin-associated periodic syndrome. N Engl J Med. 2009;360(23):2416-2425.

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Program	Program type – Prior Authorization
Change Control	
Date	Change
12/2009	New drug policy.
3/2010	Addition of Ilaris to this policy
12/2010	Annual Review
6/2011	Added new logo and replaced all AmeriChoice references with UnitedHealthcare Community & State.
6/2012	Annual Review
6/2013	Separated Ilaris and Arcalyst into individual guidelines. No changes to the clinical criteria for Ilaris. Converted policy to new UHC enterprise wide formatting.
9/2013	• Cryopyrin-Associated Periodic Syndromes indication: added 12 months length of authorization; removed age criterion; added criterion checking that patient is not taking a concomitant TNF inhibitor or IL-1 inhibitor; added diagnosis criterion asking for NRLP-3 gene mutation or evidence of clinical inflammation including clinical symptoms and elevated acute phase reactants; added prescriber requirement; added reauthorization criteria requiring positive response to therapy and patient is not taking a concomitant TNF inhibitor or IL-1 inhibitor (duration 12 months) • Added criteria for new indication of systemic juvenile idiopathic arthritis: (initial) diagnosis, prescribed or recommended by a rheumatologist, trial of NSAID or corticosteroid, patient is not taking a concomitant TNF inhibitor or IL-1 inhibitor, 12 months duration; (reauthorization) positive response to therapy and patient is not taking a concomitant TNF inhibitor or IL-1 inhibitor 12 months duration

	• Added note to prescriber regarding TB evaluation
12/2015	Annual Review
3/2016	Annual Review- Updated policy template
11/2017	Periodic Fever Syndromes: revised formatting and diagnosis, removed clinical evidence requirements, and added additional types of prescribers to specialist requirement; SJIA: revised diagnosis and added methotrexate as a trial/fail option Updated background, references, and policy template

INFLIXIMAB (REMICADE®, INFLECTRA™, RENFLEXIS™)

Policy Number: CS2018D0004V **Effective Date**: April 1, 2018

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Related Community Plan Policy

- Maximum Dosage Policy

Commercial Policy

- Infliximab (Remicade®, Inflectra™, Renflexis™)

INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

This policy refers to the following infliximab products:

- Remicade® (infliximab)
- Inflectra™ (infliximab-dyyb)
- Renflexis™ (infliximab-abda)

"Infliximab" will be used to refer to all infliximab products.

Infliximab is proven and medically necessary for the treatment of:

I. **Ankylosing spondylitis when the following criterion is met**: [1,57]
   A. Diagnosis of ankylosing spondylitis (AS).

II. **Crohn's disease when the following criterion is met**: [1,3-5,41,57,61]
   A. **One** of the following:
      1. Diagnosis of fistulizing Crohn's disease (Crohn's Disease Activity Index (CDAI) ≥ 220 and ≤ 400); **or**
      2. **Both** of the following:
         a. Diagnosis of moderately to severely active Crohn's disease; **and**

b. History of failure, contraindication, or intolerance to at least one conventional therapy (e.g., corticosteroids, 6-mercaptopurine, azathioprine, methotrexate, etc.).

III. **Noninfectious uveitis when BOTH of the following criteria are met**: [12-14,15,17]
A. Diagnosis of refractory noninfectious uveitis that is causing or threatening vision loss (e.g., noninfectious uveitis associated with Behçet's or Reiter's syndromes); **and**
B. History of failure, contraindication, or intolerance to **all** of the following:
1. Topical corticosteroids
2. Systemic corticosteroids
3. Immunosuppressive drugs (e.g., azathioprine, cyclosporine, or methotrexate).

IV. **Plaque psoriasis when BOTH of the following criteria are met**: [1,57,61]
A. Diagnosis of chronic severe plaque psoriasis (i.e., extensive and/or disabling); **and**
B. Patient is a candidate for systemic therapy.

V. **Psoriatic arthritis when the following criterion is met**: [1,57,61]
A. Diagnosis of psoriatic arthritis (PsA).

VI. **Rheumatoid arthritis when BOTH of the following criteria are met**: [1,57,61]
A. Diagnosis of moderately to severely active rheumatoid arthritis (RA); **and**
B. **One** of the following:
1. Patient is receiving concurrent therapy with methotrexate
2. History of contraindication or intolerance to methotrexate.

VII. **Sarcoidosis when ALL of the following criteria are met**: [6,25,39-40,46,52]
A. Diagnosis of sarcoidosis; **and**
B. History of failure, contraindication, or intolerance to corticosteroids (e.g., prednisone, methylprednisolone); **and**
C. History of failure, contraindication, or intolerance to one immunosuppressant (e.g., methotrexate, cyclophosphamide, azathioprine).

VIII. **Ulcerative colitis when BOTH of the following criteria are met**: [1,57,61]
A. Diagnosis of moderately to severely active ulcerative colitis (UC); **and**
B. History of failure, contraindication, or intolerance to at least one conventional therapy (e.g., 6-mercaptopurine, aminosalicylate, azathioprine, corticosteroids).

There may be other conditions that qualify as serious, rare diseases for which the use of infliximab may be appropriate. Please refer to the Benefit Considerations section of this policy for additional information.

Infliximab is unproven and not medically necessary for the treatment of:
- Still's disease
- Sjogren's syndrome
- Graft-vs-host disease
- Myelodysplastic syndromes
- Undifferentiated spondyloarthropathy
- Reiter's syndrome
- Hidradenitis suppurative
- Wegener's granulomatosis
- Juvenile idiopathic arthritis (juvenile rheumatoid arthritis)

Infliximab is unproven for the treatment of the above conditions because statistically robust randomized controlled trials are needed to address the issue of whether infliximab has sufficient superiority in clinical efficacy compared to other available treatments to justify the inherent clinical risk in the use of a monoclonal antibody anti-tumor necrosis factor agent.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Remicade is a tumor necrosis factor (TNF) blocker indicated for: [1]
- Crohn's Disease:
  - Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
  - Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease.

- Pediatric Crohn's Disease:
  - Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.
- Ulcerative Colitis:
  - Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
- Pediatric Ulcerative Colitis:
  - Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.
- Rheumatoid Arthritis in Combination with Methotrexate:
  - Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active disease.
- Plaque Psoriasis:
  - Treatment of adult patients with chronic severe (i.e., extensive and /or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.
- Psoriatic Arthritis:
  - Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.
- Ankylosing Spondylitis:
  - Reducing signs and symptoms in patients with active disease.

Inflectra (infliximab-dyyb) and Renflexis (infliximab-abda) are biosimilar* to Remicade (infliximab). Inflectra and Renflexis are tumor necrosis factor (TNF) blockers indicated for: [57-60]

- Crohn's Disease:
  - Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
  - Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease.
- Pediatric Crohn's Disease:
  - Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.
- Ulcerative Colitis:
  - Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
- Rheumatoid Arthritis in Combination with Methotrexate:
  - Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active disease.
- Ankylosing Spondylitis:
  - Reducing signs and symptoms in patients with active disease.
- Psoriatic Arthritis:
  - Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.
- Plaque Psoriasis:
  - Treatment of adult patients with chronic severe (i.e., extensive and /or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

*Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product.

The FDA issued an alert dated September 7, 2011, to inform healthcare professionals that the Boxed Warning for the entire class of Tumor Necrosis Factor-alpha (TNFα) blockers has been updated to include the risk of infection from two bacterial pathogens, *Legionella* and *Listeria*. In addition, the Boxed Warning and Warnings and Precautions sections of the labels for all of the TNFα blockers have been revised so that they contain consistent information about the risk for serious infections and the associated disease-causing pathogens. [11]

The FDA issued an update on November 3, 2011 regarding their ongoing safety review of Tumor Necrosis Factor (TNF) blockers and malignancy in children, adolescents, and young adults (30 years of age or younger). This issue was

previously communicated in June 2008, August 2009, and April 2011. The FDA is requiring the manufacturers of TNF blockers to perform enhanced safety surveillance for these products. The manufacturers will also provide FDA with annual summaries and assessments of malignancies and TNF blocker utilization data. Healthcare professionals should remain vigilant for cases of malignancy in patients treated with TNF blockers. [10]

BACKGROUND

Infliximab is a genetically engineered chimeric human/mouse monoclonal antibody (cA2) against tumor necrosis factor alfa (TNF-alfa), a key mediator of mucosal inflammation. Increased levels of TNF-alfa are found in the intestinal mucosa and stool of patients with active Crohn's disease and in the joints of rheumatoid arthritis patients. Elevated TNF-alfa concentrations are also involved in ulcerative colitis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis. TNF-alfa activity is neutralized by cA2 antibody binding to the soluble and transmembrane forms which blocks the binding of TNF-alfa with its receptors. Activities inhibited by anti-TNF-alfa antibodies include induction of interleukins, enhancement of leukocyte migration, and expression of adhesion molecules. In vitro studies have demonstrated that cells expressing transmembrane TNF-alfa bound by infliximab are lysed by complement or effector cells. In animal models, antibodies to TNF-alfa were shown to prevent or reduce inflammation. [1]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J1745	Injection, infliximab, excludes biosimilar, 10 mg
Q5103	Injection, infliximab-dyyb, biosimilar, (inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (renflexis), 10 mg

ICD-10 Diagnosis Code	Description
D86.0	Sarcoidosis of lung
D86.1	Sarcoidosis of lymph nodes
D86.2	Sarcoidosis of lung with sarcoidosis of lymph nodes
D86.3	Sarcoidosis of skin
D86.81	Sarcoid meningitis
D86.82	Multiple cranial nerve palsies in sarcoidosis
D86.83	Sarcoid iridocyclitis
D86.84	Sarcoid pyelonephritis
D86.85	Sarcoid myocarditis
D86.86	Sarcoid arthropathy
D86.87	Sarcoid myositis
D86.89	Sarcoidosis of other sites
D86.9	Sarcoidosis, unspecified
H20.041	Secondary noninfectious iridocyclitis, right eye
H20.042	Secondary noninfectious iridocyclitis, left eye
H20.043	Secondary noninfectious iridocyclitis, bilateral
H20.049	Secondary noninfectious iridocyclitis, unspecified eye
H44.131	Sympathetic uveitis, right eye
H44.132	Sympathetic uveitis, left eye
H44.133	Sympathetic uveitis, bilateral
H44.139	Sympathetic uveitis, unspecified eye
K31.6	Fistula of stomach and duodenum
K50.00	Crohn's disease of small intestine without complications

ICD-10 Diagnosis Code	Description
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication

ICD-10 Diagnosis Code	Description
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.40	Inflammatory polyps of colon without complications
K51.411	Inflammatory polyps of colon with rectal bleeding
K51.412	Inflammatory polyps of colon with intestinal obstruction
K51.413	Inflammatory polyps of colon with fistula
K51.414	Inflammatory polyps of colon with abscess
K51.418	Inflammatory polyps of colon with other complication
K51.419	Inflammatory polyps of colon with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications
K60.3	Anal fistula
K60.4	Rectal fistula
K60.5	Anorectal fistula
K63.2	Fistula of intestine
L40.0	Psoriasis vulgaris
L40.1	Generalized pustular psoriasis
L40.2	Acrodermatitis continua
L40.3	Pustulosis palmaris et plantaris
L40.4	Guttate psoriasis
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis
L40.54	Psoriatic juvenile arthropathy
L40.59	Other psoriatic arthropathy
L40.8	Other psoriasis
L40.9	Psoriasis, unspecified
M05.00	Felty's syndrome, unspecified site

ICD-10 Diagnosis Code	Description
M05.011	Felty's syndrome, right shoulder
M05.012	Felty's syndrome, left shoulder
M05.019	Felty's syndrome, unspecified shoulder
M05.021	Felty's syndrome, right elbow
M05.022	Felty's syndrome, left elbow
M05.029	Felty's syndrome, unspecified elbow
M05.031	Felty's syndrome, right wrist
M05.032	Felty's syndrome, left wrist
M05.039	Felty's syndrome, unspecified wrist
M05.041	Felty's syndrome, right hand
M05.042	Felty's syndrome, left hand
M05.049	Felty's syndrome, unspecified hand
M05.051	Felty's syndrome, right hip
M05.052	Felty's syndrome, left hip
M05.059	Felty's syndrome, unspecified hip
M05.061	Felty's syndrome, right knee
M05.062	Felty's syndrome, left knee
M05.069	Felty's syndrome, unspecified knee
M05.071	Felty's syndrome, right ankle and foot
M05.072	Felty's syndrome, left ankle and foot
M05.079	Felty's syndrome, unspecified ankle and foot
M05.09	Felty's syndrome, multiple sites
M05.20	Rheumatoid vasculitis with rheumatoid arthritis of unspecified site
M05.211	Rheumatoid vasculitis with rheumatoid arthritis of right shoulder
M05.212	Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.219	Rheumatoid vasculitis with rheumatoid arthritis of unspecified shoulder
M05.221	Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222	Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.229	Rheumatoid vasculitis with rheumatoid arthritis of unspecified elbow
M05.231	Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232	Rheumatoid vasculitis with rheumatoid arthritis of left wrist
M05.239	Rheumatoid vasculitis with rheumatoid arthritis of unspecified wrist
M05.241	Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242	Rheumatoid vasculitis with rheumatoid arthritis of left hand
M05.249	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hand
M05.251	Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252	Rheumatoid vasculitis with rheumatoid arthritis of left hip
M05.259	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hip
M05.261	Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262	Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.269	Rheumatoid vasculitis with rheumatoid arthritis of unspecified knee
M05.271	Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272	Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot
M05.279	Rheumatoid vasculitis with rheumatoid arthritis of unspecified ankle and foot
M05.29	Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.30	Rheumatoid heart disease with rheumatoid arthritis of unspecified site
M05.311	Rheumatoid heart disease with rheumatoid arthritis of right shoulder

ICD-10 Diagnosis Code	Description
M05.312	Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.319	Rheumatoid heart disease with rheumatoid arthritis of unspecified shoulder
M05.321	Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322	Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.329	Rheumatoid heart disease with rheumatoid arthritis of unspecified elbow
M05.331	Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332	Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.339	Rheumatoid heart disease with rheumatoid arthritis of unspecified wrist
M05.341	Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342	Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.349	Rheumatoid heart disease with rheumatoid arthritis of unspecified hand
M05.351	Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352	Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.359	Rheumatoid heart disease with rheumatoid arthritis of unspecified hip
M05.361	Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362	Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.369	Rheumatoid heart disease with rheumatoid arthritis of unspecified knee
M05.371	Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372	Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.379	Rheumatoid heart disease with rheumatoid arthritis of unspecified ankle and foot
M05.39	Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.40	Rheumatoid myopathy with rheumatoid arthritis of unspecified site
M05.411	Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412	Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.419	Rheumatoid myopathy with rheumatoid arthritis of unspecified shoulder
M05.421	Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422	Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.429	Rheumatoid myopathy with rheumatoid arthritis of unspecified elbow
M05.431	Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432	Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.439	Rheumatoid myopathy with rheumatoid arthritis of unspecified wrist
M05.441	Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442	Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.449	Rheumatoid myopathy with rheumatoid arthritis of unspecified hand
M05.451	Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452	Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.459	Rheumatoid myopathy with rheumatoid arthritis of unspecified hip
M05.461	Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462	Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.469	Rheumatoid myopathy with rheumatoid arthritis of unspecified knee
M05.471	Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472	Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.479	Rheumatoid myopathy with rheumatoid arthritis of unspecified ankle and foot
M05.49	Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.50	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site
M05.511	Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512	Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder

ICD-10 Diagnosis Code	Description
M05.519	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified shoulder
M05.521	Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522	Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow
M05.529	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified elbow
M05.531	Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532	Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.539	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.549	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.559	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.569	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot
M05.579	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.60	Rheumatoid arthritis of unspecified site with involvement of other organs and systems
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.619	Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.629	Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.639	Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.649	Rheumatoid arthritis of unspecified hand with involvement of other organs and systems
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.659	Rheumatoid arthritis of unspecified hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems
M05.669	Rheumatoid arthritis of unspecified knee with involvement of other organs and systems
M05.671	Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672	Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems

ICD-10 Diagnosis Code	Description
M05.679	Rheumatoid arthritis of unspecified ankle and foot with involvement of other organs and systems
M05.69	Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.70	Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement
M05.711	Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712	Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.719	Rheumatoid arthritis with rheumatoid factor of unspecified shoulder without organ or systems involvement
M05.721	Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722	Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.729	Rheumatoid arthritis with rheumatoid factor of unspecified elbow without organ or systems involvement
M05.731	Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732	Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement
M05.739	Rheumatoid arthritis with rheumatoid factor of unspecified wrist without organ or systems involvement
M05.741	Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742	Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.749	Rheumatoid arthritis with rheumatoid factor of unspecified hand without organ or systems involvement
M05.751	Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752	Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.759	Rheumatoid arthritis with rheumatoid factor of unspecified hip without organ or systems involvement
M05.761	Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762	Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement
M05.769	Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement
M05.771	Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement
M05.772	Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement
M05.779	Rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot without organ or systems involvement
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M05.80	Other rheumatoid arthritis with rheumatoid factor of unspecified site
M05.811	Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812	Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.819	Other rheumatoid arthritis with rheumatoid factor of unspecified shoulder

ICD-10 Diagnosis Code	Description
M05.821	Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822	Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.829	Other rheumatoid arthritis with rheumatoid factor of unspecified elbow
M05.831	Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832	Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.839	Other rheumatoid arthritis with rheumatoid factor of unspecified wrist
M05.841	Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842	Other rheumatoid arthritis with rheumatoid factor of left hand
M05.849	Other rheumatoid arthritis with rheumatoid factor of unspecified hand
M05.851	Other rheumatoid arthritis with rheumatoid factor of right hip
M05.852	Other rheumatoid arthritis with rheumatoid factor of left hip
M05.859	Other rheumatoid arthritis with rheumatoid factor of unspecified hip
M05.861	Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862	Other rheumatoid arthritis with rheumatoid factor of left knee
M05.869	Other rheumatoid arthritis with rheumatoid factor of unspecified knee
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.879	Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00	Rheumatoid arthritis without rheumatoid factor, unspecified site
M06.011	Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012	Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.019	Rheumatoid arthritis without rheumatoid factor, unspecified shoulder
M06.021	Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022	Rheumatoid arthritis without rheumatoid factor, left elbow
M06.029	Rheumatoid arthritis without rheumatoid factor, unspecified elbow
M06.031	Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032	Rheumatoid arthritis without rheumatoid factor, left wrist
M06.039	Rheumatoid arthritis without rheumatoid factor, unspecified wrist
M06.041	Rheumatoid arthritis without rheumatoid factor, right hand
M06.042	Rheumatoid arthritis without rheumatoid factor, left hand
M06.049	Rheumatoid arthritis without rheumatoid factor, unspecified hand
M06.051	Rheumatoid arthritis without rheumatoid factor, right hip
M06.052	Rheumatoid arthritis without rheumatoid factor, left hip
M06.059	Rheumatoid arthritis without rheumatoid factor, unspecified hip
M06.061	Rheumatoid arthritis without rheumatoid factor, right knee
M06.062	Rheumatoid arthritis without rheumatoid factor, left knee
M06.069	Rheumatoid arthritis without rheumatoid factor, unspecified knee
M06.071	Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072	Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.079	Rheumatoid arthritis without rheumatoid factor, unspecified ankle and foot
M06.08	Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.1	Adult-onset Still's disease
M06.20	Rheumatoid bursitis, unspecified site
M06.211	Rheumatoid bursitis, right shoulder

ICD-10 Diagnosis Code	Description
M06.212	Rheumatoid bursitis, left shoulder
M06.219	Rheumatoid bursitis, unspecified shoulder
M06.221	Rheumatoid bursitis, right elbow
M06.222	Rheumatoid bursitis, left elbow
M06.229	Rheumatoid bursitis, unspecified elbow
M06.231	Rheumatoid bursitis, right wrist
M06.232	Rheumatoid bursitis, left wrist
M06.239	Rheumatoid bursitis, unspecified wrist
M06.241	Rheumatoid bursitis, right hand
M06.242	Rheumatoid bursitis, left hand
M06.249	Rheumatoid bursitis, unspecified hand
M06.251	Rheumatoid bursitis, right hip
M06.252	Rheumatoid bursitis, left hip
M06.259	Rheumatoid bursitis, unspecified hip
M06.261	Rheumatoid bursitis, right knee
M06.262	Rheumatoid bursitis, left knee
M06.269	Rheumatoid bursitis, unspecified knee
M06.271	Rheumatoid bursitis, right ankle and foot
M06.272	Rheumatoid bursitis, left ankle and foot
M06.279	Rheumatoid bursitis, unspecified ankle and foot
M06.28	Rheumatoid bursitis, vertebrae
M06.29	Rheumatoid bursitis, multiple sites
M06.30	Rheumatoid nodule, unspecified site
M06.311	Rheumatoid nodule, right shoulder
M06.312	Rheumatoid nodule, left shoulder
M06.319	Rheumatoid nodule, unspecified shoulder
M06.321	Rheumatoid nodule, right elbow
M06.322	Rheumatoid nodule, left elbow
M06.329	Rheumatoid nodule, unspecified elbow
M06.331	Rheumatoid nodule, right wrist
M06.332	Rheumatoid nodule, left wrist
M06.339	Rheumatoid nodule, unspecified wrist
M06.341	Rheumatoid nodule, right hand
M06.342	Rheumatoid nodule, left hand
M06.349	Rheumatoid nodule, unspecified hand
M06.351	Rheumatoid nodule, right hip
M06.352	Rheumatoid nodule, left hip
M06.359	Rheumatoid nodule, unspecified hip
M06.361	Rheumatoid nodule, right knee
M06.362	Rheumatoid nodule, left knee
M06.369	Rheumatoid nodule, unspecified knee
M06.371	Rheumatoid nodule, right ankle and foot
M06.372	Rheumatoid nodule, left ankle and foot
M06.379	Rheumatoid nodule, unspecified ankle and foot
M06.38	Rheumatoid nodule, vertebrae
M06.39	Rheumatoid nodule, multiple sites
M06.80	Other specified rheumatoid arthritis, unspecified site

ICD-10 Diagnosis Code	Description
M06.811	Other specified rheumatoid arthritis, right shoulder
M06.812	Other specified rheumatoid arthritis, left shoulder
M06.819	Other specified rheumatoid arthritis, unspecified shoulder
M06.821	Other specified rheumatoid arthritis, right elbow
M06.822	Other specified rheumatoid arthritis, left elbow
M06.829	Other specified rheumatoid arthritis, unspecified elbow
M06.831	Other specified rheumatoid arthritis, right wrist
M06.832	Other specified rheumatoid arthritis, left wrist
M06.839	Other specified rheumatoid arthritis, unspecified wrist
M06.841	Other specified rheumatoid arthritis, right hand
M06.842	Other specified rheumatoid arthritis, left hand
M06.849	Other specified rheumatoid arthritis, unspecified hand
M06.851	Other specified rheumatoid arthritis, right hip
M06.852	Other specified rheumatoid arthritis, left hip
M06.859	Other specified rheumatoid arthritis, unspecified hip
M06.861	Other specified rheumatoid arthritis, right knee
M06.862	Other specified rheumatoid arthritis, left knee
M06.869	Other specified rheumatoid arthritis, unspecified knee
M06.871	Other specified rheumatoid arthritis, right ankle and foot
M06.872	Other specified rheumatoid arthritis, left ankle and foot
M06.879	Other specified rheumatoid arthritis, unspecified ankle and foot
M06.88	Other specified rheumatoid arthritis, vertebrae
M06.89	Other specified rheumatoid arthritis, multiple sites
M06.9	Rheumatoid arthritis, unspecified
M08.1	Juvenile ankylosing spondylitis
M45.0	Ankylosing spondylitis of multiple sites in spine
M45.1	Ankylosing spondylitis of occipito-atlanto-axial region
M45.2	Ankylosing spondylitis of cervical region
M45.3	Ankylosing spondylitis of cervicothoracic region
M45.4	Ankylosing spondylitis of thoracic region
M45.5	Ankylosing spondylitis of thoracolumbar region
M45.6	Ankylosing spondylitis lumbar region
M45.7	Ankylosing spondylitis of lumbosacral region
M45.8	Ankylosing spondylitis sacral and sacrococcygeal region
M45.9	Ankylosing spondylitis of unspecified sites in spine
M48.8X1	Other specified spondylopathies, occipito-atlanto-axial region
M48.8X2	Other specified spondylopathies, cervical region
M48.8X3	Other specified spondylopathies, cervicothoracic region
M48.8X4	Other specified spondylopathies, thoracic region
M48.8X5	Other specified spondylopathies, thoracolumbar region
M48.8X6	Other specified spondylopathies, lumbar region
M48.8X7	Other specified spondylopathies, lumbosacral region
M48.8X8	Other specified spondylopathies, sacral and sacrococcygeal region
M48.8X9	Other specified spondylopathies, site unspecified
N82.2	Fistula of vagina to small intestine
N82.3	Fistula of vagina to large intestine
N82.4	Other female intestinal-genital tract fistulae

CLINICAL EVIDENCE

Proven

Sarcoidosis

The use of infliximab in patients with chronic pulmonary sarcoidosis was assessed in a multicenter, randomized, double-blind, placebo-controlled study. [52] Patients must have been treated with at least 10 mg/d of prednisone or equivalent or one or more immunosuppressants for ≥ 3 months before screening. They received infliximab 3 mg/kg (n=46), 5 mg/kg (n=47), or placebo (n=45) at weeks 0, 2, 6, 12, 18, and 24. They were followed through 52 weeks. The primary endpoint was the change at week 24 from baseline in percent of predicted forced vital capacity (FVC). Patients receiving infliximab 3 or 5 mg/kg had a mean increase of 2.5% compared with no change for those receiving placebo (p=0.038).

Infliximab has also been studied for use in sarcoidosis in small clinical trials, small published studies and reports that also conclude that clinical evidence supports the use of infliximab for treatment-resistant sarcoidosis. [6,25,39,40,46]

Noninfectious Uveitis

Long-term safety and efficacy of treatment with infliximab in uveitis for more than 1 year in patients (n=164) with Behçet's disease (BD) was evaluated via questionnaire in a retrospective multicenter study.[12] Primary outcome measures assessed were best-corrected VA (BCVA) determined by the Landolt ring, proportion of subjects without relapse of uveitis, frequency of ocular inflammatory attacks per year, and adverse effects of the therapy. The mean age at initiation of infliximab treatment was 42.6±11.7 years, and the mean treatment duration was 32.9±14.4 months. Data before and at the last visit during infliximab treatment were analyzed in 4 groups divided by duration of treatment: group A (n=43, 12-<24 months), group B (n=62, 24-<36 months), group C (n=42, 36-<48 months), and group D (n=17, ≥48 months). The frequency of ocular attacks decreased in all groups (from 5.3±3.0 to 1.0±0.3 in group A, 4.8±4.6 to 1.4±0.3 in group B, 4.1±2.9 to 0.9±0.3 in group C, and 9.5±5.8 to 1.6±0.5 in group D; all $P < 0.05$). The BCVA was improved in approximately 55% of the eyes after treatment. Mean BCVA was improved after treatment with infliximab in groups A to C (from 0.79±1.04 to 0.59±0.94 in group A, 0.59±1.07 to 0.41±1.04 in group B, and 1.15±1.77 to 0.92±1.73 in group C; all $P < 0.05$) but not in group D. Uveitis relapsed in 59.1% of all patients after infliximab treatment, and no difference in duration until relapse was observed between individual groups. Approximately 80% of relapses occurred within 1 year after the initiation of infliximab treatment in all groups, 90% of which were controlled by increasing doses of topical corticosteroids and shortening the interval of infliximab infusion. Adverse effects were observed in 65 cases or 35% of all subjects. Infliximab treatment was continued in 85% of the patients, but 15% of the patients discontinued infliximab treatment because of adverse effects or insufficient efficacy. Researchers concluded that this study demonstrated that infliximab reduced the frequency of ocular attacks and improved VA inpatients with BD-related uveitis refractory to conventional therapies and was generally well tolerated, with few serious adverse events.

Kruh et al conducted a retrospective, interventional, noncomparative cohort study which evaluated the safety and efficacy of infliximab for the treatment of refractory noninfectious uveitis. Patients (n=88) with chronic, recalcitrant uveitis treated with infliximab were identified through an electronic medical record database.[13] All charts were reviewed for sex, diagnosis, location of inflammation, presence of vasculitis, prior immunomodulatory treatments, duration of infliximab treatment, dose received, secondary side effects, and other medications continued while receiving treatment with infliximab. The primary outcome measures assessed were the rate of remission, time to remission, relapse rate, failure rate, and patient tolerance. Additional analysis was aimed to identity risk factors that would predict a higher success rate of infliximab to treat various types of noninfectious uveitis. Of the 72 patients (81.8%) who achieved clinical remission while being treated with infliximab, 42 (58.3%) required additional immunomodulatory medications. At 7, 18.1, and 44.7 weeks, 25%, 50%, and 75% of patients, respectively, achieved clinical remission off all corticosteroids. Thirty-two patients (36.4%) experienced at least 1 side effect while on infliximab therapy, and 17 patients (19.3%) discontinued treatment secondary to 1 or more intolerable side effects. The most common adverse effects were skin rash (9.1%) and fatigue (8%). Factors associated with a higher chance to achieve clinical remission were nonidiopathic uveitis ($P < 0.001$), intermediate or panuveitis ($P < 0.001$), absence of vasculitis ($P < 0.001$), and a starting dose ≥5 mg/kg ($P < 0.011$). Researchers concluded that infliximab treatment induced a high rate of complete clinical remission in recalcitrant uveitis and is well tolerated by most patients.

Unproven

Juvenile Idiopathic Arthritis (Juvenile Rheumatoid Arthritis)

In an international, multicenter, randomized, placebo-controlled, double-blind study, 122 children with polyarticular juvenile rheumatoid arthritis (JRA) and persistent symptoms despite at least 3 months prior MTX were randomized to receive infliximab 3 mg/kg + MTX or placebo + MTX at weeks 0, 2, and 6.[24] At week 14, the placebo group was switched to infliximab 6 mg/kg + placebo. Responses were measured according to American College of Rheumatology Pediatric 30 (Pedi 30) criteria. Although a higher percentage of patients in the 3 mg/kg group achieved responses at

week 14 (63.8% vs. 49.2% in placebo group), the study failed to show the efficacy of infliximab for JRA as the difference was not statistically significant. By week 16, similar percentage response was achieved in both groups. At week 52, the percentages reaching ACR Pedi 50 and ACR Pedi 70 were 69.6% and 51.8%, respectively. The safety profile of infliximab 3 mg/kg was generally less favorable than that of infliximab 6 mg/kg, with more serious adverse events, infusion reactions, antibodies to infliximab, and newly induced antinuclear antibodies and antibodies to double-stranded DNA. Patients who completed the study also continued to receive open-label treatment for up to 2 years.

Infliximab has also been studied for use in JIA in smaller, open-label trials. [24,31-34,36,43-45] Further large scale studies are required to characterize the efficacy and safety of infliximab in JIA.

Miscellaneous

The medical literature contains a number of small open-label studies and case reports of infliximab therapy for the treatment of adult-onset Still's disease,[26,27] Sjogren's syndrome,[22,28] graft-vs-host disease,[29-30] myelodysplastic syndromes,[37] undifferentiated spondyloarthropathy,[35] Reiter's syndrome,[19] hidradenitis suppurativa,[21,49-51] and Wegener's granulomatosis. [38,47-48] While these studies and reports showed infliximab to have a positive effect on the manifestations of these diseases, the use of infliximab for these conditions has not been evaluated in large, controlled trials.

Professional Societies

Crohn's Disease

According to the American College of Gastroenterology Practice Guidelines for the Management of Crohn's Disease in Adults (ACG Practice Guidelines) published in February 2009, patients with moderate-severe disease usually have a Crohn's Disease Activity Index (CDAI) of 220-450. They have failed to respond to treatment for mild-moderate disease, or have more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia. [3]

The CDAI[52] is the sum of the following clinical or laboratory variables after multiplying by their weighting factor given in parentheses:

- Number of liquid or soft stools each day for seven days (2)
- Abdominal pain graded from 0-3 in severity each day for seven days (5)
- General well-being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days (7)
- Presence of complications where 1 point is added for each complication (20). Complications include:
  - The presence of joint pains (arthralgia) or frank arthritis
  - Inflammation of the iris or uveitis
  - Presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers
  - Anal fissures, fistulae or abscesses
  - Other fistulae (e.g. Enterocutaneous, vesicle, vaginal)
  - Fever (>37.8° C) during the previous week
- Taking diphenoxylate/atropine [Lomotil®] or opiates for diarrhea (30)
- Presence of an abdominal mass where 0 = none, 2 = questionable, 5 = definite (10);
- Absolute deviation of hematocrit from 47% in males and 42% in females (6)
- Percentage deviation from standard body weight (1)

The ACG Practice Guidelines support the use of infliximab for treatment and maintenance of patients with moderate to severely active Crohn's disease who have failed first-line therapy. [3]

Ulcerative Colitis

According to the American College of Gastroenterology Adult Ulcerative Colitis Practice Guidelines published in March 2010, moderate ulcerative colitis is characterized by more than four stools daily but with minimal signs of toxicity. The guidelines also describe severe disease as more than six bloody stools daily, along with evidence of toxicity such as fever, tachycardia, anemia, or an elevated erythrocyte sedimentation rate. The guidelines further state that the patient with severe colitis refractory to maximal oral treatment with prednisone, oral aminosalicylate drugs, and topical medications may be treated with infliximab if urgent hospitalization is not necessary. Infliximab may also be effective in avoiding colectomy in patients failing intravenous steroids but its long-term efficacy is unknown in this setting. [42]

Rheumatoid Arthritis

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDS, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (≥ 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with

RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs.[2] The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions. Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

Supplementary Appendix 5, of the 2015 ACR RA guideline, summarizes recommendations for patients with early RA, established RA, and high-risk comorbidities: [2]

Recommendations for Early RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, another target may be chosen because risk tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with early, symptomatic RA, the panel strongly recommends DMARD monotherapy over double or triple DMARD therapy in patients with low disease activity and conditionally recommends DMARD monotherapy over double or triple DMARD therapy in patients with moderate or high disease activity. Methotrexate should be the preferred initial therapy for most patients with early RA with active disease.
- For patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids), the panel strongly recommends treatment with a combination of DMARDs *or* a TNFi *or* a non-TNF biologic, with or without methotrexate (MTX) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to superior efficacy.
- For patients with moderate or high disease activity despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids (defined as ≤10 mg/day of prednisone or equivalent). Low-dose glucocorticoids may also be used in patients who need a bridge until realizing the benefits of DMARD therapy. The risk/benefit ratio of glucocorticoid therapy is favorable as long as the dose is low and the duration of therapy is short.
- For patients experiencing a flare of RA, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose for the shortest possible duration, to provide a favorable benefit-risk ratio for the patient.

Recommendations for Established RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, however, another target may be chosen because tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with low disease activity, the panel strongly recommends using DMARD monotherapy over a TNFi. For DMARD-naïve patients with moderate or high disease activity, the panel conditionally recommends DMARD monotherapy over double or triple DMARD therapy and DMARD monotherapy over tofacitinib. In general, MTX should be the preferred initial therapy for most patients with established RA with active disease.
- For patients with moderate or high disease activity despite DMARD monotherapy including methotrexate, the panel strongly recommends using combination DMARDs or adding a TNFi or a non-TNF biologic or tofacitinib (all choices with or without methotrexate) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to its superior efficacy.

For all scenarios for established RA below, treatment may be with or without MTX:

- For moderate or high disease activity despite TNFi therapy in patients currently not on a DMARD, the panel strongly recommends that one or two DMARDs be added to TNFi therapy rather than continuing TNFi therapy alone.
- If disease activity is moderate or high despite single TNFi biologic therapy, the panel conditionally recommends using a non-TNF biologic.
- If disease activity is moderate or high despite non-TNF biologic therapy, the panel conditionally recommends using another non-TNF biologic. However, if a patient has failed multiple non-TNF biologics and they are TNFi-naïve with moderate or high disease activity, the panel conditionally recommends treatment with a TNFi.
- For patients with moderate or high disease activity despite prior treatment with at least one TNFi and at least one non-TNF-biologic (sequentially, not combined), the panel conditionally recommends first treating with another

non-TNF biologic. However, when a non-TNF biologic is not an option (e.g., patient declines non-TNF biologic therapy due to inefficacy or side effects), the panel conditionally recommends treatment with tofacitinib.
- If disease activity is moderate or high despite the use of multiple (2+) TNFi therapies (in sequence, not concurrently), the panel conditionally recommends non-TNF biologic therapy and then conditionally treating with tofacitinib when a non-TNF biologic is not an option.
- If disease activity is moderate or high despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids.
- If patients with established RA experience an RA flare while on DMARD, TNFi, or non-TNF biologic therapy, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose and for shortest possible duration to provide the best benefit-risk ratio for the patient.
- In patients with established RA and low disease activity but not remission, the panel strongly recommends continuing DMARD therapy, TNFi, non-TNF biologic or tofacitinib rather than discontinuing respective medication.
- In patients with established RA currently in remission, the panel conditionally recommends tapering DMARD therapy, TNFi, non-TNF biologic, or tofacitinib.
- The panel strongly recommends not discontinuing all therapies in patients with established RA in disease remission.

Recommendations for RA Patients with High-Risk Comorbidities

Congestive Heart Failure

- In patients with established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF), the panel conditionally recommends using combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a TNFi.
- If patients in this population are treated with a TNFi and their CHF worsens while on the TNFi, the panel conditionally recommends switching to combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a different TNFi.

Hepatitis B

- In patients with established RA with moderate or high disease activity and evidence of active hepatitis B infection (hepatitis surface antigen positive > 6 months), who are receiving or have received effective antiviral treatment, the panel strongly recommends treating them the same as patients without this condition.
- For a patient with natural immunity from prior exposure to hepatitis B (i.e., HB core antibody and HBS antibody positive and normal liver function tests), the panel recommends the same therapies as those without such findings as long as the patient's viral load is monitored.
- For patients with chronic hepatitis B who are untreated, referral for antiviral therapy is appropriate prior to immunosuppressive therapy.

Hepatitis C

- In patients with established RA with moderate or high disease activity and evidence of chronic hepatitis C virus (HCV) infection, who are receiving or have received effective antiviral treatment, the panel conditionally recommends treating them the same as the patients without this condition.
- The panel recommends that rheumatologists work with gastroenterologists and/or hepatologists who would monitor patients and reassess the appropriateness of antiviral therapy. This is important considering the recent availability of highly effective therapy for HCV, which may lead to a greater number of HCV patients being treated successfully.
- If the same patient is not requiring or receiving antiviral treatment for their hepatitis C, the panel conditionally recommends using DMARD therapy rather than TNFi.

Malignancy

- Previous Melanoma and Non-Melanoma Skin Cancer:
  - In patients with established RA and moderate or high disease activity and a history of previously treated or untreated skin cancer (melanoma or non-melanoma), the panel conditionally recommends the use of DMARD therapy over biologics or tofacitinib.
- Previous Lymphoproliferative Disorders:
  - In patients with established RA with moderate or high disease activity and a history of a previously treated lymphoproliferative disorder, the panel strongly recommends using rituximab rather than a TNFi and conditionally recommends using combination DMARD therapy, abatacept or tocilizumab rather than TNFi.
- Previous Solid Organ Cancer:
  - In patients with established RA with moderate or high disease activity and previously treated solid organ cancer, the panel conditionally recommends that they be treated for RA just as one would treat an RA patient without a history of solid organ cancer.

Serious Infections

- In patients with established RA with moderate or high disease activity and previous serious infection(s), the panel conditionally recommends using combination DMARD therapy or abatacept rather than TNFi.

Plaque Psoriasis

The American Academy of Dermatology (AAD) defines moderate to severe psoriasis as affecting more than 5% of the body surface area (BSA) or affecting crucial body areas such as the hands, feet, face, or genitals. According to the AAD Practice Guidelines for the management of psoriasis, the potential importance of TNF-α in the pathophysiology of psoriasis is underscored by the observation that there are elevated levels of TNF-α in both the affected skin and serum of patients with psoriasis. These elevated levels have a significant correlation with psoriasis severity as measured by the PASI score. Furthermore, after successful treatment of psoriasis, TNF-α levels are reduced to normal levels. The guidelines support the use of infliximab for psoriasis based on evidence ranked as consistent, good quality, and patient-oriented (Strength of Recommendation: A). [18]

Psoriatic Arthritis

The American Academy of Dermatology (AAD) defines psoriatic arthritis (PsA) as mild, moderate, or severe. Where mild disease responds to NSAIDs, moderate disease requires DMARDs or TNF blockers. Appropriate treatment of severe PsA requires DMARDs plus TNF blockers or other biologic therapies. If PsA is diagnosed, treatment should be initiated to alleviate signs and symptoms of PsA, inhibit structural damage, and maximize quality of life (QOL). According to the AAD Practice Guidelines for the management of psoriatic arthritis, the potential importance of TNF-α in the pathophysiology of PsA is underscored by the observation that there are elevated levels of TNF-α in the synovium, joint fluid, and skin of patients with PsA. The guidelines support the use of infliximab for PsA based on evidence ranked as consistent, good quality, and patient-oriented. (Strength of Recommendation: A). [16]

Ankylosing Spondylitis

Evidence based recommendations for the management of ankylosing spondylitis (AS) were created as a combined effort of the 'ASsessment in AS' international working group and the European League Against Rheumatism (EULAR). According to these comprehensive guidelines, anti-TNF treatment (infliximab, etanercept, adalimumab, and golimumab) should be given to patients with persistently high disease activity despite conventional treatments. There is no evidence to support the obligatory use of DMARDs before, or concomitant with, anti-TNF treatment in patients with axial disease. There is no evidence to support a difference in efficacy of the various TNF inhibitors on the axial and articular/entheseal disease manifestations; but in the presence of IBD a difference in gastrointestinal efficacy needs to be taken into account. Switching to a second TNF blocker might be beneficial especially in patients with loss of response. [8]

Juvenile Idiopathic Arthritis

The 2011 American College of Rheumatology (ACR) recommendations for the Treatment of Juvenile Idiopathic Arthritis include the tumor necrosis factor (TNF) inhibitors adalimumab, etanercept, infliximab and do not differentiate between the agents. [34]

For JIA patients with history of arthritis of 4 or fewer joints:

- Initiation of a TNF inhibitor was recommended for patients who have received glucocorticoids joint injections and 3 months of methotrexate at the maximum tolerated typical dose and have moderate or high disease activity and features of poor prognosis (level C).
- Initiation of a TNF inhibitor was also recommended for patients who have received glucocorticoids joint injections and 6 months of methotrexate and have high disease activity without features of poor prognosis (level C).
- Initiation of a TNF inhibitor was recommended for patients specifically with the enthesitis-related arthritis category of JIA who have received glucocorticoids joint injections and an adequate trial of sulfasalazine (without prior methotrexate) and have moderate or high disease activity, irrespective of prognostic features (level C).

For JIA patients with history of arthritis of 5 or more joints:

- Initiation of a TNF inhibitor was recommended for patients who have received methotrexate or leflunomide for 3 months at the maximum tolerated typical dose and have moderate or high disease activity, irrespective of poor prognostic features (level B).
- Initiation of a TNF inhibitor was also recommended for patients who have received methotrexate or leflunomide for 6 months and have low disease activity, irrespective of poor prognostic features (level B).
- Switching from one TNF inhibitor to another was recommended as one treatment approach for patients who have received the current TNF inhibitor for 4 months and have moderate or high disease activity, irrespective of poor prognostic features (level C).
- Switching to a TNF inhibitor was recommended as one treatment approach for patients who have received abatacept for 3 months and have high disease activity and features of poor prognosis and for patients who have

received abatacept for 6 months and have moderate or high disease activity, irrespective of prognostic features (level D).

Level of evidence "B" was assigned when the recommendation was supported by nonrandomized controlled studies (e.g., cohort and case–control studies) or extrapolations from randomized clinical trials.

Level of evidence "C" was assigned when the recommendation was supported by uncontrolled studies (case series), extrapolations from nonrandomized controlled studies, or marked extrapolations from randomized clinical trials (e.g., studies of adult arthritis patients applied to juvenile arthritis or studies of polyarthritis phenotype applied to oligoarthritis).

Noninfectious Uveitis

In 2014, a subcommittee of the Executive Committee of the American Uveitis Society conducted a systematic review of published literature and developed a guideline for the use of anti-tumor necrosis factor α (TNF-α) biologic agents in patients with ocular inflammatory disorders. There recommendations are as follows:

- Strong recommendation. Anti-TNF therapy with infliximab (good-quality evidence) or adalimumab (moderate-quality evidence) should be considered early in management of patients with vision threatening ocular manifestations of Behçet's disease.
- Strong recommendation. Anti-TNF therapy with infliximab (good-quality evidence) or adalimumab (good-quality evidence) should be considered as second-line immunomodulatory therapy for children with vision-threatening uveitis secondary to JIA in whom methotrexate therapy is insufficiently effective or not tolerated. Methotrexate therapy, if tolerated, may be combined with infliximab therapy.
- Strong recommendation. Anti-TNF therapy with infliximab or potentially adalimumab should be considered as second-line immunomodulatory therapy in patients with vision-threatening chronic uveitis from seronegative spondyloarthropathy (good- to moderate-quality evidence).
- Discretionary recommendation. Anti-TNF therapy with infliximab or adalimumab for other forms of ocular inflammation, including sarcoidosis, scleritis, and panuveitis, may be considered in patients with vision-threatening, corticosteroid-dependent disease who have failed first-line immunomodulatory therapies such as antimetabolites or calcineurin inhibitors (moderate-quality evidence). The literature for adalimumab is less developed than for infliximab, but these agents seem to show similar efficacy in most studies. Until more comparative data are available, no recommendation can be made as to preferred agent, although numerous studies have suggested that adalimumab may be effective in patients who have become intolerant to or have developed reduced clinical responsiveness to infliximab.
- Strong recommendation. Use of infliximab or adalimumab should be considered before etanercept therapy for treatment of ocular inflammatory disease. Etanercept may have efficacy for treatment of some forms of ocular inflammatory disease such as mucocutaneous Behçet's disease, but it has been associated with development of uveitis in JIA patients and development of sarcoid-like disease in others. Patients presently taking etanercept for other indications with existing, incompletely controlled uveitis or new ocular inflammatory disease should consider switching to infliximab or adalimumab if possible.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) that specifically addresses Remicade® (infliximab). Local Coverage Determinations (LCDs) exist; refer to the LCDs for Drugs and Biologicals: Infliximab (REMICADE®) and Infliximab (Remicade™).

Medicare does not have an NCD that specifically addresses INFLECTRA® (infliximab-dyyb). LCDs exist; refer to the LCDs for Drugs and Biologicals, Coverage of, for Label and Off-Label Uses.

Medicare does not have an NCD that specifically addresses RENFLEXIS™ (infliximab-abda). LCDs exist; refer to the LCDs for Drugs and Biologicals, Coverage of, for Label and Off-Label Uses.

Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf. (Accessed February 14, 2018)

STATE EXCEPTIONS

State	Note
Kansas	Drug policy not approved for use in this market

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
04/01/2018	• Updated list of applicable HCPCS codes to reflect quarterly code edits: ○ Added Q5103 and Q5104 ○ Removed Q5102 and corresponding modifiers ZB (Pfizer) and ZC (Merck) • Updated supporting information to reflect the most current clinical evidence, CMS information, and references • Archived previous policy version CS2017D0004U

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Kevzara

Program	Prior Authorization
Medication	Kevzara (sarilumab)
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Jersey, New Mexico, New York, Ohio, Pennsylvania, Rhode Island
Issue Date	10/2017
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Kevzara is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying anti-rheumatic drugs (DMARDs).

2. Coverage Criteria:

A. Initial Authorization

1. Diagnosis of moderately to severely active rheumatoid arthritis (RA)

-AND-

2. Prescribed by or in consultation with a rheumatologist

-AND-

3. History of failure, contraindication, or intolerance to one non-biologic disease modifying anti-rheumatic drug (DMARD) [e.g., Rheumatrex/Trexall (methotrexate), Arava (leflunomide), Azulfidine (sulfasalazine)]

-AND-

4. **One** of the following:

   a. History of failure, contraindication, or intolerance to **two** of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-OR-

b. For continuation of prior Kevzara therapy

-AND-

5. Patient is not receiving Kevzara in combination with any of the following:

   a. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
   b. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
   c. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. <u>Reauthorization</u>

1. Documentation of positive clinical response to Kevzara therapy

-AND-

2. Patient is not receiving Kevzara in combination with any of the following:

   a. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
   b. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
   c. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

1. Kevzara Prescribing Information, Sanofi-Aventis U.S. LLC, May 2017.

Program	Prior Authorization –Kevzara (sarilumab)
Change Control	
Date	Change
10/2017	New program

2/2018	Updated number of trial/fail products from three to two to account for PDL change effective 4/1/18.

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Kineret

Program	Prior Authorization
Medication	Kineret (anakinra)
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Mexico, New York, Rhode Island, Ohio, Pennsylvania, New Jersey
Issue Date	3/2013
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Indicated for the reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying anti-rheumatic drugs (DMARDs). Kineret can be used alone or in combination with DMARDs other than Tumor Necrosis Factor (TNF) blocking agents.

Indicated for the treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID).

Off Label Uses
Systemic Juvenile Idiopathic Arthritis
Has been used for the treatment of systemic juvenile idiopathic arthritis.

2. Coverage Criteria:

A. Rheumatoid Arthritis (RA)

1. Initial Authorization

a. Diagnosis of moderately to severely active RA

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one non-biologic disease modifying anti-rheumatic drug (DMARD) [eg, methotrexate,

leflunomide, sulfasalazine, hydroxychloroquine]

-AND-

d. Patient is not receiving Kineret in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

e. **One** of the following:

(1) Both of the following:

(a) History of failure, contraindication, or intolerance to **two** of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-AND-

(b) History of failure, contraindication, or intolerance to Kevzara (sarilumab)

-OR-

(2) For continuation of prior Kineret therapy

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Kineret therapy

-AND-

b. Patient is not receiving Kineret in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Neonatal-Onset Multisystem Inflammatory Disease (NOMID)

1. Initial Authorization

a. Diagnosis of neonatal-onset multisystem inflammatory disease (NOMID)

-AND-

b. Diagnosis of NOMID has been confirmed by one of the following:
(1) NLRP-3 (nucleotide-binding domain, leucine rich family (NLR), pyrin domain containing 3] gene (also known as Cold- Induced Auto-inflammatory Syndrome-1 [CIAS1]) mutation

-OR-

(2) Evidence of active inflammation which includes both of the following:
(a) Clinical symptoms (eg, rash, fever, arthralgia)
(b) Elevated acute phase reactants (eg, ESR, CRP)

-AND-

c. Prescribed or recommended by one of the following:
(1) Allergist/Immunologist
(2) Rheumatologist

-AND-

d. Patient is not receiving Kineret in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Kineret therapy

-AND-

b. Patient is not receiving Kineret in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Systemic Juvenile Idiopathic Arthritis (SJIA) (off-label)

1. Initial Authorization

a. Diagnosis of active systemic juvenile idiopathic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one of the following:

(1) Non-steroidal anti-inflammatory drugs (NSAIDs) [e.g., Motrin (ibuprofen), Naprosyn (naproxen)]
(2) Corticosteroids (e.g., prednisone)

-AND-

d. Patient is not receiving Kineret in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Kineret therapy

-AND-

b. Patient is not receiving Kineret in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

1. Kineret Prescribing Information. Swedish Orphan Biovitrum. November 2013.
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15. Xeljanz Prescribing Information. Pfizer. March 2014.

Program	Program type – Prior Authorization
Change Control	
Date	Change
3/2013	New Guideline
2/2015	• Removed age requirement for RA and SJIA criteria • Changed requirement of one TNF trial to two TNF trials unless the request is for a continuation of therapy. Preferred TNFs were Enbrel and Humira and are now Cimzia and Humira. • Added requirement that the patient is not receiving a biologic DMARD or JAK inhibitor for the NOMID and SJIA reauthorization criteria. This was only present previously in the initial criteria for NOMID and SJIA.
3/2016	• Added Enbrel to list of prerequisite therapy for Rheumatoid Arthritis section, initial therapy • Added diagnosis confirmation requirements and prescriber requirement to NOMID section, initial therapy • Updated policy template
10/2016	• Annual Review – no change
2/2017	• Changed Enbrel to Kineret in rheumatoid arthritis section.
3/2017	• Added Otezla to list of medications that should not be used with Kineret
4/2017	• Added hydroxychloroquine to example list of non-biologic DMARDs
2/2018	• Updated step therapy medications in the rheumatoid arthritis section to a trial of two TNF inhibitors and Kevzara due to PDL

	changes effective 4/1/18.

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Orencia

Program	Prior Authorization
Medication	Orencia (abatacept) subcutaneous
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Jersey, New Mexico, New York, Ohio, Pennsylvania, Rhode Island
Issue Date	3/2013
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Orencia (abatacept) is a selective T-cell costimulation modulator indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (RA). Orencia may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists. It is also indicated for reducing signs and symptoms in pediatric patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis (JIA). Orencia may be used as monotherapy or concomitantly with methotrexate (MTX). Orencia is also indicated for the treatment of adult patients with active psoriatic arthritis (PsA).

Orencia IV is not a pharmacy benefit for the UnitedHealthcare Community Plan

2. Coverage Criteria:

A. <u>Rheumatoid Arthritis (RA)</u>

1. **<u>Initial Authorization</u>**

a. Diagnosis of moderately to severely active rheumatoid arthritis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one non-biologic

disease modifying anti-rheumatic drug (DMARD) [egg, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine]

-AND-

d. Patient is not receiving Orencia in combination with any of the following:

(1) Biologic DMARD [egg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [egg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

e. **One** of the following:

(1) **Both** of the following:

(a) History of failure, contraindication, or intolerance to **two** of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-AND-

(b) History of failure, contraindication, or intolerance to Kevzara (sarilumab)

-OR-

(2) For continuation of prior Orencia therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Orencia therapy

-AND-

b. Patient is not receiving Orencia in combination with any of the following:

(1) Biologic DMARD [egg, Enbrel (etanercept), Humira (adalimumab),

Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [egg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Psoriatic Arthritis

1. **Initial Authorization**

a. Diagnosis of active psoriatic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist or dermatologist

-AND-

c. Patient is not receiving Orencia in combination with any of the following:
i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab)]
ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

d. One of the following:

(1) History of failure, contraindication, or intolerance to **two** of the following:

(a) Humira (adalimumab)
(b) Enbrel (etanercept)
(c) Cimzia (certolizumab pegol)

-OR-

(2) For continuation of prior Orencia therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Orencia therapy

-AND-

b. Patient is not receiving Orencia in combination with any of the following:
   i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Taltz (ixekizumab)]
   ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
   iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Juvenile Idiopathic Arthritis (JIA)

1. **Initial Authorization**

a. Diagnosis of moderately to severely active juvenile idiopathic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to one non-biologic disease modifying anti-rheumatic drug (DMARD) [egg, methotrexate, leflunomide]

-AND-

d. Patient is not receiving Orencia in combination with any of the following:

(1) Biologic DMARD [egg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [egg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

e. One of the following:

(1) History of failure, contraindication, or intolerance to both of the following:

(a) Humira (adalimumab)
(b) Enbrel (etanercept)

-OR-

(2) For continuation of prior Orencia therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Orencia therapy

-AND-

b. Patient is not receiving Orencia in combination with any of the following:

(1) Biologic DMARD [egg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [egg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

1. Orencia Prescribing Information. Bristol-Myers Squibb Company, June 2017.
2. Genovese MC, Becker JC, Schiff M, et al. Abatacept for Rheumatoid Arthritis Refractory to Tumor Necrosis Factor Inhibition. N Engl J Med. 2005. 353 (11):1114-1123.
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4. Kremer JM, Genant HK, Moreland LW, et al. Effects of abatacept in patients with methotrexate-resistant active rheumatoid arthritis: a randomized trial. Ann Intern Med. 2006 Jun 20;144(12):865-76.
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7. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995; 38(6):727-735.

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10. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011 Apr;63(4):465-82.
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14. DRUGDEX System [Internet database]. Thomson Micromedex. Updated periodically. Accessed January 9, 2014.
15. Milliman Care Guidelines. Ambulatory Care 18th Edition. Abatacept. Avaialble at: http://cgi.careguidelines.com/login-careweb.htm. Accessed September 25, 2014.

Program	Program type – Prior Authorization
Change Control	
Date	Change
3/2013	New policy
2/2015	Template updated. Orencia IV formulation and criteria removed from criteria as this drug is not available on the outpatient pharmacy benefit. Removed age requirement for all indications. Added embedded step criteria requiring trial of Humira and Cimzia, or continuation of existing Orencia therapy.
3/2016	Initial therapy section: Added Enbrel to list of preferred drugs that require history of failure, contraindication, or intolerance Updated policy template
10/2016	Annual Review – no change
3/2017	Added Otezla to list of medications not to be used with Orencia. Updated background and policy template.
4/2017	Added hydroxychloroquine to example list of non-biologic DMARDs

9/2017	Added psoriatic arthritis and juvenile idiopathic arthritis to coverage criteria. Added Otezla as a trial/fail option for psoriatic arthritis since it is now a preferred product. Updated background and references.
2/2018	Updated step therapy medications in the rheumatoid arthritis section to a trial of two TNF inhibitors and Kevzara due to PDL changes effective 4/1/18. Changed number of trial products from three to two in the psoriatic arthritis section.

ORENCIA® (ABATACEPT) INJECTION FOR INTRAVENOUS INFUSION

Policy Number: CS2018D0039J **Effective Date**: March 1, 2018

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Commercial Policy

- Orencia® (Abatacept) Injection for Intravenous Infusion

INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

This policy refers to Orencia (abatacept) injection for intravenous infusion.

Orencia is proven and medically necessary for the treatment of:

I. **Polyarticular juvenile idiopathic arthritis when ALL of the following criteria are met**:[2,5,15,20]
   A. Diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA); **and**
   B. Orencia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for polyarticular juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule):
      1. 10mg/kg every 4 weeks for patients weighing <75kg
      2. 1,000mg every 4 weeks for patients weighing ≥75kg;

      and
   C. Patient is not receiving Orencia in combination with either of the following:
      1. Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)].[18]

II. **Rheumatoid arthritis when ALL of the following criteria are met**:[1,5,15,16,21]
   A. Diagnosis of moderately to severely active rheumatoid arthritis (RA); **and**
   B. Orencia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for rheumatoid arthritis up to a maximum of (or equivalent dose and interval schedule):
      1. 500mg every 4 weeks for patients weighing <60kg
      2. 750mg every 4 weeks for patients weighing 60kg to 100kg
      3. 1,000mg every 4 weeks for patients weighing >100kg;

      and
   C. Patient is not receiving Orencia in combination with either of the following:
      1. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)].[18]

III. **Psoriatic arthritis when ALL of the following criteria are met**:
   A. Diagnosis of psoriatic arthritis (PsA); **and**
   B. Orencia is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for psoriatic arthritis up to a maximum of (or equivalent dose and interval schedule):
      1. 500mg every 4 weeks for patients weighing <60kg
      2. 750mg every 4 weeks for patients weighing 60kg to 100kg
      3. 1,000mg every 4 weeks for patients weighing >100kg;

      and
   C. Patient is not receiving Orencia in combination with any of the following:
      1. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)][18]
      3. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)].

Orencia is unproven and not medically necessary for the treatment of:
- Multiple sclerosis
- Systemic lupus erythematosus
- Graft versus host disease (GVHD)
- Uveitis associated with Behçet's disease

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Orencia is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. Orencia may be used as monotherapy or concomitantly with DMARDs other than tumor necrosis factor (TNF) antagonists.[5]

Orencia is also indicated for reducing signs and symptoms in pediatric patients 6 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis. Orencia may be used as monotherapy or concomitantly with methotrexate. Orencia is also indicated for the treatment of adult patients with active psoriatic arthritis.[5]

The labeling for Orencia states that it should not be administered concomitantly with TNF antagonists or with other biologic RA therapy, such as Kineret (anakinra), an interleukin-1 receptor antagonist. In controlled clinical trials in patients with adult RA, patients receiving concomitant Orencia and TNF antagonist therapy experienced more infections (63%) and serious infections (4.4%) compared to patients treated with only TNF antagonists (43% and 0.8%, respectively). These trials failed to demonstrate superiority of results with concomitant administration of Orencia and TNF antagonists. Therefore, clinical evidence does not support concurrent therapy with Orencia and TNF antagonists.[5]

BACKGROUND

Orencia is a fully human, soluble, fusion protein, selective co-stimulation modulator which inhibits T lymphocyte activation by binding to CD80 and CD86, thereby blocking interaction with CD28.[6,7] This interaction provides a costimulatory signal necessary for full activation of T lymphocytes.[5]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J0129	Injection, abatacept, 10 mg

ICD-10 Diagnosis Code	Description
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis
L40.54	Psoriatic juvenile arthropathy
L40.59	Other psoriatic arthropathy
M05.00	Felty's syndrome, unspecified site
M05.011	Felty's syndrome, right shoulder
M05.012	Felty's syndrome, left shoulder
M05.019	Felty's syndrome, unspecified shoulder
M05.021	Felty's syndrome, right elbow
M05.022	Felty's syndrome, left elbow
M05.029	Felty's syndrome, unspecified elbow
M05.031	Felty's syndrome, right wrist
M05.032	Felty's syndrome, left wrist
M05.039	Felty's syndrome, unspecified wrist
M05.041	Felty's syndrome, right hand
M05.042	Felty's syndrome, left hand
M05.049	Felty's syndrome, unspecified hand
M05.051	Felty's syndrome, right hip
M05.052	Felty's syndrome, left hip
M05.059	Felty's syndrome, unspecified hip
M05.061	Felty's syndrome, right knee
M05.062	Felty's syndrome, left knee
M05.069	Felty's syndrome, unspecified knee
M05.071	Felty's syndrome, right ankle and foot
M05.072	Felty's syndrome, left ankle and foot
M05.079	Felty's syndrome, unspecified ankle and foot
M05.09	Felty's syndrome, multiple sites
M05.20	Rheumatoid vasculitis with rheumatoid arthritis of unspecified site
M05.211	Rheumatoid vasculitis with rheumatoid arthritis of right shoulder
M05.212	Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.219	Rheumatoid vasculitis with rheumatoid arthritis of unspecified shoulder
M05.221	Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222	Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.229	Rheumatoid vasculitis with rheumatoid arthritis of unspecified elbow
M05.231	Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232	Rheumatoid vasculitis with rheumatoid arthritis of left wrist

ICD-10 Diagnosis Code	Description
M05.239	Rheumatoid vasculitis with rheumatoid arthritis of unspecified wrist
M05.241	Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242	Rheumatoid vasculitis with rheumatoid arthritis of left hand
M05.249	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hand
M05.251	Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252	Rheumatoid vasculitis with rheumatoid arthritis of left hip
M05.259	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hip
M05.261	Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262	Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.269	Rheumatoid vasculitis with rheumatoid arthritis of unspecified knee
M05.271	Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272	Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot
M05.279	Rheumatoid vasculitis with rheumatoid arthritis of unspecified ankle and foot
M05.29	Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.30	Rheumatoid heart disease with rheumatoid arthritis of unspecified site
M05.311	Rheumatoid heart disease with rheumatoid arthritis of right shoulder
M05.312	Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.319	Rheumatoid heart disease with rheumatoid arthritis of unspecified shoulder
M05.321	Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322	Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.329	Rheumatoid heart disease with rheumatoid arthritis of unspecified elbow
M05.331	Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332	Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.339	Rheumatoid heart disease with rheumatoid arthritis of unspecified wrist
M05.341	Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342	Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.349	Rheumatoid heart disease with rheumatoid arthritis of unspecified hand
M05.351	Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352	Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.359	Rheumatoid heart disease with rheumatoid arthritis of unspecified hip
M05.361	Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362	Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.369	Rheumatoid heart disease with rheumatoid arthritis of unspecified knee
M05.371	Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372	Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.379	Rheumatoid heart disease with rheumatoid arthritis of unspecified ankle and foot
M05.39	Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.40	Rheumatoid myopathy with rheumatoid arthritis of unspecified site
M05.411	Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412	Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.419	Rheumatoid myopathy with rheumatoid arthritis of unspecified shoulder
M05.421	Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422	Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.429	Rheumatoid myopathy with rheumatoid arthritis of unspecified elbow
M05.431	Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432	Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.439	Rheumatoid myopathy with rheumatoid arthritis of unspecified wrist

ICD-10 Diagnosis Code	Description
M05.441	Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442	Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.449	Rheumatoid myopathy with rheumatoid arthritis of unspecified hand
M05.451	Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452	Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.459	Rheumatoid myopathy with rheumatoid arthritis of unspecified hip
M05.461	Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462	Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.469	Rheumatoid myopathy with rheumatoid arthritis of unspecified knee
M05.471	Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472	Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.479	Rheumatoid myopathy with rheumatoid arthritis of unspecified ankle and foot
M05.49	Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.50	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site
M05.511	Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512	Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder
M05.519	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified shoulder
M05.521	Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522	Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow
M05.529	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified elbow
M05.531	Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532	Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.539	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.549	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.559	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.569	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot
M05.579	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.60	Rheumatoid arthritis of unspecified site with involvement of other organs and systems
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.619	Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.629	Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems

ICD-10 Diagnosis Code	Description
M05.639	Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.649	Rheumatoid arthritis of unspecified hand with involvement of other organs and systems
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.659	Rheumatoid arthritis of unspecified hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems
M05.669	Rheumatoid arthritis of unspecified knee with involvement of other organs and systems
M05.671	Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672	Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems
M05.679	Rheumatoid arthritis of unspecified ankle and foot with involvement of other organs and systems
M05.69	Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.70	Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement
M05.711	Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712	Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.719	Rheumatoid arthritis with rheumatoid factor of unspecified shoulder without organ or systems involvement
M05.721	Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722	Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.729	Rheumatoid arthritis with rheumatoid factor of unspecified elbow without organ or systems involvement
M05.731	Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732	Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement
M05.739	Rheumatoid arthritis with rheumatoid factor of unspecified wrist without organ or systems involvement
M05.741	Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742	Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.749	Rheumatoid arthritis with rheumatoid factor of unspecified hand without organ or systems involvement
M05.751	Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752	Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.759	Rheumatoid arthritis with rheumatoid factor of unspecified hip without organ or systems involvement

ICD-10 Diagnosis Code	Description
M05.761	Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762	Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement
M05.769	Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement
M05.771	Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement
M05.772	Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement
M05.779	Rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot without organ or systems involvement
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M05.80	Other rheumatoid arthritis with rheumatoid factor of unspecified site
M05.811	Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812	Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.819	Other rheumatoid arthritis with rheumatoid factor of unspecified shoulder
M05.821	Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822	Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.829	Other rheumatoid arthritis with rheumatoid factor of unspecified elbow
M05.831	Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832	Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.839	Other rheumatoid arthritis with rheumatoid factor of unspecified wrist
M05.841	Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842	Other rheumatoid arthritis with rheumatoid factor of left hand
M05.849	Other rheumatoid arthritis with rheumatoid factor of unspecified hand
M05.851	Other rheumatoid arthritis with rheumatoid factor of right hip
M05.852	Other rheumatoid arthritis with rheumatoid factor of left hip
M05.859	Other rheumatoid arthritis with rheumatoid factor of unspecified hip
M05.861	Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862	Other rheumatoid arthritis with rheumatoid factor of left knee
M05.869	Other rheumatoid arthritis with rheumatoid factor of unspecified knee
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.879	Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00	Rheumatoid arthritis without rheumatoid factor, unspecified site
M06.011	Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012	Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.019	Rheumatoid arthritis without rheumatoid factor, unspecified shoulder
M06.021	Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022	Rheumatoid arthritis without rheumatoid factor, left elbow
M06.029	Rheumatoid arthritis without rheumatoid factor, unspecified elbow
M06.031	Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032	Rheumatoid arthritis without rheumatoid factor, left wrist
M06.039	Rheumatoid arthritis without rheumatoid factor, unspecified wrist
M06.041	Rheumatoid arthritis without rheumatoid factor, right hand

ICD-10 Diagnosis Code	Description
M06.042	Rheumatoid arthritis without rheumatoid factor, left hand
M06.049	Rheumatoid arthritis without rheumatoid factor, unspecified hand
M06.051	Rheumatoid arthritis without rheumatoid factor, right hip
M06.052	Rheumatoid arthritis without rheumatoid factor, left hip
M06.059	Rheumatoid arthritis without rheumatoid factor, unspecified hip
M06.061	Rheumatoid arthritis without rheumatoid factor, right knee
M06.062	Rheumatoid arthritis without rheumatoid factor, left knee
M06.069	Rheumatoid arthritis without rheumatoid factor, unspecified knee
M06.071	Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072	Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.079	Rheumatoid arthritis without rheumatoid factor, unspecified ankle and foot
M06.08	Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.1	Adult-onset Still's disease
M06.80	Other specified rheumatoid arthritis, unspecified site
M06.811	Other specified rheumatoid arthritis, right shoulder
M06.812	Other specified rheumatoid arthritis, left shoulder
M06.819	Other specified rheumatoid arthritis, unspecified shoulder
M06.821	Other specified rheumatoid arthritis, right elbow
M06.822	Other specified rheumatoid arthritis, left elbow
M06.829	Other specified rheumatoid arthritis, unspecified elbow
M06.831	Other specified rheumatoid arthritis, right wrist
M06.832	Other specified rheumatoid arthritis, left wrist
M06.839	Other specified rheumatoid arthritis, unspecified wrist
M06.841	Other specified rheumatoid arthritis, right hand
M06.842	Other specified rheumatoid arthritis, left hand
M06.849	Other specified rheumatoid arthritis, unspecified hand
M06.851	Other specified rheumatoid arthritis, right hip
M06.852	Other specified rheumatoid arthritis, left hip
M06.859	Other specified rheumatoid arthritis, unspecified hip
M06.861	Other specified rheumatoid arthritis, right knee
M06.862	Other specified rheumatoid arthritis, left knee
M06.869	Other specified rheumatoid arthritis, unspecified knee
M06.871	Other specified rheumatoid arthritis, right ankle and foot
M06.872	Other specified rheumatoid arthritis, left ankle and foot
M06.879	Other specified rheumatoid arthritis, unspecified ankle and foot
M06.88	Other specified rheumatoid arthritis, vertebrae
M06.89	Other specified rheumatoid arthritis, multiple sites
M06.9	Rheumatoid arthritis, unspecified
M08.00	Unspecified juvenile rheumatoid arthritis of unspecified site
M08.011	Unspecified juvenile rheumatoid arthritis, right shoulder
M08.012	Unspecified juvenile rheumatoid arthritis, left shoulder
M08.019	Unspecified juvenile rheumatoid arthritis, unspecified shoulder
M08.021	Unspecified juvenile rheumatoid arthritis, right elbow
M08.022	Unspecified juvenile rheumatoid arthritis, left elbow
M08.029	Unspecified juvenile rheumatoid arthritis, unspecified elbow
M08.031	Unspecified juvenile rheumatoid arthritis, right wrist

ICD-10 Diagnosis Code	Description
M08.032	Unspecified juvenile rheumatoid arthritis, left wrist
M08.039	Unspecified juvenile rheumatoid arthritis, unspecified wrist
M08.041	Unspecified juvenile rheumatoid arthritis, right hand
M08.042	Unspecified juvenile rheumatoid arthritis, left hand
M08.049	Unspecified juvenile rheumatoid arthritis, unspecified hand
M08.051	Unspecified juvenile rheumatoid arthritis, right hip
M08.052	Unspecified juvenile rheumatoid arthritis, left hip
M08.059	Unspecified juvenile rheumatoid arthritis, unspecified hip
M08.061	Unspecified juvenile rheumatoid arthritis, right knee
M08.062	Unspecified juvenile rheumatoid arthritis, left knee
M08.069	Unspecified juvenile rheumatoid arthritis, unspecified knee
M08.071	Unspecified juvenile rheumatoid arthritis, right ankle and foot
M08.072	Unspecified juvenile rheumatoid arthritis, left ankle and foot
M08.079	Unspecified juvenile rheumatoid arthritis, unspecified ankle and foot
M08.08	Unspecified juvenile rheumatoid arthritis, vertebrae
M08.09	Unspecified juvenile rheumatoid arthritis, multiple sites
M08.20	Juvenile rheumatoid arthritis with systemic onset, unspecified site
M08.211	Juvenile rheumatoid arthritis with systemic onset, right shoulder
M08.212	Juvenile rheumatoid arthritis with systemic onset, left shoulder
M08.219	Juvenile rheumatoid arthritis with systemic onset, unspecified shoulder
M08.221	Juvenile rheumatoid arthritis with systemic onset, right elbow
M08.222	Juvenile rheumatoid arthritis with systemic onset, left elbow
M08.229	Juvenile rheumatoid arthritis with systemic onset, unspecified elbow
M08.231	Juvenile rheumatoid arthritis with systemic onset, right wrist
M08.232	Juvenile rheumatoid arthritis with systemic onset, left wrist
M08.239	Juvenile rheumatoid arthritis with systemic onset, unspecified wrist
M08.241	Juvenile rheumatoid arthritis with systemic onset, right hand
M08.242	Juvenile rheumatoid arthritis with systemic onset, left hand
M08.249	Juvenile rheumatoid arthritis with systemic onset, unspecified hand
M08.251	Juvenile rheumatoid arthritis with systemic onset, right hip
M08.252	Juvenile rheumatoid arthritis with systemic onset, left hip
M08.259	Juvenile rheumatoid arthritis with systemic onset, unspecified hip
M08.261	Juvenile rheumatoid arthritis with systemic onset, right knee
M08.262	Juvenile rheumatoid arthritis with systemic onset, left knee
M08.269	Juvenile rheumatoid arthritis with systemic onset, unspecified knee
M08.271	Juvenile rheumatoid arthritis with systemic onset, right ankle and foot
M08.272	Juvenile rheumatoid arthritis with systemic onset, left ankle and foot
M08.279	Juvenile rheumatoid arthritis with systemic onset, unspecified ankle and foot
M08.28	Juvenile rheumatoid arthritis with systemic onset, vertebrae
M08.29	Juvenile rheumatoid arthritis with systemic onset, multiple sites
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.80	Other juvenile arthritis, unspecified site
M08.811	Other juvenile arthritis, right shoulder
M08.812	Other juvenile arthritis, left shoulder
M08.819	Other juvenile arthritis, unspecified shoulder
M08.821	Other juvenile arthritis, right elbow
M08.822	Other juvenile arthritis, left elbow

ICD-10 Diagnosis Code	Description
M08.829	Other juvenile arthritis, unspecified elbow
M08.831	Other juvenile arthritis, right wrist
M08.832	Other juvenile arthritis, left wrist
M08.839	Other juvenile arthritis, unspecified wrist
M08.841	Other juvenile arthritis, right hand
M08.842	Other juvenile arthritis, left hand
M08.849	Other juvenile arthritis, unspecified hand
M08.851	Other juvenile arthritis, right hip
M08.852	Other juvenile arthritis, left hip
M08.859	Other juvenile arthritis, unspecified hip
M08.861	Other juvenile arthritis, right knee
M08.862	Other juvenile arthritis, left knee
M08.869	Other juvenile arthritis, unspecified knee
M08.871	Other juvenile arthritis, right ankle and foot
M08.872	Other juvenile arthritis, left ankle and foot
M08.879	Other juvenile arthritis, unspecified ankle and foot
M08.88	Other juvenile arthritis, vertebrae
M08.89	Other juvenile arthritis, multiple sites
M08.90	Juvenile arthritis, unspecified, unspecified site
M08.911	Juvenile arthritis, unspecified, right shoulder
M08.912	Juvenile arthritis, unspecified, left shoulder
M08.919	Juvenile arthritis, unspecified, unspecified shoulder
M08.921	Juvenile arthritis, unspecified, right elbow
M08.922	Juvenile arthritis, unspecified, left elbow
M08.929	Juvenile arthritis, unspecified, unspecified elbow
M08.931	Juvenile arthritis, unspecified, right wrist
M08.932	Juvenile arthritis, unspecified, left wrist
M08.939	Juvenile arthritis, unspecified, unspecified wrist
M08.941	Juvenile arthritis, unspecified, right hand
M08.942	Juvenile arthritis, unspecified, left hand
M08.949	Juvenile arthritis, unspecified, unspecified hand
M08.951	Juvenile arthritis, unspecified, right hip
M08.952	Juvenile arthritis, unspecified, left hip
M08.959	Juvenile arthritis, unspecified, unspecified hip
M08.961	Juvenile arthritis, unspecified, right knee
M08.962	Juvenile arthritis, unspecified, left knee
M08.969	Juvenile arthritis, unspecified, unspecified knee
M08.971	Juvenile arthritis, unspecified, right ankle and foot
M08.972	Juvenile arthritis, unspecified, left ankle and foot
M08.979	Juvenile arthritis, unspecified, unspecified ankle and foot
M08.98	Juvenile arthritis, unspecified, vertebrae
M08.99	Juvenile arthritis, unspecified, multiple sites

Proven

Psoriatic Arthritis

A randomized, placebo controlled Phase 3 trial assessed the efficacy and safety of abatacept in adult patients (>18 years old) with psoriatic arthritis. Patients were randomly assigned in a double-blind manner to receive either subcutaneous abatacept 125mg weekly or placebo for 24 weeks. Patients who had not achieved ≥ 20% improvement in swollen and tender joint counts from baseline to week 16 were switched to open-label abatacept weekly for 28 weeks. At the end of the open-label period, patients had the option of entering a 1 year, long-term extension. Primary efficacy endpoint was the proportion of patients with ACR20 responses at week 24. Abatacept significantly increased ACR20 response versus placebo at week 24 (39.4% vs 22.3%; p<0.001). Although abatacept numerically increased Health Assessment Questionnaire−Disability Index response rates (reduction from baseline ≥0.35) at week 24, this was not statistically significant (31.0% vs 23.7%; p=0.097). The benefits of abatacept were seen in ACR20 responses regardless of TNF inhibitor exposure and in other musculoskeletal manifestations, but significance could not be attributed due to ranking below Health Assessment Questionnaire−Disability Index response in hierarchical testing. The benefit on psoriasis lesions was modest. Efficacy was maintained or improved up to week 52. Abatacept was well tolerated with no new safety signals. The authors concluded that abatacept treatment of PsA in achieved its primary end point, ACR20 response, showed beneficial trends overall in musculoskeletal manifestations and was well tolerated. There was only a modest impact on psoriasis lesions.

Rheumatoid Arthritis

A randomized, multicenter, active controlled Phase 3b trial, the Assessing Very Early Rheumatoid arthritis Treatment (AVERT) trial (n=351) of 24 months, with a 12-month, double-blind treatment period, evaluated clinical remission with subcutaneous abatacept plus methotrexate (MTX) and abatacept monotherapy in patients with early rheumatoid arthritis (RA), and maintenance of remission following the rapid withdrawal of all RA treatment.[17] During the 12 month treatment period, patients were randomized (1:1:1) to receive abatacept plus MTX (n=119), abatacept monotherapy (n=116), or MTX monotherapy (n=116), stratified by corticosteroid use at baseline. Patients with a Disease Activity Score (DAS)28 (CRP) <3.2 at month 12 could enter the 12 month withdrawal period where abatacept was immediately stopped and MTX and steroids tapered over 1 month. Patients with DAS28 ≥ 3.2 discontinued the study. After month 15, patients in the withdrawal period who experienced a flare could re-start open label SC abatacept 125mg plus MTX. Co-primary endpoints were the proportion of randomized and treated patients in DAS-defined remission (CRP <2.6) at month 12 and months 12 and 18 for abatacept plus MTX versus MTX. For the abatacept plus MTX versus MTX, DAS28 (CRP) < 2.6 was achieved in 60.9% versus 45.2% (p=0.010) at 12 months, and following treatment withdrawal, in 14.8% versus 7.8% (p=0.045) at both 12 and 18 months. DAS28 (CRP) <2.6 was achieved for abatacept monotherapy in 42.5% (month 12) and 12.45% (both months 12 and 18). Both abatacept arms had a safety profile comparable to MTX alone. The authors concluded that abatacept plus MTX demonstrated efficacy compared with MTX alone in early RA, with a comparable safety profile to MTX. Abatacept achieved some sustained remission following withdrawal of all RA therapy in the respective groups.

Polyarticular Juvenile Idiopathic Arthritis

The long-term extension (LTE) phase of a pivotal phase III study examining the efficacy and safety of abatacept in patients with juvenile idiopathic arthritis (JIA) reported the efficacy and safety outcomes of treatment (up to 10mg/kg every 4 weeks), with or without non-biologic DMARDs, for up to 7 years of follow-up.[19] One hundred fifty-three of 190 patients (80.5%) entered the LTE phase, with only 69 patients (36.3%) completing the study. The overall incidence rate (events per 100 patient-years) of adverse events decreased from 433.61 events during the short-term phase compared to 132.39 events during the LTE phase. Serious adverse events (6.82 vs. 5.60), malignancies (1.12 vs. 0), and autoimmune events (2.26 vs. 1.18) also were reduced. Serious infections were slightly increased (1.13 vs. 1.72). American College of Rheumatology (ACR) Pediatric 30 (Pedi 30), Pedi 70, responses, and clinically inactive disease status were maintained throughout the extension phase in those patients continuing to receive therapy. Improvements in the Child Health Questionnaire summary scores were also maintained over the course of the study. The authors concluded that long-term abatacept therapy, for up to 7 years, was associated with consistent safety, efficacy, and quality of life benefits in patients with JIA.

Unproven

Multiple Sclerosis

A randomized, double-blind, placebo-controlled Phase II study of 128 patients was initiated to evaluate the use of abatacept in patients with relapsing-remitting multiple sclerosis.[8] The primary objective was to demonstrate the relative safety and preliminary clinical efficacy of 2 different doses of abatacept (10 mg/kg and 2 mg/kg) compared with placebo in subjects with relapsing-remitting MS by showing a reduction in the cumulative number of new or recurrent gadolinium-enhancing lesions on T1-weighted (Gd-T1) magnetic resonance imaging (MRI) over Day 85 through Day 225. However, the study terminated early because the Drug Safety Monitoring Board (DSMB) responsible for reviewing blinded safety data from the study expressed concerns that one of the treatment groups (subsequently

found to be the 2 mg/kg abatacept group) had more subjects exhibiting an increase in Gd-enhancing T1-weighted MRI lesions and at least 1 multiple sclerosis exacerbation.

Systemic Lupus Erythematosus

A Phase II multi-center, randomized, double-blind, placebo-controlled study was conducted to evaluate the efficacy and safety of abatacept (n=121) versus placebo (n=59) for patients with systemic lupus erythematosus (SLE).[9] The abatacept group received the study drug (weight-tiered dosing) administered intravenously on Day 1, 15, 29, and every 28 days thereafter. Planned treatment duration for the double-blind period was 12 months. Prednisone or prednisone equivalent oral tablets was given on a defined tapering schedule at the time of randomization along with the study medication or placebo. The study failed to meet the primary efficacy endpoint, which was to assess the proportion of subjects who experienced a new SLE flare, based on adjudication of all BILAG 'A' or 'B' events, following resolution of the entry flare and/or the start of prednisone or prednisone equivalent taper schedule across the 12-month double-blind treatment period.

Graft Versus Host Disease (GVHD), Psoriatic Arthropathy, and Uveitis Associated with Behçet's Disease

Blockade of antigen non-specific co-stimulatory signals is theorized to be effective for conditions such as GVHD,[10,11] psoriatic arthropathy,[12] and Behçet's disease.[13,14] However, there is currently insufficient clinical evidence of the safety and efficacy of abatacept in published peer-reviewed medical literature for these conditions.

Professional Societies

Rheumatoid Arthritis

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDs, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (≥ 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs.[21] The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions. Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

Supplementary Appendix 5, of the 2015 ACR RA guideline, summarizes recommendations for patients with early RA, established RA, and high-risk comorbidities:[21]

Recommendations for Early RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, another target may be chosen because risk tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with early, symptomatic RA, the panel strongly recommends DMARD monotherapy over double or triple DMARD therapy in patients with low disease activity and conditionally recommends DMARD monotherapy over double or triple DMARD therapy in patients with moderate or high disease activity. Methotrexate should be the preferred initial therapy for most patients with early RA with active disease.
- For patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids), the panel strongly recommends treatment with a combination of DMARDs or a TNFi or a non-TNF biologic, with or without methotrexate (MTX) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to superior efficacy.
- For patients with moderate or high disease activity despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids (defined as ≤10 mg/day of prednisone or equivalent). Low-dose glucocorticoids may also be used in patients who need a bridge until realizing the benefits of DMARD therapy. The risk/benefit ratio of glucocorticoid therapy is favorable as long as the dose is low and the duration of therapy is short.
- For patients experiencing a flare of RA, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose for the shortest possible duration, to provide a favorable benefit-risk ratio for the patient.

Recommendations for Established RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, however, another target may be chosen because tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with low disease activity, the panel strongly recommends using DMARD monotherapy over a TNFi. For DMARD-naïve patients with moderate or high disease activity, the panel conditionally recommends DMARD monotherapy over double or triple DMARD therapy and DMARD monotherapy over tofacitinib. In general, MTX should be the preferred initial therapy for most patients with established RA with active disease.
- For patients with moderate or high disease activity despite DMARD monotherapy including methotrexate, the panel strongly recommends using combination DMARDs or adding a TNFi or a non-TNF biologic or tofacitinib (all choices with or without methotrexate) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to its superior efficacy.

For all scenarios for established RA below, treatment may be with or without MTX:

- For moderate or high disease activity despite TNFi therapy in patients currently not on a DMARD, the panel strongly recommends that one or two DMARDs be added to TNFi therapy rather than continuing TNFi therapy alone.
- If disease activity is moderate or high despite single TNFi biologic therapy, the panel conditionally recommends using a non-TNF biologic.
- If disease activity is moderate or high despite non-TNF biologic therapy, the panel conditionally recommends using another non-TNF biologic. However, if a patient has failed multiple non-TNF biologics and they are TNFi-naïve with moderate or high disease activity, the panel conditionally recommends treatment with a TNFi.
- For patients with moderate or high disease activity despite prior treatment with at least one TNFi and at least one non-TNF-biologic (sequentially, not combined), the panel conditionally recommends first treating with another non-TNF biologic. However, when a non-TNF biologic is not an option (e.g., patient declines non-TNF biologic therapy due to inefficacy or side effects), the panel conditionally recommends treatment with tofacitinib.
- If disease activity is moderate or high despite the use of multiple (2+) TNFi therapies (in sequence, not concurrently), the panel conditionally recommends non-TNF biologic therapy and then conditionally treating with tofacitinib when a non-TNF biologic is not an option.
- If disease activity is moderate or high despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids.
- If patients with established RA experience an RA flare while on DMARD, TNFi, or non-TNF biologic therapy, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose and for shortest possible duration to provide the best benefit-risk ratio for the patient.
- In patients with established RA and low disease activity but not remission, the panel strongly recommends continuing DMARD therapy, TNFi, non-TNF biologic or tofacitinib rather than discontinuing respective medication.
- In patients with established RA currently in remission, the panel conditionally recommends tapering DMARD therapy, TNFi, non-TNF biologic, or tofacitinib.
- The panel strongly recommends not discontinuing all therapies in patients with established RA in disease remission.

Recommendations for RA Patients with High-Risk Comorbidities

- Congestive Heart Failure:
  - In patients with established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF), the panel conditionally recommends using combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a TNFi.
  - If patients in this population are treated with a TNFi and their CHF worsens while on the TNFi, the panel conditionally recommends switching to combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a different TNFi.
- Hepatitis B:
  - In patients with established RA with moderate or high disease activity and evidence of active hepatitis B infection (hepatitis surface antigen positive > 6 months), who are receiving or have received effective antiviral treatment, the panel strongly recommends treating them the same as patients without this condition.
  - For a patient with natural immunity from prior exposure to hepatitis B (i.e., HB core antibody and HBS antibody positive and normal liver function tests), the panel recommends the same therapies as those without such findings as long as the patient's viral load is monitored.
  - For patients with chronic hepatitis B who are untreated, referral for antiviral therapy is appropriate prior to immunosuppressive therapy.

- Hepatitis C:
  - In patients with established RA with moderate or high disease activity and evidence of chronic hepatitis C virus (HCV) infection, who are receiving or have received effective antiviral treatment, the panel conditionally recommends treating them the same as the patients without this condition.
  - The panel recommends that rheumatologists work with gastroenterologists and/or hepatologists who would monitor patients and reassess the appropriateness of antiviral therapy. This is important considering the recent availability of highly effective therapy for HCV, which may lead to a greater number of HCV patients being treated successfully.
  - If the same patient is not requiring or receiving antiviral treatment for their hepatitis C, the panel conditionally recommends using DMARD therapy rather than TNFi.
- Malignancy:
  - Previous Melanoma and Non-Melanoma Skin Cancer:
    - In patients with established RA and moderate or high disease activity and a history of previously treated or untreated skin cancer (melanoma or non-melanoma), the panel conditionally recommends the use of DMARD therapy over biologics or tofacitinib.
  - Previous Lymphoproliferative Disorders:
    - In patients with established RA with moderate or high disease activity and a history of a previously treated lymphoproliferative disorder, the panel strongly recommends using rituximab rather than a TNFi and conditionally recommends using combination DMARD therapy, abatacept or tocilizumab rather than TNFi.
  - Previous Solid Organ Cancer:
    - In patients with established RA with moderate or high disease activity and previously treated solid organ cancer, the panel conditionally recommends that they be treated for RA just as one would treat an RA patient without a history of solid organ cancer.
- Serious Infections:
  - In patients with established RA with moderate or high disease activity and previous serious infection(s), the panel conditionally recommends using combination DMARD therapy or abatacept rather than TNFi.

Juvenile Idiopathic Arthritis

The 2011 American College of Rheumatology (ACR) recommendations for the treatment of Juvenile Idiopathic Arthritis include abatacept.[2]

- For JIA patients with history of arthritis of 5 or more joints:
  - Initiation of abatacept was recommended as one treatment approach for patients who have received a TNFα inhibitor for 4 months and have high disease activity, irrespective of features of poor prognosis, or moderate disease activity and features of poor prognosis (level B).
  - Initiation of abatacept was recommended as one treatment approach for patients who have received more than one TNFα inhibitor sequentially and have moderate or high disease activity, irrespective of poor prognostic features, or low disease activity with features of poor prognosis (level B).
- For JIA patients with systemic arthritis with active arthritis (and without active systemic features):
  - Initiation of abatacept was recommended for patients who have received methotrexate and a TNFα inhibitor and have high disease activity, irrespective of features of poor prognosis, or have moderate disease activity and poor prognostic features (level B)

The 2013 update to the 2011 ACR recommendations includes the use of abatacept in those patients with systemic JIA with continued disease activity and synovitis.[20]

- For patients with systemic JIA with active systemic features and varying degrees of synovitis:
  - Use of abatacept was recommended only for patients with an MD global ≥5 and an AJC >4 after a trial of both an interleukin-1 (IL-1) inhibitor and tocilizumab (sequentially) (level D). Use of abatacept for patients with an AJC of 0 irrespective of the MD global was inappropriate (level D), with the exception of patients who had tried both an IL-1 inhibitor and tocilizumab (sequentially), in which case it was uncertain. Use of abatacept for patients with an MD global <5 and an AJC >0 or an MD global ≥5 and an AJC <4 was inappropriate (level D), with the exception of patients who had tried both an IL-1 inhibitor and tocilizumab (sequentially) or a disease-modifying antirheumatic drug (DMARD) plus either an IL-1 inhibitor or tocilizumab, in which case it was uncertain. Use of abatacept for patients with an MD global ≥5 and an AJC >4 was inappropriate (level D), with the exception of patients who had tried both an IL-1 inhibitor and tocilizumab (sequentially), in which case it was appropriate (level D), or patients who had tried a DMARD plus either an IL-1 inhibitor or tocilizumab, in which case it was uncertain.
- For patients with systemic JIA without active systemic features and varying degrees of active synovitis:
  - Use of abatacept was recommended for patients with an AJC >0 after treatment with MTX or leflunomide (level B), anakinra (level D), or tocilizumab (level D).
- For patients with systemic JIA with features concerning for Macrophage Activation Syndrome (MAS)
  - Initiation of abatacept was inappropriate (level D).

Level of evidence "B" was assigned when the recommendation was supported by nonrandomized controlled studies (e.g., cohort and case–control studies) or extrapolations from randomized clinical trials.

Level of evidence "C" was assigned when the recommendation was supported by uncontrolled studies (case series), extrapolations from nonrandomized controlled studies, or marked extrapolations from randomized clinical trials (e.g., studies of adult arthritis patients applied to juvenile arthritis or studies of polyarthritis phenotype applied to oligoarthritis).

Level of evidence "D" was assigned when the recommendation was based upon expert opinion.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) that addresses Orencia® (abatacept). Local Coverage Determinations (LCDs) exist; refer to the LCDs for Abatacept.

Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals.
(Accessed January 5, 2018)

STATE EXCEPTIONS

State	Note
Kansas	Drug policy not approved for use in this market

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
03/01/2018	• Updated supporting information to reflect the most current CMS information; no change to coverage rationale or lists of applicable codes • Archived previous policy version CS2017D0039I

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Siliq

Program	Prior Authorization
Medication	Siliq (brodalumab)
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Mexico, New York, Ohio, Rhode Island
Issue Date	5/2017
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Siliq (brodalumab) is a human interleukin-17A receptor antagonist indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies.

2. Coverage Criteria:

A. Plaque Psoriasis

1. **Initial Authorization**

a. **Siliq** will be approved based on one of the following criteria:

(1) Submission of medical records (e.g., chart notes, laboratory values, prescription claims history) documenting **all** of the following:

(a) Diagnosis of chronic moderate to severe plaque psoriasis

-AND-

(b) Greater than or equal to 5% body surface area involvement, palmoplantar, facial, or genital involvement, or severe scalp psoriasis

-AND-

(c) History of failure, contraindication, or intolerance to **both** of the following conventional therapies:

i. Topical therapy with **one** of the following:

- Corticosteroids (e.g., betamethasone, clobetasol, desonide)
- Vitamin D analogs (e.g., calcitriol, calcipotriene)
- Tazarotene
- Calcineurin inhibitors (e.g., tacrolimus, pimecrolimus)
- Anthralin
- Coal tar

-AND-

ii. Systemic therapy of at least 3 months duration with methotrexate

-AND-

(d) History of failure, contraindication, or intolerance to **both** of the following preferred biologic products (document drug, date, and duration of trial):

i. Humira (adalimumab)
ii. Enbrel (etanercept)

-AND-

(e) **One** of the following (document drug, date, and duration of trial):

i. History of 6 month trial of Cosentyx (secukinumab) with moderate clinical response yet residual disease activity

-OR-

ii. **Both** of the following:

- History of intolerance or adverse event to Cosentyx
- Physician attests that in their clinical opinion the same intolerance or adverse event would not be expected to occur with Siliq

-AND-

(f) Patient is not receiving Siliq in combination with any of the following:

i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Cosentyx (secukinumab), Orencia (abatacept)]
ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-OR-

(2) **Both** of the following:

(a) Patient is currently on Siliq therapy

-AND-

(b) Patient is not receiving Siliq in combination with any of the following:

i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Cosentyx (secukinumab), Orencia (abatacept)]
ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Siliq** will be approved based on **both** of the following criteria:

(1) Documentation of positive clinical response to Siliq therapy

-AND-

(2) Patient is not receiving Siliq in combination with **any** of the following:

i. Biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Cosentyx (secukinumab), Orencia (abatacept)]
ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

UnitedHealthcare Community Plan

Authorization will be issued for 12 months.

3. References:

1. Siliq Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; February 2017.
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Program	Prior Authorization –Siliq (brodalumab)
Change Control	
Date	Change
5/2017	New program
9/2017	Updated preferred biologic products to include Otezla
2/2018	Removed Otezla as a step therapy medication

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Simponi

Program	Prior Authorization
Medication	Simponi (golimumab) subcutaneous
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Jersey, New Mexico, New York, Ohio, Pennsylvania, Rhode Island
Issue Date	2/2015
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Simponi (golimumab) is a tumor necrosis factor (TNF) blocker, indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis in combination with methotrexate. Simponi, alone or in combination with methotrexate, is indicated for the treatment of adult patients with active psoriatic arthritis. It is also indicated for the treatment of adult patients with active ankylosing spondylitis. Simponi is also indicated in adult patients with moderately to severely active ulcerative colitis who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine. For ulcerative colitis, it is indicated for inducing and maintaining clinical response, improving endoscopic appearance of the mucosa during induction, inducing clinical remission, and achieving and sustaining clinical remission in induction responders. An intravenous formulation of golimumab, Simponi Aria™, is also available. It is only indicated for adult patients with moderately to severely active rheumatoid arthritis.

Simponi Aria (IV) is not a pharmacy benefit for the UnitedHealthcare Community Plan

2. Coverage Criteria:

A. <u>Rheumatoid Arthritis (RA)</u>

1. **<u>Initial Authorization</u>**

a. Diagnosis of moderately to severely active RA

-AND-

b. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab),

Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

c. One of the following:

(1) Patient is receiving concurrent therapy with methotrexate (e.g., Rheumatrex, Trexall)

-OR-

(2) History of failure, contraindication, or intolerance to methotrexate

-AND-

d. Prescribed or recommended by a rheumatologist

-AND-

e. **One** of the following:

(1) **Both** of the following:

(a) History of failure, contraindication, or intolerance to **two** of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-AND-

(b) History of failure, contraindication, or intolerance to Kevzara (sarilumab)

-OR-

(2) For continuation of prior Simponi therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Simponi therapy

-AND-

b. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Psoriatic Arthritis

1. **Initial Authorization**

a. Diagnosis of active psoriatic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist or dermatologist

-AND-

c. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

d. One of the following:

(1) History of failure, contraindication, or intolerance to **two** of the following:

(a) Cimzia (certolizumab)
(b) Humira (adalimumab)
(c) Enbrel (etanercept)

-OR-

(2) For continuation of prior Simponi therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Simponi therapy

-AND-

b. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Ankylosing Spondylitis

1. **Initial Authorization**

a. Diagnosis of ankylosing spondylitis

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to two or more NSAIDs

-AND-

d. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

e. One of the following:

(1) History of failure, contraindication, or intolerance to all of the following:

(a) Cimzia (certolizumab)
(b) Humira (adalimumab)
(c) Enbrel (etanercept)

-OR-

(2) For continuation of prior Simponi therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Simponi therapy

-AND-

b. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

D. Ulcerative Colitis

1. **Initial Authorization**

a. Diagnosis of moderately to severely active ulcerative colitis

-AND-

b. One of the following:

(1) Patient is corticosteroid dependent (i.e., an inability to successfully taper corticosteroids without a return of the symptoms of UC)

-OR-

(2) History of failure, contraindication, or intolerance to one of the following

therapies:
(a) Oral aminosalicylates
(b) Oral corticosteroids
(c) Azathioprine
(d) 6-mercaptopurine

-AND-

c. Prescribed or recommended by a gastroenterologist

-AND-

d. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

e. One of the following:

(1) History of failure, contraindication, or intolerance to Humira (adalimumab)

-OR-

(2) For continuation of prior Simponi therapy

Authorization will be issued for 10 weeks.

2. **Reauthorization**

a. Documentation of positive clinical response to Simponi therapy

-AND-

b. Patient is not receiving Simponi in combination with any of the following:

(1) Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

UnitedHealthcare Community Plan

Authorization will be issued for 12 months.

3. References:

1. Simponi Prescribing Information. Janssen Biotech Inc., November 2013.
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3. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. Ann Rheum Dis. 2012;71(Supp II):i2–i45.
4. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis -- Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. J Am Acad Dermatol. 2011;65:137-174.
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8. Kavanaugh A, McInnes I, Mease P, et al. Golimumab, a new tumor necrosis factor ? antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis. Arthritis Rheum. 2009; 60(4): 976-986.
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12. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993; 36 (6): 729-740.
13. Per clinical consult with rheumatologist, June 30, 2011.
14. van der Heijde, Sieper J, Maksymowych WP, et al. 2010 update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70:905-908.
15. Kornbluth A, Sachar DB, and Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010;105(3):501-23.
16. Simponi Aria Prescribing Information. Janssen Biotech, Inc., September 2013.
17. Xeljanz Prescribing Information. Pfizer, Inc., November 2013.

Program	Program type – Prior Authorization
Change Control	
Date	Change
2/2015	New policy
3/2016	Changed trial requirement of traditional DMARDs to only methotrexate to align with the requirement of concurrent use of methotrexate. Added Enbrel to prerequisite therapy in the following initial therapy sections: rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. Updated policy template
10/2016	Annual Review – no change
3/2017	Added Otezla to list of medications that should not be used with Simponi. Updated policy template.
9/2017	Added Otezla to preferred agents for psoriatic arthritis
2/2018	Updated step therapy medications in the rheumatoid arthritis section to a trial of two TNF inhibitors and Kevzara due to PDL changes effective 4/1/18. Changed number of trial products from three to two in the psoriatic arthritis section.

SIMPONI ARIA® (GOLIMUMAB) INJECTION FOR INTRAVENOUS INFUSION

Policy Number: CS2018D0051F **Effective Date**: April 1, 2018

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Commercial Policy

- Simponi Aria® (Golimumab) Injection for Intravenous Infusion

INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

This policy refers only to Simponi Aria (golimumab) injection for intravenous infusion for the treatment of ankylosing spondylitis, psoriatic arthritis, and rheumatoid arthritis. Simponi, for self-administered subcutaneous injection, is obtained under the pharmacy benefit and is indicated in the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and ulcerative colitis.

Simponi Aria is proven and medically necessary for the treatment of:

I. **Ankylosing spondylitis when ALL of the following criteria are met**: [1]
   A. Diagnosis of active ankylosing spondylitis (AS); **and**
   B. Simponi Aria is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for ankylosing spondylitis up to a maximum of 2mg/kg every 8 weeks (or equivalent dose and interval schedule); **and**
   C. Patient is not receiving Simponi Aria in combination with either of the following:
      1. Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)]

2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]. [5]

II. **Psoriatic arthritis when ALL of the following criteria are met**: [1]
   A. Diagnosis of active psoriatic arthritis (RA); **and**
   B. Simponi Aria is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for rheumatoid arthritis up to a maximum of 2mg/kg every 8 weeks (or equivalent dose and interval schedule); **and**
   C. Patient is not receiving Simponi Aria in combination with either of the following:
      1. Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [5]
      3. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)].

III. **Rheumatoid arthritis when ALL of the following criteria are met**: [1.8]
   A. Diagnosis of moderately to severely active rheumatoid arthritis (RA); **and**
   B. **One** of the following:
      1. Patient is receiving concurrent therapy with methotrexate
      2. History of contraindication or intolerance to methotrexate;
      and
   C. Simponi Aria is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for rheumatoid arthritis up to a maximum of 2mg/kg every 8 weeks (or equivalent dose and interval schedule); **and**
   D. Patient is not receiving Simponi Aria in combination with either of the following:
      1. Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]. [5]

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Simponi Aria, for intravenous infusion, is a tumor necrosis factor (TNF) blocker indicated for the treatment of adult patients with moderately to severely active RA in combination with methotrexate (MTX), active PsA and AS. [1]

Simponi, for subcutaneous injection, is indicated in adult patients for the following: treatment of moderately to severely active RA in combination with MTX; treatment of active psoriatic arthritis (PsA) alone, or in combination with MTX; treatment of active ankylosing spondylitis (AS); and the treatment of moderately to severely active ulcerative colitis (UC) who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine for: inducing and maintaining clinical response, improving endoscopic appearance of the mucosa during induction, inducing clinical remission, and achieving and sustaining clinical remission in induction responders. [7]

BACKGROUND

Golimumab is a human anti-tumor necrosis factor (TNF) monoclonal antibody that targets both soluble and transmembrane bioactive forms of TNF-alpha, a protein that when overproduced in the body due to chronic inflammatory diseases can cause inflammation and damage to bones, cartilage and tissue. [1]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J1602	Injection, golimumab, 1 mg, for intravenous use

ICD-10 Diagnosis Code	Description
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans

ICD-10 Diagnosis Code	Description
L40.53	Psoriatic spondylitis
L40.54	Psoriatic juvenile arthropathy
L40.59	Other psoriatic arthropathy
M05.00	Felty's syndrome, unspecified site
M05.011	Felty's syndrome, right shoulder
M05.012	Felty's syndrome, left shoulder
M05.019	Felty's syndrome, unspecified shoulder
M05.021	Felty's syndrome, right elbow
M05.022	Felty's syndrome, left elbow
M05.029	Felty's syndrome, unspecified elbow
M05.031	Felty's syndrome, right wrist
M05.032	Felty's syndrome, left wrist
M05.039	Felty's syndrome, unspecified wrist
M05.041	Felty's syndrome, right hand
M05.042	Felty's syndrome, left hand
M05.049	Felty's syndrome, unspecified hand
M05.051	Felty's syndrome, right hip
M05.052	Felty's syndrome, left hip
M05.059	Felty's syndrome, unspecified hip
M05.061	Felty's syndrome, right knee
M05.062	Felty's syndrome, left knee
M05.069	Felty's syndrome, unspecified knee
M05.071	Felty's syndrome, right ankle and foot
M05.072	Felty's syndrome, left ankle and foot
M05.079	Felty's syndrome, unspecified ankle and foot
M05.09	Felty's syndrome, multiple sites
M05.20	Rheumatoid vasculitis with rheumatoid arthritis of unspecified site
M05.211	Rheumatoid vasculitis with rheumatoid arthritis of right shoulder
M05.212	Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.219	Rheumatoid vasculitis with rheumatoid arthritis of unspecified shoulder
M05.221	Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222	Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.229	Rheumatoid vasculitis with rheumatoid arthritis of unspecified elbow
M05.231	Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232	Rheumatoid vasculitis with rheumatoid arthritis of left wrist
M05.239	Rheumatoid vasculitis with rheumatoid arthritis of unspecified wrist
M05.241	Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242	Rheumatoid vasculitis with rheumatoid arthritis of left hand
M05.249	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hand
M05.251	Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252	Rheumatoid vasculitis with rheumatoid arthritis of left hip
M05.259	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hip
M05.261	Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262	Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.269	Rheumatoid vasculitis with rheumatoid arthritis of unspecified knee
M05.271	Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272	Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot

ICD-10 Diagnosis Code	Description
M05.279	Rheumatoid vasculitis with rheumatoid arthritis of unspecified ankle and foot
M05.29	Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.30	Rheumatoid heart disease with rheumatoid arthritis of unspecified site
M05.311	Rheumatoid heart disease with rheumatoid arthritis of right shoulder
M05.312	Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.319	Rheumatoid heart disease with rheumatoid arthritis of unspecified shoulder
M05.321	Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322	Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.329	Rheumatoid heart disease with rheumatoid arthritis of unspecified elbow
M05.331	Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332	Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.339	Rheumatoid heart disease with rheumatoid arthritis of unspecified wrist
M05.341	Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342	Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.349	Rheumatoid heart disease with rheumatoid arthritis of unspecified hand
M05.351	Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352	Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.359	Rheumatoid heart disease with rheumatoid arthritis of unspecified hip
M05.361	Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362	Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.369	Rheumatoid heart disease with rheumatoid arthritis of unspecified knee
M05.371	Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372	Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.379	Rheumatoid heart disease with rheumatoid arthritis of unspecified ankle and foot
M05.39	Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.40	Rheumatoid myopathy with rheumatoid arthritis of unspecified site
M05.411	Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412	Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.419	Rheumatoid myopathy with rheumatoid arthritis of unspecified shoulder
M05.421	Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422	Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.429	Rheumatoid myopathy with rheumatoid arthritis of unspecified elbow
M05.431	Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432	Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.439	Rheumatoid myopathy with rheumatoid arthritis of unspecified wrist
M05.441	Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442	Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.449	Rheumatoid myopathy with rheumatoid arthritis of unspecified hand
M05.451	Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452	Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.459	Rheumatoid myopathy with rheumatoid arthritis of unspecified hip
M05.461	Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462	Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.469	Rheumatoid myopathy with rheumatoid arthritis of unspecified knee
M05.471	Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472	Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.479	Rheumatoid myopathy with rheumatoid arthritis of unspecified ankle and foot

ICD-10 Diagnosis Code	Description
M05.49	Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.50	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site
M05.511	Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512	Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder
M05.519	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified shoulder
M05.521	Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522	Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow
M05.529	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified elbow
M05.531	Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532	Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.539	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.549	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.559	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.569	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot
M05.579	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.60	Rheumatoid arthritis of unspecified site with involvement of other organs and systems
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.619	Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.629	Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.639	Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.649	Rheumatoid arthritis of unspecified hand with involvement of other organs and systems
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.659	Rheumatoid arthritis of unspecified hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems
M05.669	Rheumatoid arthritis of unspecified knee with involvement of other organs and systems

ICD-10 Diagnosis Code	Description
M05.671	Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672	Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems
M05.679	Rheumatoid arthritis of unspecified ankle and foot with involvement of other organs and systems
M05.69	Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.70	Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement
M05.711	Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712	Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.719	Rheumatoid arthritis with rheumatoid factor of unspecified shoulder without organ or systems involvement
M05.721	Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722	Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.729	Rheumatoid arthritis with rheumatoid factor of unspecified elbow without organ or systems involvement
M05.731	Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732	Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement
M05.739	Rheumatoid arthritis with rheumatoid factor of unspecified wrist without organ or systems involvement
M05.741	Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742	Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.749	Rheumatoid arthritis with rheumatoid factor of unspecified hand without organ or systems involvement
M05.751	Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752	Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.759	Rheumatoid arthritis with rheumatoid factor of unspecified hip without organ or systems involvement
M05.761	Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762	Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement
M05.769	Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement
M05.771	Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement
M05.772	Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement
M05.779	Rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot without organ or systems involvement
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement

ICD-10 Diagnosis Code	Description
M05.80	Other rheumatoid arthritis with rheumatoid factor of unspecified site
M05.811	Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812	Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.819	Other rheumatoid arthritis with rheumatoid factor of unspecified shoulder
M05.821	Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822	Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.829	Other rheumatoid arthritis with rheumatoid factor of unspecified elbow
M05.831	Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832	Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.839	Other rheumatoid arthritis with rheumatoid factor of unspecified wrist
M05.841	Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842	Other rheumatoid arthritis with rheumatoid factor of left hand
M05.849	Other rheumatoid arthritis with rheumatoid factor of unspecified hand
M05.851	Other rheumatoid arthritis with rheumatoid factor of right hip
M05.852	Other rheumatoid arthritis with rheumatoid factor of left hip
M05.859	Other rheumatoid arthritis with rheumatoid factor of unspecified hip
M05.861	Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862	Other rheumatoid arthritis with rheumatoid factor of left knee
M05.869	Other rheumatoid arthritis with rheumatoid factor of unspecified knee
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.879	Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00	Rheumatoid arthritis without rheumatoid factor, unspecified site
M06.011	Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012	Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.019	Rheumatoid arthritis without rheumatoid factor, unspecified shoulder
M06.021	Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022	Rheumatoid arthritis without rheumatoid factor, left elbow
M06.029	Rheumatoid arthritis without rheumatoid factor, unspecified elbow
M06.031	Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032	Rheumatoid arthritis without rheumatoid factor, left wrist
M06.039	Rheumatoid arthritis without rheumatoid factor, unspecified wrist
M06.041	Rheumatoid arthritis without rheumatoid factor, right hand
M06.042	Rheumatoid arthritis without rheumatoid factor, left hand
M06.049	Rheumatoid arthritis without rheumatoid factor, unspecified hand
M06.051	Rheumatoid arthritis without rheumatoid factor, right hip
M06.052	Rheumatoid arthritis without rheumatoid factor, left hip
M06.059	Rheumatoid arthritis without rheumatoid factor, unspecified hip
M06.061	Rheumatoid arthritis without rheumatoid factor, right knee
M06.062	Rheumatoid arthritis without rheumatoid factor, left knee
M06.069	Rheumatoid arthritis without rheumatoid factor, unspecified knee
M06.071	Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072	Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.079	Rheumatoid arthritis without rheumatoid factor, unspecified ankle and foot
M06.08	Rheumatoid arthritis without rheumatoid factor, vertebrae

ICD-10 Diagnosis Code	Description
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.1	Adult-onset Still's disease
M06.20	Rheumatoid bursitis, unspecified site
M06.211	Rheumatoid bursitis, right shoulder
M06.212	Rheumatoid bursitis, left shoulder
M06.219	Rheumatoid bursitis, unspecified shoulder
M06.221	Rheumatoid bursitis, right elbow
M06.222	Rheumatoid bursitis, left elbow
M06.229	Rheumatoid bursitis, unspecified elbow
M06.231	Rheumatoid bursitis, right wrist
M06.232	Rheumatoid bursitis, left wrist
M06.239	Rheumatoid bursitis, unspecified wrist
M06.241	Rheumatoid bursitis, right hand
M06.242	Rheumatoid bursitis, left hand
M06.249	Rheumatoid bursitis, unspecified hand
M06.251	Rheumatoid bursitis, right hip
M06.252	Rheumatoid bursitis, left hip
M06.259	Rheumatoid bursitis, unspecified hip
M06.261	Rheumatoid bursitis, right knee
M06.262	Rheumatoid bursitis, left knee
M06.269	Rheumatoid bursitis, unspecified knee
M06.271	Rheumatoid bursitis, right ankle and foot
M06.272	Rheumatoid bursitis, left ankle and foot
M06.279	Rheumatoid bursitis, unspecified ankle and foot
M06.28	Rheumatoid bursitis, vertebrae
M06.29	Rheumatoid bursitis, multiple sites
M06.30	Rheumatoid nodule, unspecified site
M06.311	Rheumatoid nodule, right shoulder
M06.312	Rheumatoid nodule, left shoulder
M06.319	Rheumatoid nodule, unspecified shoulder
M06.321	Rheumatoid nodule, right elbow
M06.322	Rheumatoid nodule, left elbow
M06.329	Rheumatoid nodule, unspecified elbow
M06.331	Rheumatoid nodule, right wrist
M06.332	Rheumatoid nodule, left wrist
M06.339	Rheumatoid nodule, unspecified wrist
M06.341	Rheumatoid nodule, right hand
M06.342	Rheumatoid nodule, left hand
M06.349	Rheumatoid nodule, unspecified hand
M06.351	Rheumatoid nodule, right hip
M06.352	Rheumatoid nodule, left hip
M06.359	Rheumatoid nodule, unspecified hip
M06.361	Rheumatoid nodule, right knee
M06.362	Rheumatoid nodule, left knee
M06.369	Rheumatoid nodule, unspecified knee
M06.371	Rheumatoid nodule, right ankle and foot
M06.372	Rheumatoid nodule, left ankle and foot

ICD-10 Diagnosis Code	Description
M06.379	Rheumatoid nodule, unspecified ankle and foot
M06.38	Rheumatoid nodule, vertebrae
M06.39	Rheumatoid nodule, multiple sites
M06.80	Other specified rheumatoid arthritis, unspecified site
M06.811	Other specified rheumatoid arthritis, right shoulder
M06.812	Other specified rheumatoid arthritis, left shoulder
M06.819	Other specified rheumatoid arthritis, unspecified shoulder
M06.821	Other specified rheumatoid arthritis, right elbow
M06.822	Other specified rheumatoid arthritis, left elbow
M06.829	Other specified rheumatoid arthritis, unspecified elbow
M06.831	Other specified rheumatoid arthritis, right wrist
M06.832	Other specified rheumatoid arthritis, left wrist
M06.839	Other specified rheumatoid arthritis, unspecified wrist
M06.841	Other specified rheumatoid arthritis, right hand
M06.842	Other specified rheumatoid arthritis, left hand
M06.849	Other specified rheumatoid arthritis, unspecified hand
M06.851	Other specified rheumatoid arthritis, right hip
M06.852	Other specified rheumatoid arthritis, left hip
M06.859	Other specified rheumatoid arthritis, unspecified hip
M06.861	Other specified rheumatoid arthritis, right knee
M06.862	Other specified rheumatoid arthritis, left knee
M06.869	Other specified rheumatoid arthritis, unspecified knee
M06.871	Other specified rheumatoid arthritis, right ankle and foot
M06.872	Other specified rheumatoid arthritis, left ankle and foot
M06.879	Other specified rheumatoid arthritis, unspecified ankle and foot
M06.88	Other specified rheumatoid arthritis, vertebrae
M06.89	Other specified rheumatoid arthritis, multiple sites
M06.9	Rheumatoid arthritis, unspecified
M08.1	Juvenile ankylosing spondylitis
M45.0	Ankylosing spondylitis of multiple sites in spine
M45.1	Ankylosing spondylitis of occipito-atlanto-axial region
M45.2	Ankylosing spondylitis of cervical region
M45.3	Ankylosing spondylitis of cervicothoracic region
M45.4	Ankylosing spondylitis of thoracic region
M45.5	Ankylosing spondylitis of thoracolumbar region
M45.6	Ankylosing spondylitis lumbar region
M45.7	Ankylosing spondylitis of lumbosacral region
M45.8	Ankylosing spondylitis sacral and sacrococcygeal region
M45.9	Ankylosing spondylitis of unspecified sites in spine

CLINICAL EVIDENCE

Proven

Ankylosing Spondylitis

The efficacy and safety of golimumab were evaluated in a multicenter, randomized, double-blind, placebo-controlled trial in 208 adult patients with active ankylosing spondylitis (AS) and inadequate response or intolerance to NSAIDs. 1 Patients had a diagnosis of definite AS for at least 3 months according to modified New York criteria. Patients had symptoms of active disease [Bath AS Disease Activity Index (BASDAI) ≥ 4, VAS for total back pain of ≥ 4, on scales of 0 to 10 cm (0 to 100 mm), and a hsCRP level of ≥ 0.3 mg/dL (3 mg/L)]. Patients were randomized to receive either

golimumab 2 mg/kg (N=105) or placebo (N=103) as a 30-minute intravenous infusion at Weeks 0, 4 and 12. All patients on placebo received golimumab at Week 16, Week 20 and every 8 weeks thereafter through Week 52. Patients in the golimumab treatment group continued to receive golimumab infusions at Week 20 and every 8 weeks through Week 52. Patients were allowed to continue stable doses of concomitant methotrexate (MTX), sulfasalazine (SSZ), hydroxychloroquine (HCQ), low dose oral corticosteroids (equivalent to ≤ 10 mg of prednisone per day), and/or NSAIDs during the trial. The use of other DMARDs including cytotoxic agents or other biologics was prohibited. The primary endpoint was the percentage of patients achieving an Assessment in Ankylosing Spondylitis (ASAS) 20 response at Week 16. In this trial, golimumab, compared with placebo, resulted in a significant improvement in signs and symptoms as demonstrated by the percentage of patients with an ASAS 20 response at Week 16, where a greater percentage of patients treated with golimumab achieved a low level of disease activity (<2 [on a scale of 0 to 10 cm] in all four ASAS domains) compared with patients treated with placebo (16.2% vs. 3.9%). General health status was assessed by the 36-item Short Form Health Survey (SF-36). Patients receiving golimumab demonstrated greater improvement from baseline compared with placebo in physical component summary and mental component summary scores and in all 8 domains of the SF-36. Golimumab-treated patients showed significant improvement compared with placebo-treated patients in health related quality of life as assessed by the Ankylosing Spondylitis Quality of Life questionnaire (ASQoL).

Psoriatic Arthritis

The efficacy and safety of golimumab were evaluated in a multicenter, randomized, double-blind, placebo-controlled trial in 480 adult patients with active psoriatic arthritis despite NSAID or DMARD therapy PsA.[11] Previous treatment with a biologic was not allowed. Patients in this trial had a diagnosis of PsA for at least six months and had symptoms of active disease [≥5 swollen joints and ≥5 tender joints and a CRP level of ≥ 0.6 mg/dL]. Patients were randomized to either receive golimumab 2 mg/kg (N=241) or placebo (N=239) as a 30-minute intravenous infusion at Weeks 0, 4, 12 and 20. All patients on placebo received golimumab at Week 24, Week 28 and every 8 weeks thereafter through Week 52. Patients in the golimumab treatment group continued to receive golimumab infusions at Week 28 and every 8 weeks through Week 52. Patients were allowed to continue stable doses of MTX, NSAIDs, and low dose oral corticosteroids (equivalent to ≤ 10 mg of prednisone per day) during the trial. The use of other DMARDs including cytotoxic agents or other biologics was prohibited. The primary endpoint was the percentage of patients achieving an ACR 20 response at Week 14. Patients with each subtype of PsA were enrolled, including polyarticular arthritis with absence of rheumatoid nodules (44%), asymmetric peripheral arthritis (19%), distal interphalangeal joint involvement (8.1%), spondylitis with peripheral arthritis (25%), and arthritis mutilans (4.8%). During the trial, concomitant medications used included MTX (70%), oral corticosteroids (28%), and NSAIDs (71%). Golimumab, compared with placebo, resulted in a significant improvement in signs and symptoms as demonstrated by the percentage of patients with an ACR 20 response at Week 14. Similar ACR 20 responses at Week 24 were observed in patients with different PsA subtypes. ACR 20 responses observed in the golimumab-treated groups were similar in patients who were or were not receiving concomitant MTX. Patients with enthesitis at baseline were evaluated for mean improvement using the Leeds Enthesitis Index (LEI) on a scale of 0-6. Golimumab-treated patients showed a significantly greater improvement in enthesitis, with a mean reduction of 1.8 as compared with a mean reduction in placebo-treated patients of 0.8 at Week 14. Patients with dactylitis at baseline were evaluated for mean improvement on a scale of 0-60. golimumab-treated patients showed a significantly greater improvement, with a mean reduction of 7.8 compared with a mean reduction of 2.8 in placebo-treated patients at Week 14. Golimumab inhibited the progression of structural damage compared with placebo, as assessed by total modified vdH-S score. At Week 24, a greater proportion of patients in the golimumab group (72%) had no progression of structural damage (change in the total modified vdH-S score ≤ 0), compared to 43% of patients in the placebo group. Improvement in physical function as assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI) demonstrated that the proportion of patients who achieved clinically meaningful improvement of ≥ 0.3 in HAQ-DI score from baseline was greater in the golimumab-treated group compared to placebo at Week 14 (69% compared to 32%). General health status was assessed by the 36-item Short Form Health Survey (SF-36). Patients receiving golimumab demonstrated greater improvement from baseline compared with placebo in physical component summary, mental component summary scores and in all 8 domains of the SF-36.

Rheumatoid Arthritis

In the extension phase to the GO-FURTHER pivotal study, the long term extension study of golimumab plus methotrexate (MTX) for rheumatoid arthritis evaluated the efficacy, pharmacokinetics, immunogenicity and radiographic progression, through 100 weeks of therapy, where safety was monitored through 112 weeks. [6] In the original trial 592 patients with active RA were randomized (2:1) to receive intravenous (IV) golimumab 2mg/kg plus MTX or placebo plus MTX at weeks 0, 4, and every 8 weeks thereafter.[2] Patients receiving placebo were able to cross over at either week 16 or week 24 to active therapy. In total, 486 patients (82.1%) continued golimumab therapy for 100 weeks. Efficacy assessments included the American College of Rheumatology 20%, 50%, 70% (ACR 20, ACR50, ACR70) response criteria, 28 joint count disease activity score using the C-reactive protein level, physical function and quality of life (QoL) measures, and changes in the modified Sharp/van der Heijde scores (SHS). Following treatment at week 100, in both groups combined, 68.1% of patients had an ACR20 response, 43.8% had an ACR50, and 23.5% had an ACR70 response. More than 80% of all patients had a good or moderate DAS28-CRP response at week 100,

and approximately 28% achieved DAS28-CRP < 2.6. For patient reported outcomes, improvements in SF-36 PCS, MCS, FACIT-Fatigue, EQ-5D VAS scores were sustained through week 112 in both treatment groups. At week 100, the mean change from baseline in total SHS score was significantly lower in Group 1 than in Group 2 (0.74 vs. 2.10; P=0.005) and 61.8% (n=244 of 395) of patients in Group 1 and 54.8% (n=108 of 197) of patients in Group 2 had a change from baseline in total SHS of ≤ 0. When evaluated by progression beyond the smallest detectable change (3.22) in total SHS, 16.7% (n=66 of 395) of patients in Group 1 and 23.9% (n=47 of 197) in Group 2 demonstrated radiographic progression from baseline to week 100. The mean change in total SHS score from week 52 to week 100 when all patients were receiving golimumab was numerically lower in Group 1 (0.56) than in Group 2 (0.80); the median change was 0 in both groups. After 112 weeks, a total of 481 patients completed the safety follow-up with 79.1% had at least one adverse event, and 18.2% having had a serious adverse event. After 100 weeks of treatment only 6.7% (n=37 of 553) of patients developed antibodies to golimumab, with 86.5% positive for neutralizing antibodies. The authors concluded that treatment with IV golimumab plus MTX afforded a clinical response that was maintained through week 100. Radiographic progression following treatment was clinically insignificant between week 52 and week 100.

Professional Societies

Rheumatoid Arthritis

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDS, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (≥ 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs.[8] The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions. Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

Supplementary Appendix 5, of the 2015 ACR RA guideline, summarizes recommendations for patients with early RA, established RA, and high-risk comorbidities. [8]

Recommendations for Early RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, another target may be chosen because risk tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with early, symptomatic RA, the panel strongly recommends DMARD monotherapy over double or triple DMARD therapy in patients with low disease activity and conditionally recommends DMARD monotherapy over double or triple DMARD therapy in patients with moderate or high disease activity. Methotrexate should be the preferred initial therapy for most patients with early RA with active disease.
- For patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids), the panel strongly recommends treatment with a combination of DMARDs or a TNFi or a non-TNF biologic, with or without methotrexate (MTX) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to superior efficacy.
- For patients with moderate or high disease activity despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids (defined as ≤10 mg/day of prednisone or equivalent). Low-dose glucocorticoids may also be used in patients who need a bridge until realizing the benefits of DMARD therapy. The risk/benefit ratio of glucocorticoid therapy is favorable as long as the dose is low and the duration of therapy is short.
- For patients experiencing a flare of RA, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose for the shortest possible duration, to provide a favorable benefit-risk ratio for the patient.

Recommendations for Established RA Patients

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, however, another target may be chosen because tolerance by patients or comorbidities may mitigate the usual choices.

- For DMARD-naïve patients with low disease activity, the panel strongly recommends using DMARD monotherapy over a TNFi. For DMARD-naïve patients with moderate or high disease activity, the panel conditionally recommends DMARD monotherapy over double or triple DMARD therapy and DMARD monotherapy over tofacitinib. In general, MTX should be the preferred initial therapy for most patients with established RA with active disease.
- For patients with moderate or high disease activity despite DMARD monotherapy including methotrexate, the panel strongly recommends using combination DMARDs or adding a TNFi or a non-TNF biologic or tofacitinib (all choices with or without methotrexate) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to its superior efficacy.

For all scenarios for established RA below, treatment may be with or without MTX:
- For moderate or high disease activity despite TNFi therapy in patients currently not on a DMARD, the panel strongly recommends that one or two DMARDs be added to TNFi therapy rather than continuing TNFi therapy alone.
- If disease activity is moderate or high despite single TNFi biologic therapy, the panel conditionally recommends using a non-TNF biologic.
- If disease activity is moderate or high despite non-TNF biologic therapy, the panel conditionally recommends using another non-TNF biologic. However, if a patient has failed multiple non-TNF biologics and they are TNFi-naïve with moderate or high disease activity, the panel conditionally recommends treatment with a TNFi.
- For patients with moderate or high disease activity despite prior treatment with at least one TNFi and at least one non-TNF-biologic (sequentially, not combined), the panel conditionally recommends first treating with another non-TNF biologic. However, when a non-TNF biologic is not an option (e.g., patient declines non-TNF biologic therapy due to inefficacy or side effects), the panel conditionally recommends treatment with tofacitinib.
- If disease activity is moderate or high despite the use of multiple (2+) TNFi therapies (in sequence, not concurrently), the panel conditionally recommends non-TNF biologic therapy and then conditionally treating with tofacitinib when a non-TNF biologic is not an option.
- If disease activity is moderate or high despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids.
- If patients with established RA experience an RA flare while on DMARD, TNFi, or non-TNF biologic therapy, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose and for shortest possible duration to provide the best benefit-risk ratio for the patient.
- In patients with established RA and low disease activity but not remission, the panel strongly recommends continuing DMARD therapy, TNFi, non-TNF biologic or tofacitinib rather than discontinuing respective medication.
- In patients with established RA currently in remission, the panel conditionally recommends tapering DMARD therapy, TNFi, non-TNF biologic, or tofacitinib.
- The panel strongly recommends not discontinuing all therapies in patients with established RA in disease remission.

Recommendations for RA Patients with High-Risk Comorbidities

Congestive Heart Failure
- In patients with established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF), the panel conditionally recommends using combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a TNFi.
- If patients in this population are treated with a TNFi and their CHF worsens while on the TNFi, the panel conditionally recommends switching to combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a different TNFi.

Hepatitis B
- In patients with established RA with moderate or high disease activity and evidence of active hepatitis B infection (hepatitis surface antigen positive > 6 months), who are receiving or have received effective antiviral treatment, the panel strongly recommends treating them the same as patients without this condition.
- For a patient with natural immunity from prior exposure to hepatitis B (i.e., HB core antibody and HBS antibody positive and normal liver function tests), the panel recommends the same therapies as those without such findings as long as the patient's viral load is monitored.
- For patients with chronic hepatitis B who are untreated, referral for antiviral therapy is appropriate prior to immunosuppressive therapy.

Hepatitis C
- In patients with established RA with moderate or high disease activity and evidence of chronic hepatitis C virus (HCV) infection, who are receiving or have received effective antiviral treatment, the panel conditionally recommends treating them the same as the patients without this condition.
- The panel recommends that rheumatologists work with gastroenterologists and/or hepatologists who would monitor patients and reassess the appropriateness of antiviral therapy. This is important considering the recent

availability of highly effective therapy for HCV, which may lead to a greater number of HCV patients being treated successfully.
- If the same patient is not requiring or receiving antiviral treatment for their hepatitis C, the panel conditionally recommends using DMARD therapy rather than TNFi.

Malignancy
- Previous Melanoma and Non-Melanoma Skin Cancer:
  - In patients with established RA and moderate or high disease activity and a history of previously treated or untreated skin cancer (melanoma or non-melanoma), the panel conditionally recommends the use of DMARD therapy over biologics or tofacitinib.
- Previous Lymphoproliferative Disorders:
  - In patients with established RA with moderate or high disease activity and a history of a previously treated lymphoproliferative disorder, the panel strongly recommends using rituximab rather than a TNFi and conditionally recommends using combination DMARD therapy, abatacept or tocilizumab rather than TNFi.
- Previous Solid Organ Cancer:
  - In patients with established RA with moderate or high disease activity and previously treated solid organ cancer, the panel conditionally recommends that they be treated for RA just as one would treat an RA patient without a history of solid organ cancer.

Serious Infections
- In patients with established RA with moderate or high disease activity and previous serious infection(s), the panel conditionally recommends using combination DMARD therapy or abatacept rather than TNFi.

Psoriatic Arthritis

The American Academy of Dermatology (AAD) defines psoriatic arthritis (PsA) as mild, moderate, or severe. Where mild disease responds to NSAIDs, moderate disease requires DMARDs or TNF blockers. Appropriate treatment of severe PsA requires DMARDs plus TNF blockers or other biologic therapies. If PsA is diagnosed, treatment should be initiated to alleviate signs and symptoms of PsA, inhibit structural damage, and maximize quality of life (QOL). According to the AAD Practice Guidelines for the management of psoriatic arthritis, the potential importance of TNF-α in the pathophysiology of PsA is underscored by the observation that there are elevated levels of TNF-α in the synovium, joint fluid, and skin of patients with PsA. The guidelines support the use of infliximab for PsA based on evidence ranked as consistent, good quality, and patient-oriented. (Strength of Recommendation: A). [9]

Ankylosing Spondylitis

Evidence based recommendations for the management of ankylosing spondylitis (AS) were created as a combined effort of the 'ASsessment in AS' international working group and the European League Against Rheumatism (EULAR). According to these comprehensive guidelines, anti-TNF treatment (infliximab, etanercept, adalimumab, and golimumab) should be given to patients with persistently high disease activity despite conventional treatments. There is no evidence to support the obligatory use of DMARDs before, or concomitant with, anti-TNF treatment in patients with axial disease. There is no evidence to support a difference in efficacy of the various TNF inhibitors on the axial and articular/entheseal disease manifestations; but in the presence of IBD a difference in gastrointestinal efficacy needs to be taken into account. Switching to a second TNF blocker might be beneficial especially in patients with loss of response. [10]

American College of Rheumatology, Spondylitis Association of America and Spondyloarthritis Research developed provide evidence-based recommendations for the treatment of patients with ankylosing spondylitis (AS). In patients with active AS, the strong recommendations from the committee regardinc pharmacologic treatment include: use of nonsteroidal antiinflammatory drugs (NSAIDs), use of tumor necrosis factor inhibitors (TNFi) when persistant disease activity while on NSAID treatment, not to use systemic glucocorticoids. In addition, no specific TNFi was preferred with the exception of patients who have concomitant inflammatory bowel disease or recurrent iritis. In these patients, the committee recomends TNFi monoclonal antibodies. [12]

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination for SIMPONI® ARIA™ (golimumab). Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual, Chapter 15, Section 50 Drugs and Biologicals.
(Accessed January 8, 2018)

STATE EXCEPTIONS

State	Note
Kansas	Drug policy not approved for use in this market

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
04/01/2018	• Updated supporting information to reflect the most current clinical evidence and references; no change to coverage rationale or lists of applicable codes ○ Replaced reference to "MCG™ Ambulatory Care *20th* Edition" with "MCG™ Ambulatory Care *22nd* Edition" • Archived previous policy version CS2018D0051E

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Stelara

Program	Prior Authorization
Medication	Stelara (ustekinumab)
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Mexico, New York, Ohio, Rhode Island
Issue Date	12/2013
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Stelara (ustekinumab) is a human interleukin-12 and -23 antagonist indicated for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. It is also indicated for active psoriatic arthritis, alone or in combination with methotrexate. In addition, it is also indicated for moderately to severely active Crohn's disease in patients who have failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker or patients who have failed or were intolerant to treatment with one or more TNF blockers.

Stelara IV is not a pharmacy benefit for the UnitedHealthcare Community Plan

2. Coverage Criteria:

A. <u>Plaque Psoriasis</u>

1. <u>Initial Authorization</u>

a. Diagnosis of moderate to severe plaque psoriasis

-AND-

b. Prescribed or recommended by a dermatologist

-AND-

c. Patient is not receiving Stelara in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]

(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

d. **One** of the following:

(1) **Both** of the following:

(a) History of failure, contraindication, or intolerance to **both** of the following:

- Humira (adalimumab)
- Enbrel (etanercept)

-AND-

(b) History of failure, contraindication, or intolerance to Cosentyx (secukinumab)

-OR-

(2) For continuation of prior Stelara therapy

-AND-

e. **One** of the following:

(1) Requested medication is Stelara 45 mg/0.5 mL

-OR-

(2) Both of the following:

(a) Requested medication is Stelara 90 mg/1 mL

-AND-

(b) Patient's weight is > 100 kg (220 lbs)

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Stelara therapy

-AND-

b. Patient is not receiving Stelara in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

B. Psoriatic Arthritis

1. Initial Authorization

a. One of the following:

(1) Both of the following:

(a) Requested medication is Stelara 45 mg/0.5 mL

-AND-

(b) Diagnosis of active psoriatic arthritis

-OR-

(2) All of the following:

(a) Requested medication is Stelara 90 mg/1 mL

-AND-

(b) Patient's weight is > 100 kg (220 lbs)

-AND-

(c) Diagnosis of active psoriatic arthritis

-AND-

(d) Diagnosis of co-existent moderate to severe psoriasis

-AND-

b. Prescribed or recommended by a rheumatologist or dermatologist

-AND-

c. Patient is not receiving Stelara in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

d. **One** of the following:

(1) History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-OR-

(2) For continuation of prior Stelara therapy

Authorization will be issued for 12 months.

2. Reauthorization

a. Documentation of positive clinical response to Stelara therapy

-AND-

b. Patient is not receiving Stelara in combination with any of the following:

(1) Biologic DMARD [eg, Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(2) Janus kinase inhibitor [eg, Xeljanz (tofacitinib)]
(3) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

C. Crohn's Disease (CD)

1. Initial Authorization for Maintenance Dosing

a. Stelara 90 mg/1 mL will be approved based on **all** of the following criteria:

(1) Diagnosis of moderately to severely active Crohn's disease

-AND-

(2) **One** of the following:

(a) History of failure, contraindication or intolerance to Humira (adalimumab) and Cimzia (certolizumab)]

-OR-

(b) For continuation of prior Stelara therapy

-AND-

(3) Patient is not receiving Stelara in combination with **any** of the following:

(a) Biologic DMARD [e.g., Remicade/Inflectra (infliximab), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(b) Janus Kinase Inhibitor [e.g., Xeljanz (tofacitinib)]
(c) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

-AND-

(4) Prescribed by or in consultation with a gastroenterologist

Authorization will be issued for 12 months.

2. Reauthorization

(1) Documentation of positive clinical response to Stelara therapy

-AND-

(2) Patient is not receiving Stelara in combination with **any** of the following:

(a) Biologic DMARD [e.g., Remicade/Inflectra (infliximab), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
(b) Janus Kinase Inhibitor [e.g., Xeljanz (tofacitinib)]
(c) Phosphodiesterase 4 (PDE4) inhibitor [e.g. Otezla (apremilast)]

Authorization will be issued for 12 months.

3. References:

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Program	Program type – Prior Authorization
Change Control	
Date	Change
12/2013	New Criteria
3/2015	▪ For plaque psoriasis, removed requirement to try conventional therapies, including phototherapy (one of the following:

	ultraviolet light B [UVB] used alone or in combination with topical or systemic treatments, pulsed dye laser, psoralen and exposure to ultraviolet light A [PUVA], photochemotherapy) and systemic therapy (one of the following: methotrexate, cyclosporine, acitretin, hydroxyurea, sulfasalazine, 6-thioguanine, mycophenolate). ▪ For plaque psoriasis, changed requirement of trial of Humira and Enbrel to trial of Humira only due to Enbrel PDL deletion ▪ The examples of biologic DMARDs in the concomitant therapy criterion have been revised to list the most commonly utilized products: Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab). ▪ Reauthorization criteria revised to include concomitant therapy criteria (biologic DMARD or janus kinase inhibitor). ▪ For psoriatic arthritis (initial authorization), added rheumatologist as a prescriber. ▪ For psoriatic arthritis changed requirement of trial of Humira and Enbrel to trial of Humira and Cimzia due to Enbrel PDL deletion and Cimzia PDL addition
3/2016	Added Enbrel to prerequisite therapy requirement for both psoriasis and psoriatic arthritis initial therapy sections Removed all “notes to prescriber” Updated policy template
10/2016	Updated background. Added Phosphodiesterase 4 (PDE4) inhibitor to combination therapy requirements. Added criteria section for Crohn’s disease.
2/2017	Added statement that Stelara IV is not a pharmacy benefit. Updated policy template.
9/2017	Added Otezla to preferred products for diagnoses of psoriatic arthritis and plaque psoriasis
2/2018	Removed Otezla as a step therapy medication. Added step through Cosentyx for psoriasis section.

STELARA® (USTEKINUMAB)

Policy Number: CS2018D0045L **Effective Date**: April 1, 2018

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Related Community Plan Policy

- Maximum Dosage Policy

Commercial Policy

- Stelara® (Ustekinumab)

INSTRUCTIONS FOR USE

This Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced. The terms of the federal, state or contractual requirements for benefit plan coverage may differ greatly from the standard benefit plan upon which this Drug Policy is based. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage supersedes this Drug Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the contractual requirements for benefit plan coverage prior to use of this Drug Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the federal, state or contractual requirements for benefit coverage.

COVERAGE RATIONALE

This policy refers to Stelara (ustekinumab) injection.

Stelara is proven and medically necessary for the treatment of:

I. **Crohn's disease when ALL of the following criteria are met**: [1]
   A. Diagnosis of moderately to severely active Crohn's disease; **and**
   B. **One** of the following:
      1. History of failure, contraindication, or intolerance to at least one tumor necrosis factor (TNF) blocker [e.g., Remicade/Inflectra (infliximab), Humira (adalimumab), Cimzia (certolizumab)]; **or**
      2. **Both** of the following:
         a. History of failure, contraindication, or intolerance to at least **one** immunomodulator or corticosteroid (e.g., corticosteroids, 6-mercaptopurine, azathioprine, methotrexate, etc.)
         b. Patient has never failed a TNF blocker [e.g., Remicade/Inflectra (infliximab), Humira (adalimumab), Cimzia (certolizumab)];

   and
   C. **One** of the following:
      1. Initial therapy:

a. Stelara is to be administered as an intravenous induction dose; **and**
b. Stelara induction dosing is accordance with the United States Food and Drug Administration approved labeled dosing for Crohn's disease:
   i. 260mg for patients weighing ≤55kg
   ii. 390mg for patients weighing >55kg to ≤85kg
   iii. 520mg for patients weighing >85kg;
   and
c. Patient is not receiving Stelara in combination with **any** of the following:
   i. Biologic DMARD [e.g., Remicade/Inflectra (infliximab), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
   ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [16]
   iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)];
   and
d. Authorization will be for one induction dose;

or

2. Continuation therapy:
   a. Patient is unable to self-administer subcutaneous doses; **and**
   b. Stelara is to be subcutaneously administered 8 weeks after the initial intravenous dose; **and**
   c. Stelara continuation dosing is in accordance with the United States Food and Drug Administration approved labeled dosing for Crohn's disease:
      i. 90mg every 8 weeks subcutaneously;
      and
   d. Patient is not receiving Stelara in combination with **any** of the following:
      i. Biologic DMARD [e.g., Remicade/Inflectra (infliximab), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      ii. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [16]
      iii. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)].

II. **Plaque psoriasis when ALL of the following criteria are met**: [1]
   A. Diagnosis of moderate to severe plaque psoriasis; **and**
   B. **One** of the following:
      1. Patient is a candidate for phototherapy
      2. Patient is a candidate for systemic therapy;
      and
   C. Patient is unable to self-administer subcutaneous doses; **and**
   D. Stelara is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for plaque psoriasis up to a maximum of (or equivalent dose and interval schedule):
      1. 45mg every 12 weeks for patients weighing ≤100kg subcutaneously
      2. 90mg every 12 weeks for patients weighing >100kg subcutaneously;
      and
   E. Patient is not receiving Stelara in combination with **any** of the following:
      1. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)][16]
      3. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)].

III. **Psoriatic arthritis when ALL of the following criteria are met**: [1]
   A. Diagnosis of psoriatic arthritis; **and**
   B. Stelara is initiated and titrated according to U.S. Food and Drug Administration labeled dosing for psoriatic arthritis up to a maximum of 90mg every 12 weeks subcutaneously (or equivalent dose and interval schedule); **and**
   C. Patient is unable to self-administer subcutaneous doses; **and**
   D. Patient is not receiving Stelara in combination with **any** of the following:
      1. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
      2. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)][16]
      3. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)].

Stelara is unproven and not medically necessary for the treatment of:

- Multiple sclerosis.

In available studies, Stelara does not demonstrate efficacy in the treatment of multiple sclerosis.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Stelara is a human interleukin-12 and -23 antagonist indicated for the treatment of:

- Adult patients (18 years or older) with: [1]
  - Moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy
  - Active psoriatic arthritis, alone or in combination with methotrexate
  - Moderately to severely active Crohn's disease who have:
    - Failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker; or
    - Failed or were intolerant to treatment with one or more TNF blockers.
- Adolescent patients (12 years or older) with:
  - Moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

BACKGROUND

Stelara is a human IgG1κ monoclonal antibody that binds with high affinity and specificity to the p40 protein subunit used by both the interleukin (IL)-12 and IL-23 naturally occurring cytokines. IL-12 and IL-23 are involved in inflammatory and immune responses, such as natural killer cell activation and CD4+ T-cell differentiation and activation. [1]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J3357	Ustekinumab, for subcutaneous injection, 1 mg
J3358	Ustekinumab, for intravenous injection, 1 mg

ICD-10 Diagnosis Code	Description
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications

ICD-10 Diagnosis Code	Description
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
L40.0	Psoriasis vulgaris
L40.1	Generalized pustular psoriasis
L40.2	Acrodermatitis continua
L40.3	Pustulosis palmaris et plantaris
L40.4	Guttate psoriasis
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis
L40.54	Psoriatic juvenile arthropathy
L40.59	Other psoriatic arthropathy
L40.8	Other psoriasis
L40.9	Psoriasis, unspecified

Maximum Dosage Requirements

Maximum Allowed Quantities by HCPCS Units

This section provides information about the maximum dosage per administration for ustekinumab administered by a medical professional.

Medication Name		Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic			
Stelara	ustekinumab	90 mg	J3357	90 HCPCS units (1 mg per unit)

HCPCS Code Based Maximum Dosage Information

Maximum Allowed Quantities by National Drug Code (NDC) Units

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDC's for each drug product and is subject to change.

Medication Name		How Supplied	National Drug Code	Maximum Allowed
Brand	Generic			
Stelara	ustekinumab	45 mg/0.5 mL prefilled syringe	57894-0060-03	0.5 mL
Stelara	ustekinumab	45 mg/0.5 mL solution in vials	57894-0060-02	0.5 mL
Stelara	ustekinumab	90 mg/1 mL prefilled syringe	57894-0061-03	1 mL

CLINICAL EVIDENCE

Proven

Crohn's Disease

Ustekinumab was evaluated in three randomized, double-blind, placebo-controlled clinical studies in adult patients with moderately to severely active Crohn's disease. There were two 8-week intravenous induction studies followed by a 44-week subcutaneous randomized withdrawal maintenance study representing 52 weeks of therapy. [1,17]

In the two induction studies, 1409 patients were randomized, and 1368 (CD-1, n=741; CD-2, n=628) were included in the final efficacy analysis. Induction of clinical response at Week 6 and clinical remission at Week 8 were primary endpoints. In both studies, patients were randomized to receive a single intravenous administration of ustekinumab at

approximately 6 mg/kg, placebo, or 130 mg. In the first study, patients had failed or were intolerant to prior treatment with a TNF blocker: 29% patients had an inadequate initial response (primary non-responders), 69% responded but subsequently lost response (secondary non-responders) and 36% were intolerant to a TNF blocker. Of these patients, 48% failed or were intolerant to one TNF blocker and 52% had failed 2 or 3 prior TNF blockers. At baseline and throughout this study, approximately 46% of the patients were receiving corticosteroids and 31% of the patients were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The median baseline CDAI score was 319 in the ustekinumab approximately 6 mg/kg group and 313 in the placebo group. [1,17,18]

In the second induction study, patients had failed or were intolerant to prior treatment with corticosteroids (81% of patients), at least one immunomodulator; (68% of patients), or both (49% of patients). Additionally, 69% never received a TNF blocker and 31% previously received but had not failed a TNF blocker. At baseline, and throughout the study, approximately 39% of the patients were receiving corticosteroids and 35% of the patients were receiving immunomodulators. The median baseline CDAI score was 286 in the ustekinumab and 290 in the placebo group. [1,17,18]

In both of the induction studies, a greater proportion of patients treated with ustekinumab achieved clinical response at Week 6 and clinical remission at Week 8 compared to placebo. Clinical response and remission were significant as early as Week 3 in ustekinumab treated patients and continued to improve through Week 8. [1,17,18]

The maintenance study, evaluated 388 patients who achieved clinical response (≥100 point reduction in CDAI score) at Week 8 of induction with ustekinumab in either of the induction studies. Patients were randomized to receive a subcutaneous maintenance regimen of either 90 mg ustekinumab every 8 weeks or placebo for 44 weeks. [1,17,18]

At Week 44, 47% of patients who received ustekinumab were corticosteroid-free and in clinical remission, compared to 30% of patients in the placebo group. At Week 0 of this study, 34/56 (61%) ustekinumab treated patients who previously failed or were intolerant to TNF blocker therapies were in clinical remission and 23/56 (41%) of these patients were in clinical remission at Week 44. In the placebo arm, 27/61 (44%) patients were in clinical remission at Week 0 while 16/61 (26%) of these patients were in remission at Week 44. At Week 0 of this study, 46/72 (64%) ustekinumab treated patients who had previously failed immunomodulator therapy or corticosteroids (but not TNF blockers) were in clinical remission and 45/72 (63%) of these patients were in clinical remission at Week 44. In the placebo arm, 50/70 (71%) of these patients were in clinical remission at Week 0 while 31/70 (44%) were in remission at Week 44. In the subset of these patients who were also naïve to TNF blockers, 34/52 (65%) of ustekinumab treated patients were in clinical remission at Week 44 as compared to 25/51 (49%) in the placebo arm. Patients who were not in clinical response 8 weeks after ustekinumab induction were not included in the primary efficacy analyses; however, these patients were eligible to receive a 90 mg subcutaneous injection of ustekinumab upon entry into the maintenance study. Of these patients, 102/219 (47%) achieved clinical response eight weeks later and were followed for the duration of the study. [1,17,18]

Plaque Psoriasis

A phase 3, multi-center, double-blind, placebo-controlled, randomized study evaluated the safety and efficacy of ustekinumab in patients age 12 to 17 years who had moderate-to-severe psoriasis.[17] Patients (n = 110) were randomly assigned (2:2:1:1) ratio to ustekinumab (SD; 0.75 mg/kg [≤60 kg], 45 mg [>60 - ≤100 kg], and 90 mg [>100 kg]) or half-standard dosing (HSD; 0.375 mg/kg [≤60 kg], 22.5 mg [>60 - ≤100 kg], and 45 mg [>100 kg]) at weeks 0 and 4 and every 12 weeks or placebo at weeks 0 and 4 with crossover to ustekinumab SD or HSD at weeks 12 and 16 and thereafter every 12 weeks through week 40. At week 8, patients with a PASI increase ≥50% from baseline were eligible to commence treawtment with moderate-to-high potency topical steroid preparations through week 12. The primary endpoint was the proportion of patients with a Physician's Global Assessment (PGA) 0/1 at week 12. Major secondary endpoints were the proportions of patients achieving at least 75% improvement in PASI (PASI 75) and at least 90% improvement in PASI (PASI 90) at week 12 and the change from baseline in Childrens' Dermatology Life Quality Index (CDLQI) at week 12. Assessments were performed through week 52. At week 12, the proportions of patients achieving PGA 0/1 were significantly greater in the HSD (67.6%) and SD (69.4%) groups versus placebo (5.4%; P < 0.001 for both dose groups). Approximately one-third of patients in each ustekinumab group achieved PGA 0/1 at week 4. Significantly greater proportions of patients in the HSD (32.4%) and SD (47.2%) groups achieved a PGA of 0 at week 12 compared to placebo (2.7%, bot P < 0.001). Significantly greater proportions of patients receiving ustekinumab achieved PASI 75 (HSD, 78.4%; SD, 80.6%; placebo, 10.8%; P < 0.001) or PASI 90 (HSD, 54.1%; SD, 61.1%; placebo, 5.4%; P < 0.001). Additionally, 21.6% of patients in the HSD group and 38.9% in the SD group achieved a PASI score of 0 (cleared) at week 12 compared with 2.7% in the placebo group (P = .014 and P < 0.001, respectively). The treatment effect of both the HSD and SD of ustekinumab through week 12 for patients <60 kg was consistent with that observed in patients >60 kg to ≤100 kg. Placebo patients who crossed over to ustekinumab at week 12, PASI 75 response rates increased by week 16 and were maintained through week 52. The proportions of patients achieving PGA 0/1, PASI 75, or PASI 90 after crossover were generally similar to those observed in patients who started ustekinumab at baseline. Through week 40, all 110 patients received at least 1 injection of ustekinumab; among these, 81.8% reported an adverse event (AE) through week 60. By week 12, only one serious AE (SAE) was reported in the HSD group. After week 12, 5 additional

singular SAEs were reported (total, 6; HSD, 5; SD, 1) through week 60. The investigators concluded that ustekinumab, in patients 12 to 17 years, the standard dose provided response comparable to that in adults with no unexpected adverse events through 1 year.

Griffiths et al. conducted a blinded, multi-center, head-to-head comparison of ustekinumab versus etanercept in the treatment of moderate-to-severe plaque psoriasis.[11] Patients (n=903) were randomly assigned in a 3:5:5 ratio to receive subcutaneous injections of ustekinumab 45 mg (n=209) at weeks 0 and 4, ustekinumab 90 mg (n=347) at weeks 0 and 4, or etanercept 50 mg (n=347) twice weekly for 12 weeks. The primary end point was the proportion of patients with at least 75% improvement in the PASI index at week 12. A secondary end point was the proportion with cleared or minimal disease on the basis of the physician's global assessment. At week 12, a total of 67.5% of patients who received 45 mg of ustekinumab and 73.8% of patients who received 90 mg of ustekinumab had at least 75% improvement in the PASI score, as compared with 56.8% of those who received high-dose etanercept (p=0.01 and p<0.001, respectively). Similarly, 65.1% of patients who received 45 mg of ustekinumab and 70.6% of patients who received 90 mg of ustekinumab had cleared or minimal disease according to the physician's global assessment, as compared with 49.0% of those who received etanercept (p<0.001 for both comparisons). Among patients who did not have a response to etanercept, 48.9% had at least 75% improvement in the PASI within 12 weeks after crossover to ustekinumab. One or more adverse events occurred through week 12 in 66.0% of patients who received 45 mg of ustekinumab and 69.2% of patients who received 90 mg of ustekinumab and in 70.0% who received etanercept; 1.9%, 1.2%, and 1.2%, respectively, had serious adverse events. Safety patterns were similar before and after crossover from etanercept to ustekinumab. The investigators concluded that ustekinumab at a dose of 45 or 90 mg had superior efficacy to high-dose etanercept over a 12-week period in patients with psoriasis.

Unproven

Multiple Sclerosis

Kasper et al. conducted a phase I, double-blind, placebo-controlled, sequential dose escalation study in 20 subjects with multiple sclerosis (MS).[8] Subjects were randomized (4:1) to receive a single subcutaneous injection of either ustekinumab (0.3, 0.75, 1.5, and 3 mg/kg) or placebo. Clinical and laboratory evaluations were performed through 16 weeks following administration. Single subcutaneous administrations of ustekinumab in this first study of relapsing MS were generally well tolerated. Adverse events were generally mild or moderate, with no apparent dose-related trends. There was a large degree of variability in T2 lesion volume and total number of gadolinium-positive lesions, both unaffected by dose escalation. Three relapses of MS occurred in two placebo-treated subjects. Over the range of single doses studied, the median Tmax ranged from 9.0 to 16.5 days, and the median $T_{1/2}$ ranged from 20.2 to 30.9 days. The authors concluded that safety of ustekinumab in MS needs to be tested in a study of longer duration and involving a larger cohort of subjects.

In a phase II, multicenter, randomized, double-blind, placebo-controlled trial, Segal et al. studied repeated injections of ustekinumab in patients (n=249) with relapsing-remitting multiple sclerosis (RRMS).[9] Subjects aged 18-65 years were assigned to one of five groups: placebo (n=49) or four different ustekinumab dosages (n=50 for all) at weeks 0, 1, 2, 3, 7, 11, 15, and 19. Ustekinumab doses were 27 mg, 90 mg q8w, 90 mg, or 180 mg; the 90 mg q8w dosage group received placebo substitute at weeks 7 and 15. The primary endpoint was the cumulative number of new gadolinium-enhancing T1-weighted lesions on serial cranial MRI through week 23. Patients were followed up through week 37. In the intent to treat analysis, ustekinumab treatment did not show a significant reduction in the primary endpoint for any dosage groups versus placebo. At week 37, adverse events occurred in 38 (78%) placebo-treated patients and 170 (85%) ustekinumab-treated patients, with infections most commonly reported. Serious adverse events occurred in one (2%) placebo-treated patient and six (3%) ustekinumab-treated patients. Malignant diseases were reported in two patients shortly after the initiation of ustekinumab treatment; both patients were withdrawn from the trial and given appropriate treatment, which resulted in complete remission. No serious infections, cardiovascular events, or exacerbation of demyelinating events occurred. A dose-dependent increase in serum concentrations of ustekinumab was recorded. The investigators concluded that ustekinumab is generally well tolerated but does not show efficacy in reducing the cumulative number of gadolinium-enhancing T1-weighted lesions in multiple sclerosis.

Professional Societies

The American Academy of Dermatology guidelines of care for the management of psoriasis and psoriatic arthritis (PsA) state that patients with limited skin disease should not automatically be treated with systemic treatment if they do not improve, because treatment with systemic therapy may carry more risk than the disease itself. [10]

The strength of AAD recommendations for the treatment of moderate to severe plaque psoriasis using ustekinumab is A (highest recommendation; level I evidence). Compared with the TNF-alfa inhibitors, the most comprehensive ustekinumab safety data to date come from a pooled analysis of phase II and phase III clinical trials involving slightly more than 3,000 patients with just over 3 years of continuous therapy. Therefore, the use of registries to monitor the long-term safety of ustekinumab and other new agents currently under development, and to monitor the long-term

safety of all of the systemic agents available, is an essential step in defining the long-term adverse effects of ustekinumab and other new agents. [11]

When considering the use of ustekinumab for PsA, the AAD states that until the results of ongoing phase III trials of ustekinumab for PsA become available, the TNF-alfa inhibitors should be considered the biologic class of choice for this patient population. [11]

Technology Assessments

A 2016 Cochrane review was published to assess the efficacy and safety of anti-IL-12/23p40 antibodies for induction of remission in Crohn's disease. The review evaluated six studies with 2324 participants. The authors concluded that the high quality evidence suggests that ustekinumab is effective for induction of clinical remission and clinical improvement in patients with moderate to severe Crohn's disease. Moderate to high quality evidence suggests that the optimal dosage of ustekinumab is 6 mg/kg. Briakinumab and ustekinumab appear to be safe. Moderate quality evidence suggests no increased risk of serious adverse events. Future studies are required to determine the long-term efficacy and safety of ustekinumab in patients with moderate to severe Crohn's disease. [19]

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for STELARA® (ustekinumab). Local Coverage Determinations (LCDs) do not exist at this time.

Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf. (Accessed January 11, 2018)

STATE EXCEPTIONS

State	Note
Kansas	Drug policy not approved for use in this market

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
04/01/2018	• Updated supporting information to reflect the most current FDA information and references; no change to coverage rationale or lists of applicable codes • Archived previous policy version CS2018D0045K

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Xeljanz/Xeljanz XR

Program	Prior Authorization
Medication	Xeljanz and Xeljanz XR (tofacitinib)
Markets in Scope	California, Florida-CHIP, Hawaii, Maryland, Nevada, New Jersey, New Mexico, New York, Ohio, Pennsylvania, Rhode Island
Issue Date	3/2013
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy or in combination with methotrexate or other disease-modifying antirheumatic drugs (DMARDs).

XELJANZ/XELJANZ XR is also indicated for the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other DMARDs.

2. Coverage Criteria:

A. Rheumatoid Arthritis (RA)

1. **Initial Authorization**

a. Diagnosis of moderately to severely active RA (e.g., swollen, tender joints with limited range of motion)

-AND-

b. Prescribed or recommended by a rheumatologist

-AND-

c. History of failure, contraindication, or intolerance to methotrexate

-AND-

d. **One** of the following:

(1) **Both** of the following:

(a) History of failure, contraindication, or intolerance to **two** of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-AND-

(b) History of failure, contraindication, or intolerance to Kevzara (sarilumab)

-OR-

(2) For continuation of prior Xeljanz/Xeljanz XR therapy

-AND-

e. Patient is not receiving Xeljanz/Xeljanz XR in combination with a biologic DMARD [e.g. Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

-AND-

f. Patient is not receiving Xeljanz/Xeljanz XR in combination with a potent immunosuppressant (e.g., azathioprine or cyclosporine)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Xeljanz/Xeljanz XR therapy

-AND-

b. Patient is not receiving Xeljanz/Xeljanz XR in combination with a biologic DMARD [e.g. Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

-AND-

c. Patient is not receiving Xeljanz/Xeljanz XR in combination with a potent immunosuppressant (e.g., azathioprine or cyclosporine)

Authorization will be issued for 12 months.

B. Psoriatic Arthritis (PsA)

1. **Initial Authorization**

a. Diagnosis of active psoriatic arthritis

-AND-

b. Prescribed or recommended by a rheumatologist or dermatologist

-AND-

c. History of failure, contraindication, or intolerance to one non-biologic disease modifying anti-rheumatic drug (DMARD) [eg, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine]

-AND-

d. **One** of the following:

(1) History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Enbrel (etanercept)

-OR-

(2) For continuation of prior Xeljanz/Xeljanz XR therapy

-AND-

e. Patient is not receiving Xeljanz/Xeljanz XR in combination with a biologic DMARD [e.g. Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

-AND-

f. Patient is not receiving Xeljanz/Xeljanz XR in combination with a potent immunosuppressant (e.g., azathioprine or cyclosporine)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. Documentation of positive clinical response to Xeljanz/Xeljanz XR therapy

-AND-

b. Patient is not receiving Xeljanz/Xeljanz XR in combination with a biologic DMARD [e.g. Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]

-AND-

c. Patient is not receiving Xeljanz/Xeljanz XR in combination with a potent immunosuppressant (e.g., azathioprine or cyclosporine)

Authorization will be issued for 12 months.

3. References:

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Program	Program type – Prior Authorization
Change Control	
Date	Change
3/2013	New Guideline
2/2015	Template updated Removed age requirement for all indications. Changed requirement that there is a trial of two of the following: Cimzia, Enbrel, Humira, Simponi to new requirement of trial of both Humira and Cimzia or continuation of existing Xeljanz therapy. Added requirement to the reauthorization criteria that the patient is not using Xeljanz in combination with a biologic DMARD
3/2016	Added Enbrel to prerequisite therapy list Updated policy template
10/2016	Annual Review – no change
1/2017	Added "Xeljanz XR" where only Xeljanz was listed previously – criteria applies to both Xeljanz and Xeljanz XR Updated policy template
3/2017	Minor updates to policy template
2/2018	Updated step therapy medications in the rheumatoid arthritis section to a trial of two TNF inhibitors and Kevzara due to PDL changes effective 4/1/18. Added review criteria for psoriatic arthritis. Updated background and references.

Clinical Policy: Lenalidomide (Revlimid)

Reference Number: CP.PHAR.71
Effective Date: 07.01.11
Last Review Date: 05.18
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Lenalidomide (Revlimid®) is an immunomodulatory agent with antiangiogenic and antineoplastic properties.

FDA Approved Indication

Revlimid is indicated for the treatment of patients with:

- Transfusion-dependent anemia due to low- or intermediate-risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities
- Multiple myeloma (MM), in combination with dexamethasone
- MM as maintenance following autologous hematopoietic stem cell transplantation
- Mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib (Velcade)

Limitation of use: Revlimid is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Revlimid is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Will be used for one of the following indications (a, b, or c):
   a. In combination with dexamethasone;
   b. As maintenance therapy as a single agent following autologous hematopoietic stem cell transplantation;
   c. As maintenance therapy as a single agent for active (symptomatic) myeloma after response to primary myeloma therapy;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 25 mg/day;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

B. Myelodysplastic Syndrome (must meet all):
1. Diagnosis of MDS;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has symptomatic or transfusion-dependent anemia due to MDS;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

C. Mantle Cell Lymphoma (must meet all):
1. Diagnosis of MCL;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Will be used for one of the following indications (a, b, or c):
   a. Relapsed or progressive disease after two prior therapies, one of which included bortezomib;
   b. In combination with rituximab;
   c. Second-line therapy as a single agent;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 25 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

D. Other NCCN Compendium Supported Diagnoses/Indications (off-label) (must meet all):
1. Prescribed for one of the following NCCN category 1 or 2a recommended indications (Refer to :
   a. Myelofibrosis-associated anemia;
   b. Systemic light chain amyloidosis in combination with dexamethasone;
   c. Classic Hodgkin lymphoma as subsequent therapy for relapsed or refractory disease, or as palliative therapy;
   d. Any of the following non-Hodgkin lymphoma subtypes:
      i. T-cell leukemia/lymphoma as second-line therapy;

ii. AIDS-related B-cell lymphoma as second-line or subsequent therapy;
iii. Castleman's disease (CD) as subsequent therapy following treatment of relapsed, refractory, or progressive disease;
iv. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) as first or second-line maintenance therapy, or for relapsed or refractory disease;
v. Diffuse large B-cell lymphoma;
vi. Follicular lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
vii. Gastric MALT lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
viii. Mycosis fungoides /Sezary syndrome;
ix. Nodal marginal zone lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
x. Nongastric MALT lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
xi. Peripheral T-cell lymphoma as second-line and subsequent therapy;
xii. Primary cutaneous CD30+ T-cell lymphoproliferative disorders as therapy for relapsed or refractory anaplastic large cell lymphoma with multifocal lesions or regional nodes;
xiii. Splenic marginal zone lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
xiv. Post-transplant lymphoproliferative disorders of B-cell lymphomas as second-line or subsequent therapy

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 25 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

E. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or documentation supports that member is currently receiving Revlimid and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):

a. New dose does not exceed 25 mg/day for MM and MCL and 10 mg/day for MDS;
b. Requested new dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 12 months
Commercial - Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AIDS: acquired immune deficiency syndrome
FDA: Food and Drug Administration
MALT: mucosa-associated lymphoid tissue
MCL: mantle cell lymphoma
MDS: myelodysplastic syndrome
MM: multiple myeloma
CD: Castleman's disease
CLL: chronic lymphocytic leukemia
NCCN: National Comprehensive Cancer Network
REMS: Risk Evaluation and Mitigation Strategy
SLL: small lymphocytic lymphoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
melphalan/ prednisone (MP)	**Multiple Myeloma** (Conventional primary therapy) melphalan 8 mg/m^2/day PO days 1-4; prednisone 60 mg/m2/day PO days 1-4. Repeat cycle every 28 days	As recommended in dosing regimen
vincristine*/ doxorubicin*/ dexamethasone (VAD)	**Multiple Myeloma** (Conventional primary therapy) vincristine 0.4 mg/day IV continuous infusion days 1- 4; doxorubicin 9 mg/m2/day IV continuous infusion days 1-4; dexamethasone 40 mg PO days 1-4, 9-12, 17-20. Repeat cycle every 28-35 days	As recommended in dosing regimen
dexamethasone (pulse dose as single agent)	**Multiple Myeloma** (Conventional primary therapy) dexamethasone 40 mg PO days 1-4, 9-12, 17-20	As recommended in dosing regimen
Thalomid® (thalidomide)/ dexamethasone	**Multiple Myeloma** (Conventional primary therapy) thalidomide 200 mg/day PO daily; dexamethasone 40 mg/day days 1-4, 9-12,17-20 for odd cycles and days 1-4 for even cycles. Repeat cycle every 28 days	As recommended in dosing regimen
Pomalyst® (pomalidomide)	**Multiple Myeloma** 4 mg PO QD on days 1-21 of repeated 28-day cycles until disease progression. Pomalyst may be given in combination with dexamethasone. Pomalyst may be given in combination with Kyprolis/dexamethasone Avoid Pomalyst in patients with a serum creatinine greater than 3.0 mg/dL	4 mg/day
Velcade® (bortezomib)*	**Mantle Cell Lymphoma**	1.3 mg/m^2/dose

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	1.3 mg/m^2/dose SC or IV BIW for 2 weeks (Days 1, 4, 8, and 11) followed by a 10-day rest period (Days 12-21) for six 3-week cycles. For extended therapy of more than 8 cycles, Velcade may be administered on the standard schedule or on a maintenance schedule of once weekly for 4 weeks (Days 1, 8, 15, and 22) followed by a 13-day rest period (Days 23 to 35). At least 72 hours should elapse between consecutive doses of Velcade	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- Anemia is defined as hemoglobin level less than 10 g/dl.
- Transfusion dependence was defined in two different studies as either greater than 2 units or greater than 4 units of RBCs within 8 weeks prior to enrollment into the studies.
- According to National Comprehensive Cancer Network (NCCN) guideline, the following are 2A recommendations: a) MDS with no deletion of 5q with a poor probability of response to immunosuppressive therapy or following no response to hematopoietic cytokines, b) systemic light chain amyloidosis, and c) second line therapy for Non-Hodgkins Lymphoma (Adult T-cell leukemia/lymphoma, AIDS Related B-Cell Lymphoma, Castleman's disease, Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), Diffuse Large B-Cell Lymphoma, Follicular Lymphoma, Gastric and Nongastric MALT Lymphoma, Mycosis fungoides /Sezary syndrome, Nodal marginal zone lymphoma, Peripheral T-cell lymphoma, Primary cutaneous CD30+ T-cell lymphoproliferative disorders, and Splenic Marginal Zone Lymphoma).
- According to NCCN guideline, current drug therapies for MCL include: a) induction therapy (including CHOP [Cytoxan, Adriamycin, vincristine, and prednisone] and hyperCVAD [Cytoxan, vincristine, Adriamycin, and dexamethasone] - given in frequent smaller doses, and b) second-line therapy (including Velcade+Rituxan and Revlimid+Rituxan).
- In the pivotal trial, patients with MCL were required to have received prior treatment with an anthracycline or mitoxantrone, cyclophosphamide, Rituxan, and Velcade, alone or in combination. Among these agents, Velcade is the only FDA approved medication indicated for the treatment of MCL.
- Inclusion criteria for studies with Revlimid allowed for previous use of Thalomid in patients with refractory/relapsing MM. Eight percent of patients previously treated with Thalomid demonstrated a complete response with 53.3% showing an overall response to Revlimid + Dexamethasone and 45.2% demonstrating a partial response.

- The FDA notified the public of an increased risk of second primary malignancies in patients with newly-diagnosed MM who received Revlimid. Clinical trials conducted after Revlimid was approved showed that newly-diagnosed patients treated with Revlimid had an increased risk of developing acute myelogenous leukemia, myelodysplastic syndromes, and Hodgkin lymphoma.
- Revlimid is only available under a restricted distribution program called the Revlimid REMS program due to the black box warning for fetal risk, hematologic toxicity, and deep vein thrombosis/pulmonary embolism. Patient and physician enrollment in the manufacturer's REMS program is required.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Myelodysplastic Syndrome	10 mg PO QD Dosing is modified based upon clinical and laboratory findings	10 mg/day
Multiple Myeloma (maintenance therapy)	10 mg PO QD continuously (Days 1-28 of repeated 28-day cycles) until disease progression or unacceptable toxicity. After 3 cycles of maintenance therapy, the dose can be increased to 15 mg once daily if tolerated. Dosing is modified based upon clinical and laboratory findings	15 mg/day
Multiple Myeloma (primary therapy for newly diagnosed patients)	25 mg PO QD days 1-21 of repeated 28 day cycles with dexamethasone 40 mg PO QD on days 1, 8, 15, 22 of each 28 day cycle Dosing is modified based upon clinical and laboratory findings	25 mg/day
Multiple Myeloma (previously treated patients)	25 mg PO QD days 1-21 of repeated 28 days cycles with dexamethasone 40 mg QD days 1-4, 9-12 and 17- 20 of each 28	25 mg/day

Indication	Dosing Regimen	Maximum Dose
	day cycle for the first 4 cycles then 40 mg QD for days 1-4 every 28 days Dosing is modified based upon clinical and laboratory findings	
Relapsed Multiple Myeloma (previously treated patients)	25 mg PO QD days 1-21 of repeated 28 day cycles with dexamethasone 40 mg PO QD on days 1, 8, 15, 22 and Kyprolis. Maximum 18 cycles for Kyprolis. <u>Cycle 1:</u> 20 mg/m^2 IV over 10 minutes on days 1-2. If tolerated, increase to target dose of 27 mg/m^2 IV over 10 minutes on days 8, 9, 15, 16 <u>Cycles 2-12:</u> 27 mg/m^2 IV over 10 minutes on days 1, 2, 8, 9, 15, 16 <u>Cycles 3-18</u> 27 mg/m^2 IV over 10 minutes on days 1, 2, 15, 16 Kyprolis dosed at a maximum body surface area of 2.2 m^2	25 mg/day
Mantle Cell Lymphoma	25 mg PO QD on Days 1-21 of repeated 28-day cycles Dosing is modified based upon clinical and laboratory findings	25 mg/day
Amyloidosis	25 mg PO QD days 1-21 of repeated 28 days cycles with dexamethasone 40 mg once per week. Dosing of Revlimid can be reduced to 15 mg/day for tolerability and can be	25 mg/day

Indication	Dosing Regimen	Maximum Dose
	combined with dexamethasone and either melphalan or cyclophosphamide	

VI. Product Availability

Capsule: 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg

VII. References

1. Revlimid Prescribing Information. Summit, NJ: Celgene Corporation; December 2017. Available at: http://media.celgene.com/content/uploads/revlimid-pi.pdf. Accessed January 18, 2017.
2. List A, Kurtin S, Roe D, et al. Efficacy of Lenalidomide in Myelodysplastic Syndromes. N Engl J Med. 2005; 352 (6): 549-557.
3. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 1.2018. Available at: http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed January 22, 2018.
4. National Comprehensive Cancer Network. Multiple Myeloma Version 3.2018. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed January 22, 2018.
5. National Comprehensive Cancer Network. B-cell Lymphomas Version 7.2017. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed January 22, 2018.
6. National Comprehensive Cancer Network. Systemic Light Chain Amyloidosis Version 1.2018. Available at http://www.nccn.org/professionals/physician_gls/PDF/amyloidosis.pdf. Accessed January 22, 2018.
7. Weber DM, Chen C, et.al. Lenalidomide plus dexamethasone for relapsed multiple myeloma in North America. N Engl J Med. 2007 Nov 22; 357(21):2133-42.
8. Lacy MQ, Ertz MA, et.al. Long-term results of response to therapy, time to progression, and survival with lenalidomide plus dexamethasone in newly diagnosed myeloma. Mayo Clinic Proceedings. 2007 Oct; 82 (10):1179-84.
9. FDA Drug Safety Communication: Safety review update of cancer drug Revlimid (lenalidomide) and risk of developing new types of malignancies. Available at: https://www.fda.gov/Drugs/DrugSafety/ucm302939.htm. Accessed January 22, 2018.
10. Revlimid. American Hospital Formulary Service Drug Information. Available at: http://www.medicinescomplete.com/mc/ahfs/current/. Accessed June 22, 2018.
11. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 22, 2018.
12. Clinical Pharmacology Web site. Available at: http://clinicalpharmacologyip.com/default.aspx. Accessed: January 22, 2018.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added efficacy data for all 3 indications Reviewed and added references Added appendix A, B, C Changed authorization period to 3 months in algorithm for safety purposes	07.14	07.14
Added pregnancy testing and age requirements to narrative and algorithm Removed requirement to try other therapies before Revlimid for MM in algorithm as Figure 1: Added age requirement and REMS questions; removed requirement to try other therapies before Revlimid for MM in algorithm as Revlimid is for both newly diagnosed and relapsed/refractory MM – removed corresponding Appendix of possible previous therapies for MM; edited approval periods in algorithm per Centene policy. Updated safety information	05.15	06.15
Converted policy to new template. Documentation requests removed. Age requirement removed. NCCN recommended uses added. Added REMS program and safety information to background.	05.16	06.16
Converted policy to new template. Updated FDA indication for use as maintenance therapy as a single agent following autologous hematopoietic stem cell transplantation. Removed hypersensitivity criteria.	03.17	06.17
For MM, NCCN recommended uses updated to include 1) regimens for primary therapy or subsequent therapy for disease relapse after 6 months with same regimen, 2) subsequent therapies for relapsed, progressive or refractory disease in addition to single agent therapy. Under myelodysplastic syndrome, NCCN recommended use changed from "serum erythropoietin levels ≤ 500 mU/mL, no response to erythropoietins," to "serum erythropoietin levels ≤ 500 mU/mL, in combination with epoetin alpha or darbepoetin alpha if no response to erythropoietins alone". Under MCL, NCCN recommended uses updated to include 1) induction therapy, 2) change from "use as second-line therapy for stage I-II disease or aggressive stage II bulky, III, or IV disease for relapsed, refractory, or progressive disease" to "second-line therapy as a single agent, with rituximab, or with ibrutinib and rituximab for stage I-IV disease". Under "other indications," added myelofibrosis-associated anemia and marginal zone lymphoma. Maximum dose added. Safety information removed. Global Biopharm language added under "Other Diagnoses/ Indications". Approval durations increased from 3/6 to 6/12 months.	05.17	06.17
2Q 2018 annual review: added HIM line of business; policies combined for Commercial and Medicaid lines of business; MDS:	01.22.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
removed criteria requirements for low-risk disease and deletion 5q cytogenetic abnormality; MCL: removed disease staging; removed off-label use for primary cutaneous B-cell lymphoma; references reviewed and updated.		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

Clinical Policy: Thalidomide (Thalomid)

Reference Number: CP.PHAR.78
Effective Date: 09.01.11
Last Review Date: 05.18
Line of Business: HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Thalomid, α-(N-phthalimido) glutarimide, is an immunomodulatory agent.

FDA Approved Indication(s)

Thalomid is indicated:

- For the treatment of patients with newly diagnosed multiple myeloma (MM) in combination with dexamethasone
- For the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)
- As maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence

Limitation of use: Thalomid is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Thalomid is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥12 years;
4. Prescribed in combination with dexamethasone;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 200 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Erythema Nodosum Leprosum (must meet all):

1. Diagnosis of ENL;

2. Prescribed by or in consultation with an infectious disease specialist, immunologist, or dermatologist;
3. Age ≥12 years;
4. Dose does not exceed 400 mg/day.

Approval duration: 6 months

C. Myeloproliferative Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of myeloproliferative neoplasms (myelofibrosis);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥12 years;
4. Prescribed in combination with prednisone for management of myelofibrosis-associated anemia;
5. Member meets one of the following (a or b):
   a. Serum EPO ≥ 500 mU/mL;
   b. Serum EPO < 500 mU/mL, and no response or loss of response to erythropoietic stimulating agents;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 400 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Castleman's Disease (off-label) (must meet all)**:**
1. Diagnosis of multicentric Castleman's disease;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥12 years;
4. Prescribed as subsequent therapy with or without rituximab for disease that has progressed following treatment of relapsed/refractory or progressive disease;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 400 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

E. Kaposi Sarcoma (off-label) (must meet all)**:**
1. Diagnosis of AIDS-related Kaposi Sarcoma;
2. Prescribed by or in consultation with an oncologist or immunologist;
3. Age ≥12 years;
4. Prescribed in combination with antiretroviral therapy;
5. Disease has progressed or not responded to doxorubicin and paclitaxel;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 400 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

F. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma (off-label) (must meet all)**:**
1. Diagnosis of Waldenstrom's macroglobulinemia or lymphoplasmacytic lymphoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥12 years;
4. Prescribed as a single agent or in combination with rituximab for one of the following (a or b):
   a. Primary therapy;
   b. Therapy for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 400 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

G. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or documentation supports that member is currently receiving Thalomid and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose meets one of the following (a or b):
   a. Dose does not exceed 400 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies –

HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ENL: erythema nodosum leprosum
FDA: Food and Drug Administration
MM: multiple myeloma
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Doxorubicin	Kaposi Sarcoma: 20 mg/m^2 IV every3 weeks	20 mg/m^2/dose
Paclitaxel	Kaposi Sarcoma: 100 mg/m^2 IV every 2 weeks	100 mg/m^2/dose

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- Thalomid is only available under a restricted distribution program called the Thalomid REMS program due to a black box warning for embryo-fetal toxicity. Patient and physician enrollment in the manufacturer's REMS program is required.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	200 mg orally once daily	200 mg/day
ENL	100 to 300 mg orally once daily	400 mg/day

VI. Product Availability

Capsules: 50 mg, 100 mg, 150 mg, 200 mg

VII. References

1. Thalomid Prescribing Information. Summit, NJ: Celgene Corporation; December 2017. Available at http://media.celgene.com/content/uploads/thalomid-pi.pdf. Accessed January 22, 2018.
2. Thalidomide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 22, 2018.
3. Multiple myeloma (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed January 22, 2018.
4. AIDS-Related Kaposi Sarcoma (Version 1.2018). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed January 31, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added background and safety information to include MOA and clinical response requirements. Added Appendix A and B Modified black box warning Changed approval period on algorithm Deleted "Intent to treat" question	08.14	08.14
Background: Edited for clarity Figure 1: Added REMS question and age requirement Updated safety information	06.15	06.15
Converted policy to new template. FDA approved uses: max dose added for multiple myeloma and ENL. Age requirement removed. NCCN recommended uses added. Added safety information to background.	05.16	06.16
Under multiple myeloma, NCCN recommended uses updated 1) maintenance therapy is removed, 2) non-transplant option removed under primary therapy or therapy 6 months after the same regimen, 3) for transplant candidates, "in combination with dexamethasone" is changed to "in combination with bortezomib and dexamethasone", 4) under relapsed, progressive or refractory disease, uses as a single agent and in combination with dexamethasone are removed; subsequent therapy as part of the VTD-PACE regimen is added. Maximum dose added. Under "other indications", myelofibrosis-associated anemia is added. Safety information removed. Global Biopharm language added under "Other Diagnoses/Indications". Approval durations are increased from 3/6 to 6/12 months.	05.17	06.17
2Q 2018 annual review: added HIM line of business; added prescriber and age requirements; removed off label indication for systemic light chain amyloidosis that is no longer included in NCCN Compendium; added off-label use for Kaposi Sarcoma; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; references reviewed and updated.	01.22.18	05.18

Important Reminder

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plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

Clinical Policy: Pomalidomide (Pomalyst)

Reference Number: CP.PHAR.116
Effective Date: 07.01.13 Revision Log
Last Review Date: 05.18
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Pomalidomide (Pomalyst®) is a thalidomide analogue.

FDA Approved Indication(s)

Pomalyst is indicated, in combination with dexamethasone, for patients with multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Pomalyst is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of an immunomodulatory agent (e.g., lenalidomide*, thalidomide*) and a proteasome inhibitor (e.g., bortezomib*, carfilzomib*) unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required.*
5. Dose does not exceed 4 mg/day on days 1-21 of repeated 28-day cycles.

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

B. AIDS-Related Kaposi Sarcoma (off-label) (must meet all)**:**

1. Diagnosis of AIDS-related Kaposi sarcoma;
2. Failure of at least two prior therapies;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 4 mg/day on days 1-21 of repeated 28-day cycles;

b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

C. Systemic Light Chain Amyloidosis (off-label) (must meet all)**:**
1. Diagnosis of systemic light chain amyloidosis;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is relapsed or refractory to prior therapy;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 4 mg/day on days 1-21 of repeated 28-day cycles;
   b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

D. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (meets all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Pomalyst for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 4 mg/day on days 1-21 of repeated 28-day cycles;
   b. Requested new dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM - 12 months
Commercial - Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MM: multiple myeloma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Revlimid® (lenalidomide)	*MM* 25 mg PO QD days 1-21 of repeated 28 day cycles.	25 mg/day
Thalomid® (thalidomide)	*MM* 200 mg PO QD.	200 mg/day
Velcade® (bortezomib)	*MM* 1.3 mg/m^2/dose for 9 multi-dose treatment cycles with retreatment if indicated.	1.3 mg/m^2/dose
First- and second-line therapies: • Liposomal doxorubicin (Doxil, Lipodox 50) • paclitaxel	*AIDS-related Kaposi Sarcoma* • Liposomal doxorubicin: 20 mg/m^2 IV once every 21 days • Paclitaxel: 135 mg/m^2 IV over 3 hours every 3 weeks **or** 100 mg/m^2 over 3 hours every 2 weeks	Varies
Drugs central to first-line therapy regimens: • bortezomib (Velcade®) • Revlimid® (lenalidomide) • melphalan (Alkeran®)	*Systemic Light Chain Amyloidosis* • Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	4 mg PO QD on days 1-21 of repeated 28-day cycles.	4 mg/day

VI. Product Availability

Capsule: 1 mg, 2 mg, 3 mg, 4 mg

VII. References

1. Pomalyst Prescribing Information. Summit, NJ: Celgene Corporation; Dcember 2017. Available at http://www.celgene.com/content/uploads/pomalyst-pi.pdf. Accessed January 2018.
2. Pomalidomide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 2018.
3. Multiple myeloma (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed January 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Updated background information; added Appendix A and B; reviewed and added references	07.14	07.14
Background: Added age criteria, and pregnancy/renal/hepatic monitoring information; updated safety information Figure 1: Added REMS question, and questions around labs and age; edited question about previous therapy per PI – removed related appendix since was no longer necessary; edited approval periods per Centene policy. Updated references	06.15	06.15
Converted policy to new template. FDA approve use: max dose added for multiple myeloma. Age requirement removed. NCCN recommended uses added. Added REMS program and safety information to background.	05.16	06.16
For MM, added thalidomide and lenalidomide as an example of prior immunomodulatory therapy. Maximum dose added. Pregnancy contraindication removed; toxicity after dose reduction to 1 mg and dermatologic reactions removed as reasons to discontinue. Global Biopharm language added under "Other Diagnoses/Indications". Approval durations are increased from 3/6 to 6/12 months.	05.17	06.17
2Q 2018 annual review: policies combined for Commercial and Medicaid; HIM line of business added; added age and COC; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; off-label Kaposi sarcoma and amyloidosis added; references updated.	02.13.18	05.18

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Immunomodulator Utilization

July 1, 2017 - June 30, 2018
Fee for Service
POS

QuarterFilled	Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
2017 Q3	ACTEMRA	4	12	336	43.2	$ 32,915.61
2017 Q3	CIMZIA	8	18	510	18	$ 66,691.26
2017 Q3	CIMZIA STARTER KIT	1	1	30	3	$ 11,583.57
2017 Q3	COSENTYX	1	1	56	4	$ 8,859.71
2017 Q3	COSENTYX SENSOREADY PEN	6	14	392	37	$ 103,677.14
2017 Q3	ENBREL	12	21	814	116.52	$ 105,723.63
2017 Q3	ENBREL SURECLICK	32	79	2374	337.12	$ 371,317.28
2017 Q3	ENTYVIO	1	2	112	2	$ 10,861.78
2017 Q3	HUMIRA	20	35	996	82	$ 176,417.34
2017 Q3	HUMIRA PEN	64	136	3999	314	$ 644,970.64
2017 Q3	HUMIRA PEN-CROHNS DISEASE	1	1	30	6	$ 12,961.07
2017 Q3	HUMIRA PEN-PSORIASIS STAR	7	7	209	28	$ 60,509.82
2017 Q3	KINERET	2	5	140	131.32	$ 25,924.53
2017 Q3	ORENCIA	2	6	170	24	$ 22,064.65
2017 Q3	OTEZLA	6	14	420	840	$ 31,226.02
2017 Q3	REMICADE	1	1	1	7	$ 7,924.29
2017 Q3	RITUXAN	3	9	119	740	$ 64,036.05
2017 Q3	SIMPONI	1	3	84	1.5	$ 12,008.88
2017 Q3	STELARA	4	5	316	4.5	$ 82,276.10
2017 Q3	TALTZ	2	5	140	12	$ 57,379.05
2017 Q3	TREMFYA	1	1	56	1	$ 9,694.17
2017 Q3	XELJANZ	6	12	360	720	$ 43,873.32
2017 Q3	XELJANZ XR	5	12	360	360	$ 33,011.59
2017 Q4	ACTEMRA	4	9	252	32.4	$ 30,117.29
2017 Q4	CIMZIA	8	21	600	21	$ 78,027.00
2017 Q4	COSENTYX	3	3	72	13	$ 31,003.90
2017 Q4	COSENTYX SENSOREADY PEN	6	18	566	41	$ 116,684.56
2017 Q4	ENBREL	8	18	508	65.08	$ 58,358.39
2017 Q4	ENBREL SURECLICK	32	77	2216	321.44	$ 354,063.73
2017 Q4	HUMIRA	22	57	1717	140	$ 300,991.83
2017 Q4	HUMIRA PEN	56	126	3832	316	$ 663,616.50
2017 Q4	HUMIRA PEN-CROHNS DISEASE	6	6	147	36	$ 77,766.42
2017 Q4	HUMIRA PEN-PSORIASIS STAR	3	3	119	12	$ 25,932.78
2017 Q4	KINERET	2	5	140	150.08	$ 29,620.77
2017 Q4	ORENCIA	4	8	224	32	$ 29,554.00
2017 Q4	ORENCIA CLICKJECT	1	2	56	8	$ 7,677.48
2017 Q4	OTEZLA	7	14	416	830	$ 32,934.85
2017 Q4	RITUXAN	2	3	132	290	$ 25,220.78
2017 Q4	SIMPONI	1	3	84	1.5	$ 12,052.44
2017 Q4	STELARA	4	4	286	3.5	$ 64,186.99

2017 Q4	TALTZ	2	4	112	5	$ 23,927.43
2017 Q4	TREMFYA	1	2	112	2	$ 19,388.34
2017 Q4	XELJANZ	3	9	270	540	$ 33,147.26
2017 Q4	XELJANZ XR	5	7	210	210	$ 21,958.36
2018 Q1	ACTEMRA	5	7	202	25.2	$ 24,521.21
2018 Q1	CIMZIA	6	14	452	16	$ 62,678.71
2018 Q1	COSENTYX	3	5	146	7	$ 23,325.14
2018 Q1	COSENTYX SENSOREADY PEN	9	21	658	41	$ 104,261.51
2018 Q1	ENBREL	9	20	622	86.88	$ 65,702.97
2018 Q1	ENBREL SURECLICK	32	69	2101	309.68	$ 342,196.08
2018 Q1	ENTYVIO	1	2	112	2	$ 11,746.44
2018 Q1	HUMIRA	23	48	1425	120	$ 270,531.86
2018 Q1	HUMIRA PEN	71	151	4750	390	$ 834,443.89
2018 Q1	HUMIRA PEN-CROHNS DISEASE	2	2	70	12	$ 28,434.62
2018 Q1	HUMIRA PEN-PSORIASIS STAR	1	1	28	4	$ 8,644.26
2018 Q1	KINERET	3	7	196	206.36	$ 40,733.14
2018 Q1	ORENCIA	4	10	280	40	$ 39,687.16
2018 Q1	ORENCIA CLICKJECT	2	5	140	20	$ 20,274.24
2018 Q1	OTEZLA	6	12	400	690	$ 27,031.33
2018 Q1	RITUXAN	1	3	84	270	$ 24,421.77
2018 Q1	SIMPONI	1	3	86	1.5	$ 13,122.42
2018 Q1	STELARA	9	10	588	8.5	$ 118,508.17
2018 Q1	TALTZ	3	8	224	13	$ 66,797.91
2018 Q1	TREMFYA	1	2	112	2	$ 20,337.38
2018 Q1	XELJANZ	5	8	240	480	$ 31,575.58
2018 Q1	XELJANZ XR	5	7	210	210	$ 19,538.81
2018 Q2	ACTEMRA	3	5	146	18	$ 16,623.11
2018 Q2	CIMZIA	5	10	282	10	$ 39,299.90
2018 Q2	COSENTYX	2	6	168	12	$ 42,472.44
2018 Q2	COSENTYX SENSOREADY PEN	7	13	458	36	$ 85,830.16
2018 Q2	ENBREL	10	26	742	86.96	$ 102,084.22
2018 Q2	ENBREL SURECLICK	23	48	1580	239.12	$ 289,691.56
2018 Q2	ENTYVIO	1	1	56	1	$ 5,873.22
2018 Q2	HUMIRA	21	42	1284	104	$ 241,869.00
2018 Q2	HUMIRA PEN	71	145	4469	363	$ 814,995.75
2018 Q2	HUMIRA PEN-CROHNS DISEASE	5	5	126	30	$ 71,086.55
2018 Q2	HUMIRA PEN-PSORIASIS STAR	1	1	28	4	$ 9,481.76
2018 Q2	KINERET	3	5	140	112.56	$ 15,296.54
2018 Q2	ORENCIA	3	4	112	16	$ 16,012.76
2018 Q2	ORENCIA CLICKJECT	2	5	140	20	$ 19,986.40
2018 Q2	OTEZLA	7	14	460	810	$ 27,914.23
2018 Q2	RITUXAN	4	8	321	870	$ 78,675.42
2018 Q2	SIMPONI	1	3	90	1.5	$ 13,122.42
2018 Q2	STELARA	7	8	504	6.5	$ 109,613.62
2018 Q2	TALTZ	4	10	308	17	$ 87,539.20
2018 Q2	TREMFYA	1	1	56	1	$ 10,168.69
2018 Q2	XELJANZ	4	7	270	540	$ 35,943.47
2018 Q2	XELJANZ XR	3	5	150	150	$ 19,943.85

PAD

QuarterFilled	Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
2017 Q3	ACTEMRA	1	6	6	90	$ 4,629.00
2017 Q3	COSENTYX	1	1	1	1	$ 25.00
2017 Q3	ENTYVIO	4	5	5	5	$ 21,807.98
2017 Q3	HUMIRA PEN	1	4	4	85	$ 10.00
2017 Q3	INFLECTRA	1	2	2	36	$ 17,047.80
2017 Q3	ORENCIA	12	29	29	83	$ 50,002.55
2017 Q3	REMICADE	21	36	36	121.05	$ 108,042.49
2017 Q3	RITUXAN	24	58	58	3030	$ 220,378.43
2017 Q3	TREMFYA	1	2	2	2	$ 40.00
2017 Q4	ACTEMRA	2	12	12	116	$ 8,642.96
2017 Q4	CIMZIA	1	4	4	4	$ 15,265.05
2017 Q4	ENTYVIO	3	4	4	4	$ 11,529.20
2017 Q4	HUMIRA PEN	1	1	1	40	$ 2.50
2017 Q4	INFLECTRA	2	4	4	14	$ 13,247.92
2017 Q4	ORENCIA	12	28	28	86	$ 47,845.43
2017 Q4	REMICADE	19	35	35	138	$ 128,313.45
2017 Q4	RITUXAN	30	75	75	4290	$ 290,121.85
2017 Q4	TREMFYA	1	2	2	2	$ 40.00
2018 Q1	ACTEMRA	2	9	9	142	$ 14,796.40
2018 Q1	CIMZIA	1	4	4	4	$ 16,177.28
2018 Q1	ENTYVIO	4	7	7	306	$ 78,135.70
2018 Q1	HUMIRA PEN	1	1	1	2.5	$ 2.50
2018 Q1	INFLECTRA	3	9	9	26	$ 24,603.28
2018 Q1	ORENCIA	13	38	38	105	$ 53,657.52
2018 Q1	REMICADE	17	32	32	120	$ 105,543.26
2018 Q1	RITUXAN	33	75	75	4850	$ 367,655.04
2018 Q1	STELARA	1	1	1	45	$ 32.00
2018 Q1	TALTZ	1	1	1	1	$ 20.00
2018 Q1	TREMFYA	1	1	1	1	$ 20.00
2018 Q2	ACTEMRA	2	7	7	88	$ 9,169.60
2018 Q2	ENTYVIO	5	8	8	8	$ 40,756.02
2018 Q2	INFLECTRA	2	6	6	19	$ 17,979.32
2018 Q2	ORENCIA	11	26	26	80	$ 39,160.40
2018 Q2	REMICADE	17	31	31	103.4	$ 89,925.65
2018 Q2	RITUXAN	28	67	67	3590	$ 225,549.27
2018 Q2	STELARA	1	1	1	45	$ 32.00

Anthem IMMUNOMOD	3Q 2017	4Q 2017	1Q 2018	2Q 2018	Total
ACTEMRA 162 MG/0.9 ML SYRINGE	3	1		3	7
CIMZIA 200 MG VIAL KIT	1				1
CIMZIA 200 MG/ML SYRINGE KIT	4	5	5	5	19
COSENTYX 150 MG/ML PEN INJECT		2	3	2	7
COSENTYX 300 MG DOSE-2 PENS	3	4	4	3	14
ENBREL 25 MG KIT	2	2	2	4	10
ENBREL 25 MG/0.5 ML SYRINGE	4	5	6	6	21
ENBREL 50 MG/ML SURECLICK SYR	29	37	41	43	150
ENBREL 50 MG/ML SYRINGE	5	4	11	9	29
ENTYVIO 300 MG VIAL	3				3
HUMIRA 20 MG/0.4 ML SYRINGE	3	2	1	1	7
HUMIRA 40 MG/0.8 ML PEN	100	100	106	118	424
HUMIRA 40 MG/0.8 ML SYRINGE	12	6	4	9	31
HUMIRA PEN CROHN-UC-HS 40 MG	1	2	2	7	12
HUMIRA PEN PSORIA-UVEITIS 40MG	3	1	3	3	10
KEVZARA 200 MG/1.14 ML SYRINGE	1				1
ORENCIA 125 MG/ML SYRINGE	2	3	3	4	12
ORENCIA 250 MG VIAL	1				1
ORENCIA CLICKJECT 125 MG/ML			1	1	2
OTEZLA 28 DAY STARTER PACK			1		1
OTEZLA 30 MG TABLET	1	6	6	8	21
REMICADE 100 MG VIAL	12	9	8	11	40
STELARA 45 MG/0.5 ML SYRINGE	3	3	5	5	16
STELARA 90 MG/ML SYRINGE	1	2	1	2	6
TREMFYA 100 MG/ML SYRINGE				1	1
XELJANZ 5 MG TABLET		3	3		6
XELJANZ XR 11 MG TABLET	2				2
Grand Total	**196**	**197**	**216**	**245**	**854**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Immunomodulator Utilization

July 1, 2017 - June 30, 2018

Q3 2017 - POS				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
CIMZIA KIT STARTER	7	7	58	21
CIMZIA PREFL KIT 200MG/ML	20	46	58	47
COSENTYX INJ 150MG/ML	1	1	28	4
COSENTYX INJ 300DOSE	2	5	28	10
COSENTYX PEN INJ 150MG/ML	2	6	28	6
COSENTYX PEN INJ 300DOSE	4	6	42	20
ENBREL INJ 25/0.5ML	2	5	28	10
ENBREL INJ 25MG	2	4	28	24
ENBREL INJ 50MG/ML	6	10	28	39
ENBREL SRCLK INJ 50MG/ML	30	57	42	250
HUMIRA KIT 40MG/0.8	18	46	28	96
HUMIRA PEN INJ 40MG/0.8	152	355	28	740
HUMIRA PEN INJ CROHNS	2	2	28	12
HUMIRA PEN INJ PSORIASI	9	9	28	36
KEVZARA INJ 200/1.14	1	3	28	6
KINERET INJ	2	4	42	46
ORENCIA INJ 125MG/ML	2	4	28	16
ORENCIA CLCK INJ 125MG/ML	3	7	28	28
SIMPONI INJ 100MG/ML	3	8	56	8
SIMPONI INJ 50/0.5ML	3	9	30	4.5
STELARA INJ 45MG/0.5	13	16	112	8
STELARA INJ 90MG/ML	7	11	198	11
XELJANZ TAB 5MG	4	8	30	480
XELJANZ XR TAB 11MG	3	7	30	210

Q3 2017 - PAD			
Drug Name	Count of Members	Count of Claims	Sum of Qty
ABATACEPT INJECTION	8	8	10
CANAKINUMAB INJECTION	3	3	3
INJECTION, INFLIXIMAB, EXCLUDES BIOSIMILAR, 10 MG	21	21	28
INJECTION, TOCILIZUMAB, 1MG	2	2	2
INJECTION, VEDOLIZUMAB, 1 MG	4	4	4

J-CODE PROCESSED INLCUDE: J0129, J0638, J1745, J3262, J3380

Q4 2017 - POS				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
CIMZIA KIT STARTER	3	3	30	9
CIMZIA PREFL KIT 200MG/ML	21	53	28	53
COSENTYX INJ 150MG/ML	1	3	28	3
COSENTYX INJ 300DOSE	2	3	28	6
COSENTYX PEN INJ 150MG/ML	4	8	28	14
COSENTYX PEN INJ 300DOSE	6	15	28	48
ENBREL INJ 25/0.5ML	4	10	28	30
ENBREL INJ 25MG	3	6	28	36
ENBREL INJ 50MG/ML	11	22	28	94
ENBREL SRCLK INJ 50MG/ML	38	95	28	431.2
HUMIRA KIT 40MG/0.8	21	39	28	82
HUMIRA PEN INJ 40MG/0.8	144	355	28	732
HUMIRA PEN INJ CROHNS	12	12	28	72
HUMIRA PEN INJ PSORIASI	8	8	28	32
KEVZARA INJ 200/1.14	2	2	28	4
KINERET INJ	7	12	42	318
ORENCIA INJ 125MG/ML	1	3	28	12
ORENCIA CLCK INJ 125MG/ML	4	7	28	28
SIMPONI INJ 100MG/ML	3	10	56	10
SIMPONI INJ 50/0.5ML	3	8	30	4
STELARA INJ 45MG/0.5	10	10	142	5
STELARA INJ 90MG/ML	8	8	198	8
XELJANZ TAB 5MG	2	5	30	300
XELJANZ XR TAB 11MG	4	9	30	270

Q4 2017 - PAD			
Drug Name	Count of Members	Count of Claims	Sum of Qty
ABATACEPT INJECTION	6	6	6
CANAKINUMAB INJECTION	3	3	3
INJECTION, INFLIXIMAB, EXCLUDES BIOSIMILAR, 10 MG	23	23	34
INJECTION, TOCILIZUMAB, 1MG	2	2	2
INJECTION, VEDOLIZUMAB, 1 MG	4	4	4

J-CODE PROCESSED INLCUDE: J0129, J0638, J1745, J3262, J3380

Q1 2018 - POS				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
CIMZIA KIT STARTER	5	5	58	15
CIMZIA PREFL KIT 200MG/ML	21	44	28	44
COSENTYX INJ 150MG/ML	2	5	28	8
COSENTYX INJ 300DOSE	1	1	28	2
COSENTYX PEN INJ 150MG/ML	3	6	28	6
COSENTYX PEN INJ 300DOSE	7	18	28	42
ENBREL INJ 25/0.5ML	2	4	58	8
ENBREL INJ 25MG	3	7	28	48
ENBREL INJ 50MG/ML	13	25	28	117
ENBREL SRCLK INJ 50MG/ML	37	77	28	321
HUMIRA KIT 40MG/0.8	15	29	28	58
HUMIRA PEN INJ 40MG/0.8	144	337	58	714
HUMIRA PEN INJ CROHNS	8	8	28	48
HUMIRA PEN INJ PSORIASI	6	6	28	24
KEVZARA INJ 200/1.14	3	7	28	15
KINERET INJ	5	10	28	300
ORENCIA INJ 125MG/ML	3	5	28	20
ORENCIA CLCK INJ 125MG/ML	4	8	28	32
SIMPONI INJ 100MG/ML	1	3	28	3
SIMPONI INJ 50/0.5ML	3	10	30	5
STELARA INJ 45MG/0.5	10	11	112	5
STELARA INJ 90MG/ML	9	10	170	10
XELJANZ TAB 5MG	4	6	30	360
XELJANZ XR TAB 11MG	5	10	30	300

Q1 2018 - PAD			
Drug Name	Count of Members	Count of Claims	Sum of Qty
ABATACEPT INJECTION	10	10	11
CANAKINUMAB INJECTION	3	3	3
INJECTION, INFLIXIMAB, EXCLUDES BIOSIMILAR, 10 MG	24	24	38
INJECTION, TOCILIZUMAB, 1MG	2	2	2
INJECTION, VEDOLIZUMAB, 1 MG	4	4	4

J-CODE PROCESSED INLCUDE: J0129, J0638, J1745, J3262, J3380

Q2 2018 - POS				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
CIMZIA KIT STARTER	10	10	58	30
CIMZIA PREFL KIT 200MG/ML	22	47	28	47
COSENTYX INJ 150MG/ML	2	4	28	4
COSENTYX INJ 300DOSE	2	2	28	4
COSENTYX PEN INJ 150MG/ML	2	4	28	7
COSENTYX PEN INJ 300DOSE	7	14	28	28
ENBREL INJ 25/0.5ML	4	10	58	20
ENBREL INJ 25MG	5	7	28	36
ENBREL INJ 50MG/ML	13	30	28	125
ENBREL SRCLK INJ 50MG/ML	32	73	28	317
HUMIRA KIT 40MG/0.8	14	35	28	70
HUMIRA PEN INJ 40/0.4ML	1	1	28	2
HUMIRA PEN INJ 40MG/0.8	134	336	28	710
HUMIRA PEN INJ CROHNS	3	3	28	18
HUMIRA PEN INJ PSORIASI	6	6	28	24
ILARIS INJ 150MG/ML	1	1	28	1
KEVZARA INJ 200/1.14	6	10	28	22
KINERET INJ	4	10	28	300
ORENCIA INJ 125MG/ML	3	4	28	16
ORENCIA CLCK INJ 125MG/ML	4	7	28	28
SIMPONI INJ 100MG/ML	1	3	28	3
SIMPONI INJ 50/0.5ML	5	13	30	6
STELARA INJ 45MG/0.5	10	10	112	5
STELARA INJ 90MG/ML	8	8	198	8
XELJANZ TAB 5MG	3	5	30	300
XELJANZ XR TAB 11MG	4	10	30	300

Q2 2018 - PAD			
Drug Name	Count of Members	Count of Claims	Sum of Qty
ABATACEPT INJECTION	6	6	7
CANAKINUMAB INJECTION	2	2	2
INJECTION, INFLIXIMAB, EXCLUDES BIOSIMILAR, 10 MG	13	13	21
INJECTION, TOCILIZUMAB, 1MG	2	2	3
INJECTION, VEDOLIZUMAB, 1 MG	3	3	3

J-CODE PROCESSED INLCUDE: J0129, J0638, J1745, J3262, J3380

Immunomodulator Drugs Utilization - Q3 2017–Q2 2018

SilverSummith Healthplan

REPORT NAME	REPORT DATE	TOTAL CLAIMS	UNIQUE MEMBERS	NUMBER OF UNITS	DAYS SUPPLY
Immunomodulator Drugs	04/01/2017-06/30/2018	11	4	203	273

L. Immunomodulator Drugs

Therapeutic Class: Immunomodulators
Last Reviewed by the DUR Board: January 25, 2018

Actemra® (tocilizumab)	Ilaris® (canakinumab)	Stelara® (ustekinumab)
Amevive® (alefacept)	Kevzara® (sarilumab)	Xeljanz® (tofacitinib)
Arcalyst® (rilonacept)	Kineret® (ankinra)	
Cimzia® (certolizumab pegol)	Orencia® (abatacept)	
Consentyx® (secukinumab)	Remicade® (infliximab)	
Enbrel® (etanercept)	Siliq® (brodalumab)	
Entyvio® (vedolizumab)	Simponi® (golimumab)	
Humira® (adalimumab)	Simponi® ARIA™ (golimumab)	

Immunomodulator Drugs are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the SSA and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

Approval will be given if the following criteria are met and documented:

a. For all recipients:

1. The recipient has had a negative tuberculin test; and

2. The recipient does not have an active infection or a history of recurring infections; and

3. The approval will not be given for the use of more than one biologic at a time (combination therapy); and

4. Each request meets the appropriate diagnosis-specific criteria (b-j).

b. Rheumatoid Arthritis (RA):

1. The recipient has a diagnosis of moderately to severely active RA; and

2. The recipient is 18 years of age or older; and

3. The recipient has had a rheumatology consultation, including the date of the visit; and one of the following:

a. The recipient has had RA for ≤ six months (early RA) and has high disease activity; and an inadequate or adverse reaction to a disease modifying antirheumatic drug (DMARD) (methotrexate,

hydroxychloroquine, leflunomide, minocycline and sulfasalazine); or

b. The recipient has had RA for ≥ six months (intermediate or long-term disease duration) and has moderate disease activity and has an inadequate response to a DMARD (methotrexate, hydroxychloroquine, leflunomide, minocycline or sulfasalazine); or

c. The recipient has had RA for ≥ six months (intermediate or long-term disease duration) and has high disease activity.

c. Psoriatic Arthritis:

1. The recipient has a diagnosis of moderate or severe psoriatic arthritis; and

2. The recipient is 18 years of age or older; and

3. The recipient has had a rheumatology consultation including the date of the visit or a dermatology consultation including the date of the visit; and

4. The recipient had an inadequate response or a contraindication to treatment with any one nonsteroidal anti-inflammatory (NSAID) or to any one of the following DMARDs: methotrexate, leflunomide, cyclosporine or sulfasalazine.

d. Ankylosing Spondylitis:

1. The recipient has a diagnosis of ankylosing spondylitis; and

2. The recipient is 18 years or older; and

3. The recipient has had an inadequate response to NSAIDs; and

4. The recipient has had an inadequate response to any one of the DMARDs (methotrexate, hydroxychloroquine, sulfasalzine, leflunomide, minocycline).

e. Juvenile Rheumatoid Arthritis/Juvenile Idiopathic Arthritis:

1. The recipient has a diagnosis of moderately or severely active juvenile RA or juvenile idiopathic arthritis; and

2. The recipient is at an appropriate age, based on the requested agent, and:

a. Abatacept: Six years of age or older.

b. Adalimumab, canakinumab, etanercept, tocilizumab: Two years of age or older.

3. And the recipient has at least five swollen joints; and

4. The recipient has three or more joints with limitation of motion and pain, tenderness or both; and

5. The recipient has had an inadequate response to one DMARD.

f. Plaque Psoriasis:

1. The recipient has a diagnosis of chronic, moderate to severe plaque psoriasis; and

2. The recipient is 18 years of age of older; and

3. The agent is prescribed by a dermatologist; and

4. The recipient has failed to adequately respond to a topical agent; and

5. The recipient has failed to adequately respond to at least one oral treatment.

g. Crohn's Disease:

1. The recipient has a diagnosis of moderate to severe Crohn's Disease; and

2. The recipient is at an appropriate age, based on the requested agent:

a. Adalimumab, infliximab: Six years of age or older.

b. All others: 18 years of age or older.

3. And the recipient has failed to adequately respond to conventional therapy (e.g. sulfasalzine, mesalamine, antibiotics, corticosteroids, azathioprine, 6-mercaptopurine, leflunomide); or

4. The recipient has fistulizing Crohn's Disease.

h. Ulcerative Colitis:

1. The recipient has a diagnosis of moderate to severe ulcerative colitis; and

2. The recipient is at an appropriate age, based on the requested agent:

a. Infiximab: Six years of age or older.

b. All others: 18 years of age or older.

3. And the recipient has failed to adequately respond to one or more of the following standard therapies:

a. Corticosteroids;

b. 5-aminosalicylic acid agents;

c. Immunosuppresants; and/or

d. Thiopurines.

i. Cryopyrin-Associated Periodic Syndromes (CAPS): Familial Cold Autoinflamatory Syndromes (FCAS) or Muckle-Wells Syndrome (MWS):

1. The recipient has a diagnosis of FCAS or MWS; and

2. The recipient is at an appropriate age, based on the requested agent:

a. Canakinumab: Four years of age or older.

b. Rilonacept: 12 years of age or older.

j. Cryopyrin-Associated Periodic Syndromes (CAPS): Neonatal-Onset Multisystem Inflammatory Disease (NOMID):

1. The recipient has a diagnosis of NOMID.

2. Prior Authorization Guidelines

Prior Authorization forms are available at:
http://www.medicaid.nv.gov/providers/rx/rxforms.aspx

Prior authorization approval will be for one year.

Therapeutic Class Overview
Immunomodulators

INTRODUCTION

- Immunomodulators treat a wide variety of conditions, including rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), plaque psoriasis (PsO), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC), hidradenitis suppurativa (HS), and uveitis (UV), as well as several less common conditions.
- T cells, B cells, and cytokines such as tumor necrosis factor (TNF), interleukin-1 (IL-1) and interleukin-6 (IL-6) play a key role in the inflammatory and immune process (*Choy et al 2001*). This has led to the development of biologic agents to target these areas. The Food and Drug Administration (FDA) has currently approved 5 originator TNF inhibitors: Cimzia (certolizumab), Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab), and Simponi/Simponi Aria (golimumab), as well as 6 biosimilar TNF inhibitors: Amjevita (adalimumab-atto), Erelzi (etanercept-szzs), Inflectra (infliximab-dyyb), Renflexis (infliximab-abda), Cyltezo (adalimumab-adbm), and Ixifi (infliximab-qbtx). Other agents targeting different cells and cytokines are also FDA-approved for RA treatment. These include Orencia (abatacept), which inhibits CD28-B7 mediated costimulation of the T-cell; Rituxan (rituximab), which targets CD20, a molecule that is found on the surface of B-cells; Actemra (tocilizumab) and Kevzara (sarilumab), which have activity directed against the IL-6 receptor; and Kineret (anakinra), which targets the IL-1 receptor. Oral agents on the market, Xeljanz and Xeljanz XR (tofacitinib) and Olumiant (baricitinib), target Janus-associated kinase (JAK) pathways. By inhibiting the JAK pathway, the ability of cytokines to produce inflammation is reduced.
- Other immunomodulators include Ilaris (canakinumab), which binds to the IL-1ß receptor and is approved to treat JIA; and Entyvio (vedolizumab), which binds to the α4β7 integrin and is approved to treat CD and UC. Otezla (apremilast), an oral, small-molecule phosphodiesterase 4 (PDE-4) inhibitor, and Stelara (ustekinumab), which targets the IL-12 and IL-23 cytokines, are each approved for the treatment of PsA and PsO; Stelara is additionally indicated for the treatment of CD. Cosentyx (secukinumab) and Taltz (ixekizumab) bind and neutralize IL-17A and are indicated for the treatment of PsO and PsA; Cosentyx is additionally indicated to treat PsA and AS. Siliq (brodalumab), an IL-17 receptor antagonist, as well as Tremfya (guselkumab) and Ilumya (tildrakizumab-asmn), both IL-23 antagonists, are indicated for selected patients with PsO.
- Certain rare conditions for which immunomodulators are indicated are mentioned in this review but are not discussed in detail; these include:
    - Ilaris for the treatment of 1) cryopyrin-associated periodic syndromes (CAPS), specifically the subtypes familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS); 2) TNF receptor associated periodic syndrome (TRAPS); 3) hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD); and 4) familial Mediterranean fever (FMF)
    - Kineret for the treatment of CAPS, specifically neonatal-onset multisystem inflammatory disease (NOMID)
    - Actemra for giant cell arteritis (GCA) and cytokine release syndrome (CRS).
- Rituxan is also approved for non–Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), and granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis) and microscopic polyangiitis (MPA). These indications will not be discussed in this review.
- Tysabri (natalizumab), an integrin receptor antagonist, is indicated for multiple sclerosis and CD for patients who have had an inadequate response to, or are unable to tolerate conventional therapies and TNF inhibitors; it is not included as a drug product in this review (*Tysabri prescribing information 2018*). Arcalyst (rilonacept), an interleukin-1 blocker indicated for CAPS, is also not included in this review (*Arcalyst prescribing information 2016*).
- Although FDA-approved, the launch plans for the biosimilar drugs Amjevita (adalimumab-atto), Erelzi (etanercept-szzs), Cyltezo (adalimumab-adbm) and Ixifi (infliximab-qbtx) are pending and may be delayed; therefore, these agents are not currently included in this review. The manufacturer of Ixifi to date does not have plans to launch Ixifi in the United States.
- Medispan Classes: Antineoplastic-Monoclonal Antibodies, Antipsoriatics, Antirheumatic-Enzyme Inhibitors, Anti-TNF-Alpha-Monoclonal Antibodies, Integrin Receptor Antagonists, Interleukin-1 Receptor Antagonists, Interleukin-1beta Receptor Inhibitors, Interleukin-6 Receptor Inhibitors, PDE-4 Inhibitors, Selective Costimulation Modulators, Soluble Tumor Necrosis Factor Receptor Agents, Tumor Necrosis Factor Alpha Blockers

Table 1. Medications Included Within Class Review

Drug	Manufacturer	FDA Approval Date	Biosimilar or Generic Availability	Type of Agent
Actemra (tocilizumab)	Genentech	01/08/2010	-	Human monoclonal antibody targeting the IL-6 receptor
Cimzia (certolizumab)	UCB	04/22/2008	-	TNFα inhibitor
Cosentyx (secukinumab)	Novartis	01/21/2015	-	Human monoclonal antibody to IL-17A
Enbrel (etanercept)	Amgen	11/02/1998	-*	sTNFR fusion protein, TNFα inhibitor
Entyvio (vedolizumab)	Takeda Pharmaceuticals America, Inc.	05/20/2014	-	Human monoclonal antibody binds to the α4β7 integrin
Humira (adalimumab)	AbbVie	12/31/2002	-*	TNFα inhibitor
Ilaris (canakinumab)	Novartis	06/17/2009	-	Human monoclonal antibody that binds to IL-1ß
Ilumya (tildrakizumab-asmn)	Sun Pharma Global	03/20/2018	-	Human monoclonal antibody to IL-23
Inflectra (infliximab-dyyb)	Celltrion/ Hospira/Pfizer	04/05/2016	N/A†	TNFα inhibitor
Kevzara (sarilumab)	Sanofi Genzyme Regeneron	05/22/2017	-	Human monoclonal antibody targeting IL-6 receptor
Kineret (anakinra)	Swedish Orphan Biovitrum	11/14/2001	-	IL-1 receptor antagonist
Olumiant (baricitinib)	Eli Lilly	05/31/2018	-	Small molecule Janus kinase (JAK) inhibitor
Orencia (abatacept)	Bristol Myers Squibb	12/23/2005	-	sCTLA-4-Ig recombinant fusion protein
Otezla (apremilast)	Celgene Corporation	03/21/2014	-	Small-molecule phosphodiesterase 4 inhibitor
Remicade (infliximab)	Janssen Biotech	8/24/1998	-†	TNFα inhibitor
Renflexis (infliximab-abda)	Merck	04/21/2017	N/A†	TNFα inhibitor
Rituxan (rituximab)	Genentech	11/26/1997	-	Anti-CD20 monoclonal antibody
Siliq (brodalumab)	Valeant	02/15/2017	-	Human monoclonal antibody directed against the IL-17 receptor A (IL-17RA)
Simponi/ Simponi Aria (golimumab)	Janssen Biotech	04/24/2009 and 07/18/2013	-	TNFα inhibitor
Stelara (ustekinumab)	Janssen Biotech	09/25/2009	-	Human monoclonal antibody targeting the IL-12 and IL-23 cytokines
Taltz (ixekizumab)	Eli Lilly	03/22/2016	-	Human monoclonal antibody to IL-17A
Tremfya (guselkumab)	Janssen Biotech	07/13/2017	-	Human monoclonal antibody to IL-23 cytokine
Xeljanz / Xeljanz XR (tofacitinib)	Pfizer	11/06/2012 and 02/23/2016	-	Small molecule Janus kinase (JAK) inhibitor

*Erelzi (etanercept-szzs) has been FDA-approved as a biosimilar to Enbrel (etanercept). Amjevita (adalimumab-atto) and Cyltezo (adalimumab-adbm) have been FDA-approved as biosimilars to and Humira (adalimumab). The specific launch dates for these products are pending and may be delayed. Further information on Erelzi, Amjevita, and Cyltezo will be included in this review after these products have launched.
†Inflectra (infliximab-dyyb), Renflexis (infliximab-abda), and Ixifi (infliximab-qbtx) have been FDA-approved as biosimilar agents to Remicade (infliximab), however, they are not FDA-approved as interchangeable biologics.
(Drugs@FDA, 2018; Prescribing information: Actemra, 2018; Cimzia, 2018; Cosentyx, 2018; Enbrel, 2018; Entyvio, 2018; Humira, 2018; Ilaris, 2017; Ilumya 2018; Inflectra, 2018; Kevzara, 2018; Kineret, 2018; Olumiant 2018; Orencia, 2017; Otezla, 2017; Remicade, 2018; Renflexis, 2017; Rituxan, 2018; Siliq, 2017; Simponi, 2018; Simponi Aria, 2018; Stelara, 2018; Taltz, 2018; Tremfya, 2017; Xeljanz/Xeljanz XR, 2018)

Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

INDICATIONS

Table 2. Food and Drug Administration Approved Indications (see footnotes for less common indications: CAPS, CRS, FMF, GCA, HIDS/MKD, and TRAPS)

Drug	Rheumatoid Arthritis (RA)	Crohn's Disease (CD)	Systemic Juvenile Idiopathic Arthritis (SJIA)	Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Ulcerative Colitis (UC)	Hidradenitis Suppurativa (HS)	Uveitis (UV)
Actemra[ŷ] (tocilizumab)	✔ *		✔ **	✔ **						
Cimzia (certolizumab)	✔	✔			✔ ‡	✔	✔			
Cosentyx (secukinumab)					✔ ‡	✔	✔			
Enbrel (etanercept)	✔ †			✔ **	✔ ‡	✔ †	✔			
Entyvio (vedolizumab)		✔						✔		
Humira (adalimumab)	✔ ‡‡	✔ ⌐		✔ ∫	✔ ‡	✔ ∫∫	✔	✔	✔	✔ ▼
Ilaris" (canakinumab)			✔ **							

Drug	Rheumatoid Arthritis (RA)	Crohn's Disease (CD)	Systemic Juvenile Idiopathic Arthritis (SJIA)	Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Ulcerative Colitis (UC)	Hidradenitis Suppurativa (HS)	Uveitis (UV)
Ilumya (tildrakizumab-asmn)					✔ ‡					
Inflectra (infliximab-dyyb)	✔ ⊥	✔ ⌐⌐			✔ ‡‡‡	✔	✔	✔ ⊥⊥		
Kevzara (sarilumab)	✔ *									
Kineret▼▼ (anakinra)	✔ ∞									
Olumiant (baricitinib)	✔									
Orencia (abatacept)	✔ ∞∞			✔ ⌂		✔				
Otezla (apremilast)					✔ ‡	✔				

Drug	Rheumatoid Arthritis (RA)	Crohn's Disease (CD)	Systemic Juvenile Idiopathic Arthritis (SJIA)	Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Ulcerative Colitis (UC)	Hidradenitis Suppurativa (HS)	Uveitis (UV)
Remicade (infliximab)	✓	✓			✓	✓	✓	✓		
Renflexis (infliximab-abda)	✓	✓			✓	✓	✓	✓		
Rituxan‴ (rituximab)	✓									
Siliq (brodalumab)					✓					
Simponi (golimumab)	✓					✓	✓	✓		
Simponi Aria (golimumab)	✓					✓	✓			
Stelara (ustekinumab)		✓			✓	✓				

Drug	Rheumatoid Arthritis (RA)	Crohn's Disease (CD)	Systemic Juvenile Idiopathic Arthritis (SJIA)	Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Ulcerative Colitis (UC)	Hidradenitis Suppurativa (HS)	Uveitis (UV)
Taltz (ixekizumab)					✔ ‡	✔				
Tremfya (guselkumab)					✔ ‡					
Xeljanz/ Xeljanz XR (tofacitinib)	✔ ǂǂ					✔		✔ (Xeljanz only)		

ϒActemra is also indicated for treatment of giant cell arteritis in adults and chimeric antigen receptor T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients ≥ 2 years.
*Patients with moderately to severely active RA who have had an inadequate response (or intolerance [Kevzara]) to ≥ 1 Disease-Modifying Anti-Rheumatic Drugs (DMARDs).
**Patients 2 years and older.
†In combination with methotrexate (MTX) or used alone.
‡Indicated for the treatment of adult patients (18 years or older) with chronic moderate to severe PsO who are candidates for systemic therapy or phototherapy, with the exception of Enbrel, which is indicated for the treatment of patients 4 years and older with chronic moderate to severe PsO who are candidates for systemic therapy or phototherapy, and Stelara, which is indicated for the treatment of patients 12 years and older with moderate to severe PsO.
‡‡Indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA. Can be used alone or in combination with MTX or other DMARDs.
ǂǂǂ Indicated for the treatment of adult patients with chronic severe (ie, extensive and/or disabling) PsO who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.
∫Indicated for reducing signs and symptoms of JIA for patients 2 years of age and older. Can be used alone or in combination with MTX.
∫∫Indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA. Can be used alone or in combination with non-biologic DMARDs.
▼Treatment of non-infectious intermediate, posterior and panuveitis in adult patients.
▼▼Kineret is also indicated for the treatment of cryopyrin-associated periodic syndromes (CAPS) including neonatal-onset multisystem inflammatory disease (NOMID).
"Ilaris also indicated for the treatment of CAPS in adults and children 4 years of age and older including: familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS); tumor necrosis factor receptor associated periodic syndrome (TRAPS) in adult and pediatric patients; hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD) in adult and pediatric patients; and familial Mediterranean fever (FMF) in adult and pediatric patients.
∞Indicated for the reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active RA, in patients 18 years of age or older who have failed one or more DMARDs. Can be used alone or in combination with DMARDs other than TNF blocking agents.
∞∞Indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA. May be used as monotherapy or concomitantly with DMARDs other than TNF antagonists.
⌂ Indicated for reducing signs and symptoms in pediatric patients 2 years and older with moderate to severely active PJIA. May be used as monotherapy or with MTX.
⌐For all patients 6 years of age and older, indicated for reducing signs and symptoms and inducing and maintaining clinical remission in patients who have had an inadequate response to conventional therapy. For adults, also indicated for reducing signs and symptoms and inducing clinical remission if patients have also lost a response to or are intolerant of infliximab.

⌐⌐Indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy and for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD. And for patients 6 years of age and older for reducing signs and symptoms and inducing and maintaining clinical remission with moderately to severely active disease who have had an inadequate response to conventional therapy.
⌐⌐⌐Indicated for treatment of adult patients with moderately to severely active CD who have: 1) failed or were intolerant to treatment with immunomodulators or corticosteroids but never failed a TNF blocker, or 2) failed or were intolerant to treatment with ≥ 1 TNF blockers
┴In combination with MTX, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active RA.
┴┴For reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy. Also for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy (Remicade only). The biosimilars Inflectra and Renflexis did not receive FDA approval for pediatric UC due to existing marketing exclusivity for Remicade for this indication (not for clinical reasons).
'‘Rituxan also indicated for Non–Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), and granulomatosis with polyangiitis (GPA) (Wegener's Granulomatosis) and microscopic polyangiitis (MPA).
╪In combination with MTX is indicated for the treatment of adult patients with moderately- to severely- active RA who have had an inadequate response to ≥ 1TNF antagonist therapies.
╪╪Treatment of moderate to severe PsO in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies.
┤ In combination with MTX, is indicated for the treatment of adult patients with moderately to severely active RA.
┤ ┤ Alone or in combination with MTX, is indicated for the treatment of adult patients with active PsA.
╪╪Indicated for the treatment of adult patients with moderately to severely active RA who have had an inadequate response or intolerance to MTX. It may be used as monotherapy or in combination with MTX or other nonbiologic DMARDs. Use in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
˜Indicated in adult patients with moderately to severely active UC who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine for: inducing and maintaining clinical response; improving endoscopic appearance of the mucosa during induction; inducing clinical remission; and achieving and sustaining clinical remission in induction responders.

CLINICAL EFFICACY SUMMARY

Rheumatoid arthritis (RA)

- The approval of the subcutaneous (SQ) formulation of Orencia (abatacept) was based on a double-blind, double-dummy, randomized trial demonstrating noninferiority to the intravenous (IV) formulation. The trial enrolled patients with RA who had an inadequate response to methotrexate (MTX). The proportion of patients achieving American College of Rheumatology 20% improvement (ACR 20) was not significantly different between the groups (*Genovese et al 2011*).
- Orencia (abatacept), Remicade (infliximab), and placebo were compared in a Phase 3, randomized, double-blind trial (n = 431). Enrolled patients had an inadequate response to MTX, and background MTX was continued during the trial. Although efficacy was comparable between abatacept and infliximab after 6 months of treatment, some differences in favor of abatacept were evident after 1 year of treatment. After 1 year, the mean changes from baseline in disease activity score based on erythrocyte sedimentation rate (DAS28-ESR) were -2.88 and -2.25 in the abatacept and infliximab groups, respectively (estimate of difference, -0.62; 95% confidence interval [CI], -0.96 to -0.29). Abatacept demonstrated greater efficacy vs infliximab on some (but not all) secondary endpoints, including the proportion of patients with a good European League Against Rheumatism (EULAR) response (32.0% vs 18.5%), low disease activity score (LDAS) (35.3% vs 22.4%), ACR 20 responses (72.4% vs 55.8%), and improvements in the Medical Outcomes Study short-form-36 (SF-36) physical component summary (PCS) (difference of 1.93). Overall, abatacept had a relatively more acceptable safety and tolerability profile, with fewer serious adverse events (AEs) and discontinuations due to AEs than the infliximab group (*Schiff et al 2008*).
- Treatment with Orencia (abatacept) was directly compared to treatment with Humira (adalimumab), when added to MTX, in a multicenter, investigator-blind, randomized controlled trial (n = 646) of RA patients with inadequate response to MTX. After 2 years, the proportions of patients achieving ACR 20 responses were comparable between abatacept and adalimumab treatment groups (59.7 and 60.1%, respectively; difference 1.8%; 95% CI, -5.6 to 9.2%). ACR 50 and ACR 70 responses were also similar between the 2 groups after 2 years of treatment. Rates of AEs were similar between treatment groups (*Schiff et al 2014*).
- The RAPID-1 and RAPID-2 studies compared Cimzia (certolizumab) in combination with MTX to placebo plus MTX in adults with active RA despite MTX therapy (*Keystone et al 2008, Smolen et al 2009a*). A significantly greater proportion of patients on certolizumab 400 mg plus MTX at weeks 0, 2, and 4 then 200 or 400 mg every 2 weeks attained greater ACR 20, ACR 50 and ACR 70 responses compared to patients on placebo and MTX, respectively, after 24 weeks ($p \leq 0.01$). The response rates were sustained with active treatment over 52 weeks (*Keystone et al 2008*). The Modified Total Sharp Score (mTSS) was significantly lower with certolizumab in combination with MTX compared to MTX in combination with placebo (*Keystone et al 2008, Smolen et al 2009a*). A trial evaluated Cimzia (certolizumab) monotherapy vs placebo in patients with active disease who had failed at least 1 prior DMARD. After 24 weeks, ACR 20 response rates were significantly greater with active treatment (45.5%) compared to placebo (9.3%; $p < 0.001$). Significant improvements in secondary endpoints (ACR 50, ACR 70, individual ACR component scores, and patient reported outcomes) were also associated with certolizumab therapy (*Fleischmann et al 2009*).
- More Cimzia (certolizumab)-treated patients achieved clinical disease activity index (CDAI) remission than placebo-treated patients (18.8% vs 6.1%, $p \leq 0.05$) in a randomized, double-blind, placebo-controlled trial of certolizumab over 24 weeks in 194 patients with RA who were on DMARD therapy with MTX, leflunomide, sulfasalazine and/or hydroxychloroquine for at least 6 months (*Smolen et al 2015a*).
- A randomized, double-blind, placebo-controlled trial (n = 316) conducted in Japan compared Cimzia (certolizumab) plus MTX to placebo plus MTX in MTX-naïve patients with early RA (≤ 12 months persistent disease) and poor prognostic factors: high anti-cyclic citrullinated peptide (anti-CCP) antibody and either positive rheumatoid factor and/or presence of bone erosions (*Atsumi et al 2016*). The primary endpoint was inhibition of radiographic progression (change from baseline in mTSS at week 52). The certolizumab plus MTX group showed significantly greater inhibition of radiographic progression vs MTX alone (mTSS change, 0.36 vs 1.58; $p < 0.001$). Clinical remission rates were higher in patients treated with certolizumab plus MTX vs MTX alone. The authors suggest that certolizumab plus MTX could be used as possible first-line treatment in this patient population. In a long-term extension, a higher percentage of patients treated with certolizumab plus MTX experienced inhibition of radiographic progression (change from baseline in mTSS) at week 104 vs MTX alone (84.2% vs 67.5%; $p < 0.001$) (*Atsumi et al 2017*).
- The FDA approval of Simponi (golimumab) for RA was based on 3 multicenter, double-blind, randomized, controlled trials in 1,542 patients ≥ 18 years of age with moderate to severe active disease. A greater percentage of patients from all 3 trials treated with the combination of golimumab and MTX achieved ACR responses at week 14 and week 24 vs patients treated with MTX alone (*Emery et al 2009, Keystone et al 2009, Smolen et al 2009b*). Additionally, the golimumab 50 mg groups demonstrated a greater improvement compared to the control groups in the change in

mean Health Assessment Questionnaire (HAQ) Disability Index (HAQ-DI) (*Keystone et al 2009, Smolen et al 2009b*). Response with golimumab + MTX was sustained for up to 5 years (*Keystone et al 2013a, Smolen et al 2015b*).

- Simponi Aria (golimumab) was studied in patients with RA. In 1 trial, 643 patients could receive golimumab 2 mg/kg or 4 mg/kg intravenously (IV) every 12 weeks with or without MTX, or placebo with MTX. The proportion of patients meeting the primary endpoint of ACR 50 response was not significantly different between the golimumab with or without MTX groups and the placebo group. However, significantly more patients receiving golimumab plus MTX achieved an ACR 20 response at week 14 compared with patients receiving placebo plus MTX (53 vs 28%; $p < 0.001$) (*Kremer et al 2010*). In the GO-FURTHER trial (n = 592), golimumab 2 mg/kg IV or placebo was given at weeks 0, 4 and then every 8 weeks. An increased percentage of patients treated with golimumab + MTX achieved ACR 20 response at week 14 (58.5% [231/395] of golimumab + MTX patients vs 24.9% [49/197] of placebo + MTX patients [$p < 0.001$]) (*Weinblatt et al 2013*). In an open-label extension period, treatment was continued through week 100, with placebo-treated patients crossing over to golimumab at week 16 (early escape) or week 24. Clinical response was maintained through week 100, with an ACR 20 response of 68.1%. There was a very low rate of radiographic progression throughout the study, and patients treated with IV golimumab plus MTX from baseline had significantly less radiographic progression to week 100 compared to patients who had initially received placebo plus MTX. No unexpected AEs occurred (*Bingham et al 2015*). In the GO-MORE trial, investigators treated patients with golimumab SQ for 6 months. If patients were not in remission, they could be randomized to receive golimumab SQ or IV. The percentages of patients who achieved DAS28-ESR remission did not differ between the combination SQ + IV group and the SQ golimumab group (*Combe et al 2014*).
- The efficacy and safety of Actemra (tocilizumab) were assessed in several randomized, double-blind, multicenter studies in patients age ≥ 18 years with active RA. Patients were diagnosed according to ACR criteria, with at least 8 tender and 6 swollen joints at baseline. Tocilizumab was given every 4 weeks as monotherapy (AMBITION), in combination with MTX (LITHE and OPTION) or other DMARDs (TOWARD) or in combination with MTX in patients with an inadequate response to TNF antagonists (RADIATE). In all studies, mild to moderate AEs were reported, occurring in similar frequencies in all study groups. The most common AEs in all studies were infections and gastrointestinal symptoms (*Emery et al 2008, Genovese et al 2008, Jones et al 2010, Kremer et al 2011, Smolen et al 2008*).
    - AMBITION evaluated the safety and efficacy of tocilizumab monotherapy vs MTX in patients with active RA for whom previous treatment with MTX or biological agents had not failed. A total of 673 patients were randomized to 1 of 3 treatment arms, tocilizumab 8 mg/kg every 4 weeks, MTX 7.5 mg/week and titrated to 20 mg/week within 8 weeks, or placebo for 8 weeks followed by tocilizumab 8 mg/kg. The primary endpoint was the proportion of patients achieving ACR 20 response at week 24. The results showed that tocilizumab monotherapy when compared to MTX monotherapy produced greater improvements in RA signs and symptoms, and a favorable benefit-risk ratio in patients who had not previously failed treatment with MTX or biological agents. Additionally, more patients treated with tocilizumab achieved remission at week 24 when compared to patients treated with MTX (*Jones et al 2010*).
    - LITHE evaluated 1,196 patients with moderate to severe RA who had an inadequate response to MTX. Patients treated with tocilizumab had 3 times less progression of joint damage, measured by Total Sharp Score, when compared to patients treated with MTX alone. Significantly more patients treated with tocilizumab 8 mg/kg were also found to achieve remission at 6 months as compared to MTX (33% vs 4%), and these rates continued to increase over time to 1 year (47% vs 8%) (*Kremer et al 2011*). These benefits were maintained or improved at 2 years with no increased side effects (*Fleishmann et al 2013*).
    - OPTION evaluated tocilizumab in 623 patients with moderate to severely active RA. Patients received tocilizumab 8 mg/kg, 4 mg/kg, or placebo IV every 4 weeks, with MTX at stable pre-study doses (10 to 25 mg/week). Rescue therapy with tocilizumab 8 mg/kg was offered at week 16 to patients with < 20% improvement in swollen and tender joint counts. The primary endpoint was ACR 20 at week 24. The findings showed that ACR 20 was seen in significantly more patients receiving tocilizumab than in those receiving placebo at week 24 ($p < 0.001$). Significantly more patients treated with tocilizumab achieved ACR 50 and ACR 70 responses at week 24 as well ($p < 0.001$). Greater improvements in physical function, as measured by the HAQ-DI, were seen with tocilizumab when compared to MTX (-0.52 vs -0.55 vs -0.34; $p < 0.0296$ for 4 mg/kg and $p < 0.0082$ for 8 mg/kg) (*Smolen et al 2008*).
    - TOWARD examined the efficacy and safety of tocilizumab combined with conventional DMARDs in 1220 patients with active RA. Patients remained on stable doses of DMARDs and received tocilizumab 8 mg/kg or placebo every 4 weeks for 24 weeks. At week 24, significantly more patients taking tocilizumab with DMARDs achieved an ACR 20 response than patients in the control group. The authors concluded that tocilizumab, combined with any of the DMARDs evaluated (MTX, chloroquine, hydroxychloroquine, parenteral gold, sulfasalazine, azathioprine, and leflunomide), was safe and effective in reducing articular and systemic

symptoms in patients with an inadequate response to these agents. A greater percentage of patients treated with tocilizumab also had clinically meaningful improvements in physical function when compared to placebo (60% vs 30%; p value not reported) (*Genovese et al 2008).*

- RADIATE evaluated the safety and efficacy of tocilizumab in patients with RA refractory to TNF antagonist therapy. A total of 499 patients with inadequate response to ≥ 1TNF antagonists were randomly assigned to 8 or 4 mg/kg tocilizumab or placebo every 4 weeks with stable MTX doses (10 to 25 mg/week) for 24 weeks. ACR 20 responses and safety endpoints were assessed. This study found that tocilizumab plus MTX is effective in achieving rapid and sustained improvements in signs and symptoms of RA in patients with inadequate response to TNF antagonists and has a manageable safety profile. The ACR 20 response in both tocilizumab groups was also found to be comparable to those seen in patients treated with Humira (adalimumab) and Remicade (infliximab), irrespective of the type or number of failed TNF antagonists (*Emery et al 2008*). In the ADACTA trial, patients with severe arthritis who could not take MTX were randomized to monotherapy with tocilizumab or adalimumab. The patients in the tocilizumab group had a significantly greater improvement in DAS28 at week 24 than patients in the adalimumab group (*Gabay et al 2013*).

- More recently, results of a randomized, double-blind trial evaluating Actemra (tocilizumab) in early RA were published (*Bijlsma et al 2016*). Patients (n = 317) had been diagnosed with RA within 1 year, were DMARD-naïve, and had a DAS28 score of ≥ 2.6. Patients were randomized to 1 of 3 groups: tocilizumab plus MTX, tocilizumab plus placebo, or MTX plus placebo. Tocilizumab was given at a dose of 8 mg/kg every 4 weeks (maximum 800 mg per dose), and MTX was given at a dose of 10 mg orally per week, increased to a maximum of 30 mg per week as tolerated. Patients not achieving remission switched from placebo to active treatments, and patients not achieving remission in the tocilizumab plus MTX group switched to a standard of care group (usually a TNF inhibitor plus MTX). The primary endpoint was the proportion of patients achieving sustained remission (defined as DAS28 < 2.6 with a swollen joint count ≤4, persisting for at least 24 weeks). The percentages of patients achieving a sustained remission on the initial regimen were 86%, 84%, and 44% in the tocilizumab plus MTX, tocilizumab monotherapy, and MTX monotherapy groups, respectively (p < 0.0001 for both comparisons vs MTX). The percentages of patients achieving sustained remission during the entire study were 86%, 88%, and 77% in the tocilizumab plus MTX, tocilizumab monotherapy, and MTX monotherapy groups, respectively (p = 0.06 for tocilizumab plus MTX vs MTX; p = 0.0356 for tocilizumab vs MTX). The authors concluded that immediate initiation of tocilizumab is more effective compared to initiation of MTX in early RA.
- The FDA approval of the SQ formulation of Actemra (tocilizumab) was based on 1 multicenter, double-blind, randomized, controlled trial in patients (n = 1262) with RA. Weekly tocilizumab SQ 162 mg was found to be non-inferior to tocilizumab IV 8 mg/kg every 4 weeks through 24 weeks. A higher incidence of injection-site reactions were reported with the SQ formulation (*Burmester et al 2014a*). In an open-label extension period, patients in both treatment arms were re-randomized to receive either IV or SQ tocilizumab through week 97. The proportions of patients who achieved ACR 20/50/70 responses, DAS28 remission, and improvement from baseline in HAQ-DI ≥ 0.3 were sustained through week 97 and comparable across arms. IV and SQ treatments had a comparable safety profile with the exception of higher injection-site reactions with the SQ formulation (*Burmester et al 2016*). A placebo-controlled trial in 656 patients further confirmed the efficacy of SQ Actemra administered every other week (*Kivitz et al 2014*).
- A phase 3 trial (MONARCH) evaluating the efficacy of Kevzara (sarilumab) monotherapy vs Humira (adalimumab) monotherapy for the treatment of patients with active RA with an inadequate response or intolerance to MTX reported superiority of sarilumab over adalimumab based on change from baseline in DAS28-ESR at week 24 (-3.28 vs -2.20; difference, -1.08; 95% CI, -1.36 to -0.79; p < 0.0001) (*Burmester et al 2017*). DAS28-ESR remission, ACR 20/50/70 response rates, and improvements in HAQ-DI scores were also more likely with sarilumab. Aside from the MONARCH trial, sarilumab has not been directly compared to any other biologic or tofacitinib. Nonetheless, 2 pivotal trials have shown the agent to be superior in achievement of ACR 50 when compared to MTX plus placebo, in both MTX inadequate responders and TNF inhibitor inadequate responder patients (*Genovese et al 2015, Fleischmann et al 2017*). Additionally, a meta-analysis of 4 randomized controlled trials (RCTs) has shown that ACR 50 response rates were significantly higher with sarilumab 200 mg and sarilumab 200 mg plus MTX when compared to MTX plus placebo (OR, 4.05; 95% CI, 2.04 to 8.33 and OR, 3.75; 95% CI, 2.37 to 5.72, respectively). Ranking probability based on the surface under the cumulative ranking curve (SUCRA) suggested that sarilumab 200 mg was most likely to achieve ACR 50 response rate, followed by sarilumab 200 mg plus MTX, sarilumab 150 mg plus MTX, adalimumab 40 mg, and MTX plus placebo (*Bae et al 2017).*
- In a Phase 3 trial, the percentage of patients who met criteria for RA disease remission was not significantly different in the Xeljanz (tofacitinib) groups (5 mg and 10 mg twice daily) vs placebo. However, significantly more patients in the tofacitinib groups did meet criteria for decrease of disease activity. The tofacitinib groups also had significant decreases in fatigue and pain (*Fleishmann et al 2012*). In another Phase 3 study, Xeljanz (tofacitinib), when

administered with background MTX, was superior to placebo with respect to all clinical outcomes. Although not directly compared to Humira (adalimumab), the clinical efficacy of tofacitinib was numerically similar to that observed with adalimumab. Safety of tofacitinib continues to be monitored for long term effects (*van Vollenhoven et al 2012*). The ORAL Scan trial showed the ACR 20 response rates at month 6 for patients receiving tofacitinib 5 mg and 10 mg twice daily were 51.5% and 61.8%, respectively, vs 25.3% for patients receiving placebo ($p < 0.0001$ for both comparisons) (*van der Heijde et al 2013*). The ORAL START trial evaluated tofacitinib and MTX in 956 patients with active RA over 24 months. The primary endpoint of mean change from baseline in modified total Sharp score was significantly less with tofacitinib (0.6 for 5 mg; 0.3 for 10 mg) compared to MTX (2.1; $p < 0.001$) (*Lee et al 2014*). No radiographic progression was defined as a change from baseline in the modified total Sharp score of < 0.5 points. However, a minimal clinically important difference in modified total Sharp score is 4.6 points; this study did not meet this minimal clinical meaningful difference threshold.

- In the ORAL Step study, patients with RA who had an inadequate response to ≥ 1 TNF inhibitors were randomized to Xeljanz (tofacitinib) 5 mg or 10 mg twice daily or placebo; all patients were on MTX (*Burmester et al 2013a, Strand et al 2015a*). The primary outcome, ACR 20 response rate, was significantly higher with tofacitinib 5 mg (41.7%; 95% CI, 6.06 to 28.41; $p = 0.0024$) and 10 mg (48.1%; 95% CI, 12.45 to 34.92; $p < 0.0001$) compared to placebo (24.4%). Improvements in HAQ-DI was reported as -0.43 (95% CI, -0.36 to -0.157; $p < 0.0001$) for tofacitinib 5 mg and -0.46 (95% CI, -0.38 to -0.17; $p < 0.0001$) for tofacitinib 10 mg groups compared to -0.18 for placebo. Common AEs included diarrhea, nasopharyngitis, headache, and urinary tract infections in the tofacitinib groups.
- The approval of Olumiant (baricitinib) was based on 2 confirmatory, 24-week, phase 3 trials in patients with active RA. In RA-BEACON, enrolled patients (N = 527) had moderate to severe RA and an inadequate response or intolerance to ≥ 1 TNF antagonist(s) (*Genovese et al 2016*). Patients received baricitinib once daily or placebo along with continuing a stable dose of a conventional DMARD. The primary endpoint, ACR 20 response at week 12, was achieved by 49% and 27% of patients in the baricitinib 2 mg and placebo groups, respectively ($p \leq 0.001$). In RA-BUILD, enrolled patients (N = 684) had moderate to severe RA and an inadequate response or intolerance to ≥ 1 conventional DMARD(s) (*Dougados et al 2017*). Patients received baricitinib once daily or placebo; concomitant conventional DMARDs were permitted but not required. The primary endpoint, ACR20 response at week 12, was achieved by 66% and 39% of patients in the baricitinib 2 mg and placebo groups, respectively ($p \leq 0.001$).
- Inflectra (infliximab-dyyb) was evaluated and compared to Remicade (infliximab; European Union formulation) in PLANETRA (N=606), a double-blind, multicenter, randomized trial (*Yoo et al 2013, Yoo et al 2016, Yoo et al 2017*). The primary endpoint, ACR 20 at week 30, was achieved by 58.6% and 60.9% of patients in the Remicade and Inflectra groups, respectively (treatment difference [TD], 2%; 95% CI, -6% to 10%) (intention-to-treat population). Corresponding results in the per-protocol population were 69.7% and 73.4%, respectively (TD, 4%; 95% CI, -4% to 12%). Equivalence was demonstrated between the 2 products.
    - Secondary endpoints included several other disease activity scales and a quality-of-life scale; no significant differences were noted in any of these endpoints at either the 30-week or 54-week assessments.
    - In the extension study (n = 302) through 102 weeks, all patients received Inflectra. Response rates were maintained, with no differences between the Inflectra maintenance group and the group who switched from Remicade to Inflectra.
- Renflexis (infliximab-abda) was evaluated and compared to Remicade (infliximab; European Union formulation) in 584 patients in a double-blind, multicenter, randomized phase 3 trial (*Choe et al 2017*). The primary endpoint, ACR 20 at week 30, was achieved by 64.1% and 66.0% of patients in the Renflexis and Remicade groups, respectively (TD, -1.88%; 95% CI, -10.26% to 6.51%) (per-protocol population). Equivalence was demonstrated between the 2 products.
    - Secondary endpoints were also very similar between the 2 groups.
    - At week 54 of this trial, patients transitioned into the switching/extension phase, in which patients initially taking Remicade were re-randomized to continue Remicade or switch to Renflexis; patients initially taking Renflexis continued on the same treatment. Although slight numerical differences were observed, there was consistent efficacy over time across treatments and the proportions of patients achieving ACR responses were comparable between groups (*Renflexis FDA clinical review 2017*).
- Two studies, 1 double-blind and 1 open-label, evaluated Rituxan (rituximab) in patients who had failed treatment with a TNF blocker (*Cohen et al 2006, Haraoui et al 2011*). All patients continued to receive MTX. Both studies showed > 50% of patients achieving ACR 20 response. AEs were generally mild to moderate in severity.
- A Cochrane review (*Lopez-Olivo et al 2015*) examined Rituxan (rituximab) for the treatment of RA. Eight studies and a total of 2720 patients were included. Rituximab plus MTX, compared to MTX alone, resulted in more patients achieving ACR 50 at 24 weeks (29% vs 9%, respectively) and clinical remission at 52 weeks (22% vs 11%). In addition, rituximab plus MTX compared to MTX alone resulted in more patients having no radiographic progression (70% vs 59% at 24 weeks, with similar results at 52 through 56 and 104 weeks). Benefits were also shown for physical function and quality of life.

- In the open-label ORBIT study (n = 295), adults with active, seropositive RA and an inadequate response to DMARDs who were biologic-naïve were randomized to either Rituxan (rituximab) (n = 144) or a TNF inhibitor (physician/patient choice of Enbrel [etanercept] or Humira [adalimumab]; n = 151) (*Porter et al 2016*). Medication doses were generally consistent with FDA-approved recommendations. Patients were able to switch over to the alternative treatment due to side effects or lack of efficacy. The primary endpoint was the change in DAS28-ESR in the per-protocol population at 12 months.
    - The changes in DAS28-ESR were -2.6 and -2.4 in patients in the rituximab and TNF inhibitor groups, respectively. The difference of -0.19 (95% CI, -0.51 to 0.13) was within the prespecified non-inferiority margin of 0.6 units. The authors concluded that initial treatment with rituximab was non-inferior to initial TNF inhibitor treatment in this patient population. However, interpretation of these results is limited due to the open-label study design and the high percentage of patients switching to the alternative treatment (32% in the TNF inhibitor group and 19% in the rituximab group). The indication for rituximab is limited to patients with an inadequate response to TNF inhibitor(s).
- A randomized, open-label trial evaluated biologic treatments in patients with RA who had had an inadequate response to a TNF inhibitor (*Gottenberg et al 2016*). Patients (n = 300) were randomized to receive a second TNF inhibitor (n = 150) or a non-TNF-targeted biologic (n = 150) of the prescriber's choice. The second TNF inhibitors, in order of decreasing frequency, included Humira (adalimumab), Enbrel (etanercept), Cimzia (certolizumab), and Remicade (infliximab), and the non-TNF biologics included Actemra (tocilizumab), Rituxan (rituximab), and Orencia (abatacept). The primary endpoint was the proportion of patients with a good or moderate EULAR response at week 24, defined as a decrease in DAS28-ESR of > 1.2 points resulting in a score of ≤ 3.2.
    - At week 24, 52% of patients in the second anti-TNF group and 69% of patients in the non-TNF group achieved a good or moderate EULAR response (p = 0.003 or p = 0.004, depending on how missing data were handled). Secondary disease activity scores also generally supported better efficacy for the non-TNF biologics; however, HAQ scores did not differ significantly between groups. Among the non-TNF biologics, the proportion of EULAR good and moderate responders at week 24 did not significantly differ between abatacept, rituximab, and tocilizumab (67%, 61%, and 80%, respectively). There were 8 patients (5%) in the second TNF inhibitor group and 16 patients (11%) in the non-TNF biologic group that experienced serious AEs (p = 0.10), predominantly infections and cardiovascular events. There were some limitations to this trial; notably, it had an open-label design, and adherence may have differed between groups because all non-TNF biologics were given as infusions under observation and most of the TNF inhibitor drugs were self-injected by patients. The authors concluded that among patients with RA inadequately treated with TNF inhibitors, a non-TNF biologic was more effective in achieving a good or moderate disease activity response at 24 weeks; however, a second TNF inhibitor was also often effective in producing clinical improvement.
- Another recent randomized trial (*Manders et al 2015*) evaluated the use of Orencia (abatacept) (n = 43), Rituxan (rituximab) (n = 46), or a different TNF inhibitor (n = 50) in patients (n =139) with active RA despite previous TNF inhibitor treatment. Actemra (tocilizumab) was not included. In this trial, there were no significant differences with respect to DAS28, HAQ-DI, or SF-36 over the 1-year treatment period, and AEs also appeared similar. A cost-effectiveness analysis was also included in this publication, but results are not reported in this review.
- A Cochrane review examined Orencia (abatacept) for the treatment of RA. ACR 50 response was not significantly different at 3 months but was significantly higher in the abatacept group at 6 and 12 months compared to placebo (relative risk [RR], 2.47; 95% CI, 2 to 3.07 and RR, 2.21; 95% CI, 1.73 to 2.82). Similar results were seen in ACR 20 and ACR 70 (*Maxwell et al 2009*).
- The safety and efficacy of Humira (adalimumab) for the treatment of RA were assessed in a Cochrane systematic review. Treatment with adalimumab in combination with MTX was associated with a RR of 1.52 to 4.63, 4.63 (95% CI, 3.04 to 7.05) and 5.14 (95% CI, 3.14 to 8.41) for ACR 20, ACR 50, and ACR 70 responses, respectively, at 6 months when compared to placebo in combination with MTX. Adalimumab monotherapy was also proven efficacious (*Navarro-Sarabia et al 2005*). In another study, patients received adalimumab 20 mg or 40 mg every other week for 1 year, and then could receive 40 mg every other week for an additional 9 years. At Year 10, 64.2%, 49%, and 17.6% of patients achieved ACR 50, ACR 70, and ACR 90 responses, respectively (*Keystone et al 2013b*).
- A Phase 3, open-label study evaluated the long-term efficacy of Humira (adalimumab) for RA. Patients receiving adalimumab in 1 of 4 early assessment studies could receive adalimumab for up to 10 years in the extension study. Of 846 enrolled patients, 286 (33.8%) completed 10 years of treatment. In patients completing 10 years, adalimumab led to sustained clinical and functional responses, with ACR 20, ACR 50, and ACR 70 responses being achieved by 78.6%, 55.5%, and 32.8% of patients, respectively. The authors stated that patients with shorter disease duration achieved better outcomes, highlighting the need for early treatment. No unexpected safety findings were observed. This study demonstrated that some patients with RA can be effectively treated with adalimumab on a long-term basis;

however, the study is limited by its open-label design, lack of radiographic data, and the fact that only patients who continued in the study were followed (*Furst et al 2015*).

- A Cochrane review was performed to compare Kineret (anakinra) to placebo in adult patients with RA. Significant improvements in both primary (ACR 20, 38% vs 23%; RR, 1.61; 95% CI, 1.32 to 1.98) and secondary (ACR 50 and ACR 70) outcomes were detected. The only significant difference in AEs noted with anakinra use was the rate of injection site reactions (71% vs 28% for placebo) (*Mertens et al 2009*).
- In another Cochrane review, Enbrel (etanercept) was compared to MTX or placebo in adult patients with RA and found that at 6 months, 64% of individuals on etanercept 25 mg twice weekly attained an ACR 20 vs 15% of patients on either MTX alone or placebo (RR, 3.8; number needed to treat [NNT], 2). An ACR 50 and ACR 70 were achieved by 39% and 15%, respectively, in the etanercept group compared to 4% (RR, 8.89; NNT, 3) and 1% (RR, 11.31; NNT, 7) in the control groups, respectively. Etanercept 10 mg twice weekly was only associated with significant ACR 20 (51% vs 11% of controls; RR, 4.6; 95% CI, 2.4 to 8.8; NNT, 3) and ACR 50 responses (24% vs 5% of controls; RR, 4.74; 95% CI, 1.68 to 13.36; NNT, 5). Seventy-two percent of patients receiving etanercept had no increase in Sharp erosion score compared to 60% of MTX patients. Etanercept 25 mg was associated with a significantly reduced total Sharp score (weighted mean difference, -10.5; 95% CI, -13.33 to -7.67). The Sharp erosion scores and joint space narrowing were not significantly reduced by either etanercept dose (*Blumenauer et al 2003*). In a trial of 353 patients with RA, patients received a triple therapy combination of sulfasalazine, hydroxychloroquine and MTX or etanercept and MTX. Triple therapy was shown to be noninferior to etanercept + MTX (*O'Dell et al 2013*).
- A more recent Cochrane review (*Singh et al 2016a*) evaluated the benefits and harms of 10 agents for the treatment of RA in patients failing treatment with MTX or other DMARDs. Agents included Xeljanz (tofacitinib) and 9 biologics (Orencia [abatacept], Humira [adalimumab], Kineret [anakinra], Cimzia [certolizumab], Enbrel [etanercept], Simponi [golimumab], Remicade [infliximab], Rituxan [rituximab], and Actemra [tocilizumab]), each in combination with MTX or other DMARDS, compared to comparator agents such as DMARDs or placebo. Data from 79 randomized trials (total 32,874 participants) were included. Key results from this review are as follows:
    - ACR 50: Biologic plus MTX/DMARD was associated with a statistically significant and clinically meaningful improvement in ACR 50 vs comparators. TNF inhibitors did not differ significantly from non-TNF biologics. Differences between treatments in individual comparisons were small.
    - HAQ: Biologic plus MTX/DMARD was associated with a clinically and statistically significant improvement in function measured by HAQ vs comparators. TNF inhibitors did not differ significantly from non-TNF biologics.
    - Remission: Biologic plus MTX/DMARD was associated with clinically and statistically significantly greater proportion of patients achieving RA remission, defined by DAS < 1.6 or DAS28 < 2.6, vs comparators. TNF inhibitors did not differ significantly from non-TNF biologics.
    - Radiographic progression: Radiographic progression was statistically significantly reduced in those on biologic plus MTX/DMARD vs comparator. The absolute reduction was small and clinical relevance is uncertain.
    - Safety: Biologic plus MTX/DMARD was associated with a clinically significantly increased risk of serious AEs; statistical significance was borderline. TNF inhibitors did not differ significantly from non-TNF biologics.
- A similar Cochrane review focused on the use of biologic or Xeljanz (tofacitinib) monotherapy for RA in patients with traditional DMARD failure (*Singh et al 2016b*). A total of 41 randomized trials (n = 14,049) provided data for this review. Key results are as follows:
    - Biologic monotherapy was associated with a statistically significant and clinically meaningful improvement in ACR 50 and HAQ vs placebo and vs MTX or other DMARDs.
    - Biologic monotherapy was associated with a statistically significant and clinically meaningful greater proportion of patients with disease remission vs placebo.
    - Based on a single study, the reduction in radiographic progression was statistically significant for biologic monotherapy compared to active comparators, but the absolute reduction was small and of unclear clinical relevance.
- Another Cochrane review evaluated the use of biologics or Xeljanz (tofacitinib) in patients with RA who had been unsuccessfully treated with a previous biologic (*Singh et al 2017[a]*). The review included 12 randomized trials (n = 3,364). Key results are as follows:
    - Biologics, compared to placebo, were associated with statistically significant and clinically meaningful improvement in RA as assessed by ACR 50 and remission rates. Information was not available for HAQ or radiographic progression.
    - Biologics plus MTX, compared to MTX or other traditional DMARDs, were associated with statistically significant and clinically meaningful improvement in ACR 50, HAQ, and RA remission rates. Information was not available for radiographic progression.
    - There were no published data for tofacitinib monotherapy vs placebo.

  - Based on a single study, tofacitinib plus MTX, compared to MTX, was associated with a statistically significant and clinically meaningful improvement in ACR 50 and HAQ. RA remission rates were not statistically significantly different, and information was not available for radiographic progression.
- In another meta-analysis, ACR 20 and ACR 70 response rates for Xeljanz (tofacitinib) 5 mg and 10 mg were comparable to the other monotherapies (Orencia [abatacept], Humira [adalimumab], Kineret [anakinra], Cimzia [certolizumab], Enbrel [etanercept], Simponi [golimumab], Remicade [infliximab], Actemra [tocilizumab]) at 24 weeks (*Bergrath et al 2017*). ACR 50 response rates were also comparable for tofacitinib 10 mg and other monotherapies. At 24 weeks, ACR 20/50/70 response rates for the combination of tofacitinib 5 mg or 10 mg plus conventional DMARD were comparable to other biologic plus conventional DMARD therapies except tofacitinib 5 mg plus conventional DMARD and tofacitinib 10 mg plus conventional DMARD were both superior to certolizumab 400 mg every 4 weeks plus conventional DMARD for achieving ACR 70 response (OR, 59.16; [95% CI, 2.70 to infinity]; and OR, 77.40; [95% CI, 3.53 to infinity], respectively).
- Another recent Cochrane review (*Hazlewood et al 2016*) compared MTX and MTX-based DMARD combinations for RA in patients naïve to or with an inadequate response to MTX; DMARD combinations included both biologic and non-biologic agents. A total of 158 studies and over 37,000 patients were included. Evidence suggested that efficacy was similar for triple DMARD therapy (MTX plus sulfasalazine plus hydroxychloroquine) and MTX plus most biologic DMARDs or Xeljanz (tofacitinib). MTX plus some biologics were superior to MTX in preventing joint damage in MTX-naïve patients, but the magnitude of effect was small.
- An additional Cochrane review evaluated biologics for RA in patients naïve to MTX in 19 studies (*Singh et al 2017[b]*). Agents included in the review were Humira (adalimumab), Enbrel (etanercept), Simponi (golimumab), Remicade (infliximab), Orencia (abatacept), and Rituxan (rituximab). When combined with MTX, use of biologics showed a benefit in ACR 50 vs comparator (MTX/MTX plus methylprednisolone) (RR, 1.40; 95% CI, 1.30 to 1.49) and in RA remission rates (RR, 1.62; 95% CI, 1.33 to 1.98), but no difference was found for radiographic progression. When used without MTX, there was no significant difference in efficacy between biologics and MTX.
- A meta-analysis evaluated the efficacy of Remicade (infliximab) in combination with MTX compared to placebo plus MTX. There was a higher proportion of patients in the infliximab group that achieved an ACR 20 at 30 weeks compared to patients in the placebo group (RR, 1.87; 95% CI, 1.43 to 2.45). These effects were similar in the proportion of patients achieving ACR 50 and ACR 70 (RR, 2.68; 95% CI, 1.79 to 3.99 and RR, 2.68; 95% CI, 1.78 to 4.03) (*Wiens et al 2009*).
- Another meta-analysis of randomized controlled trials included Humira (adalimumab), Kineret (anakinra), Enbrel (etanercept), and Remicade (infliximab) with or without MTX. The odds ratio (OR) for an ACR 20 was 3.19 (95% CI, 1.97 to 5.48) with adalimumab, 1.7 (95% CI, 0.9 to 3.29) with anakinra, 3.58 (95% CI, 2.09 to 6.91) with etanercept and 3.47 (95% CI, 1.66 to 7.14) with infliximab compared to placebo. The OR to achieve an ACR 50 with adalimumab was 3.97 (95% CI, 2.73 to 6.07), 2.13 (95% CI, 1.27 to 4.22) with anakinra, 4.21 (95% CI, 2.74 to 7.43) and with etanercept 4.14 (95% CI, 2.42 to 7.46) compared to placebo. Further analysis of each agent against another was performed, and no significant difference was determined between individual agents in obtaining an ACR 20 and ACR 50. However, the TNF-blockers as a class showed a greater ACR 20 and ACR 50 response compared to anakinra (OR, 1.96; 95% CI, 1.03 to 4.01 and OR, 1.93; 95% CI,1.05 to 3.5; $p < 0.05$) (*Nixon et al 2007*).
- The Agency for Healthcare Research and Quality published a review of drug therapy to treat adults with RA (*Donahue et al 2012*). They concluded that there is limited head-to-head data comparing the biologics. Studies that are available are generally observational in nature or mixed treatment comparison meta-analysis. At this time, there appears to be no significant differences amongst the agents. Clinical trials have shown better efficacy with combination biologics and MTX and no additional increased risk of AEs. However, combinations of 2 biologic agents showed increased rate of serious AEs with limited or no increase in efficacy.
- A meta-analysis of 6 trials (n = 1,927) evaluated the efficacy of withdrawing biologics from patients with RA who were in sustained remission or had low disease activity (*Galvao et al 2016*). The biologics in the identified trials were TNF inhibitors, most commonly Enbrel (etanercept) or Humira (adalimumab). Compared to withdrawing the medication, continuing the biologic increased the probability of having low disease activity (RR, 0.66; 95% CI, 0.51 to 0.84) and remission (RR, 0.57; 95% CI, 0.44 to 0.74). Although outcomes were worse in patients withdrawing the biologic, the investigators noted that almost half of the patients maintained a low disease activity after withdrawal. The authors suggested that further research is necessary to identify subgroups for which withdrawal may be more appropriate.

Ankylosing spondylitis (AS)

- The FDA-approval of Humira (adalimumab) for the treatment of AS was based on 1 randomized, double-blind, placebo-controlled study (n = 315) in which a significantly greater proportion of patients achieved a 20% improvement in the Assessment of SpondyloArthritis International Society criteria (ASAS 20) (primary endpoint) with adalimumab (58% vs 21% with placebo; $p < 0.001$). A greater than 50% improvement in Bath Ankylosing Spondylitis Disease

Activity Index (BASDAI) score, a measure of fatigue severity, spinal and peripheral joint pain, localized tenderness, and morning stiffness which is considered clinically meaningful, was detected in 45% of adalimumab-treated patients compared to 16% of placebo-treated patients ($p < 0.001$) at week 12. This response was sustained through week 24, with 42% in the adalimumab group achieving a greater than or equal to 50% improvement in BASDAI score compared to 15% in the placebo group ($p < 0.001$) (*van der Heijde et al 2006*).

- In 2 double-blind, randomized, placebo-controlled trials, the efficacy of Enbrel (etanercept) was evaluated in patients with AS (*Calin et al 2004, Gorman et al 2002*). Etanercept had a significantly greater response to treatment compared to placebo ($p < 0.001$) (*Gorman et al 2002*). More patients achieved an ASAS 20 response compared to placebo ($p < 0.001$) (*Calin et al 2004*). An open-label extension study, evaluating the long-term safety and efficacy of etanercept in patients with AS, was conducted. Safety endpoints included AEs, serious AEs, serious infection, and death while efficacy endpoints included ASAS 20 response, ASAS 5/6 response and partial remission rates. After up to 192 weeks of treatment, the most common AEs were injection site reactions, headache and diarrhea. A total of 71% of patients were ASAS 20 responders at week 96 and 81% of patients were responders at week 192. The ASAS 5/6 response rates were 61% at week 96 and 60% at week 144, and partial remission response rates were 41% at week 96 and 44% at week 192. Placebo patients who switched to etanercept in the open-label extension trial showed similar patterns of efficacy maintenance (*Davis et al 2008*). A multicenter, randomized, double-blind trial compared etanercept and sulfasalazine in adult patients with active AS that failed treatment with nonsteroidal anti-inflammatory drugs (NSAIDs). A significantly greater proportion of patients treated with etanercept compared to patients treated with sulfasalazine achieved the primary outcome of ASAS 20 at week 16 ($p < 0.0001$). There were also significantly more patients that achieved ASAS 40 and ASAS 5/6 in the etanercept group compared to the sulfasalazine group ($p < 0.0001$ for both) (*Braun et al 2011*).
- The FDA-approval of Simponi (golimumab) for AS was based on a multicenter, randomized, double-blind, placebo-controlled trial in adult patients with active disease for at least 3 months (n = 356). Golimumab with or without a DMARD was compared to placebo with or without a DMARD and was found to significantly improve the signs and symptoms of AS as demonstrated by the percentage of patients achieving an ASAS 20 response at week 14 (*Inman et al 2008*). Sustained improvements in ASAS 20 and ASAS 40 response rates were observed for up to 5 years in an open-label extension trial (*Deodhar et al 2015*). Safety profile through 5 years was consistent with other TNF inhibitors.
- The efficacy of Remicade (infliximab) in the treatment of AS was demonstrated in 12- and 24-week double-blind, placebo-controlled trials. There was significantly more patients that achieved a 50% BASDAI score in the infliximab group compared to the placebo group at 12 weeks ($p < 0.0001$)(*Braun et al 2002*), At 24 weeks, significantly more patients in the infliximab group achieved ASAS 20 compared to the placebo group ($p < 0.001$)(*van der Heijde et al 2005*).
- Inflectra (infliximab-dyyb) was evaluated alongside Remicade (infliximab; European Union formulation) for the treatment of AS in PLANETAS (n = 250), a double-blind, multicenter, randomized trial (*Park et al 2013, Park et al 2016, Park et al 2017*). The primary endpoints related to pharmacokinetic equivalence. Secondary efficacy endpoints supported similar clinical activity between Inflectra and Remicade. An ASAS 20 response was achieved by 72.4% and 70.5% of patients in the Remicade and Inflectra groups, respectively, at 30 weeks, and by 69.4% and 67.0% of patients at 54 weeks. Other disease activity endpoints and a quality-of-life scale were also similar between groups.
    - In the extension study (n = 174) through 102 weeks, all patients received Inflectra. From weeks 54 to 102, the proportion of patients achieving a clinical response was maintained at a similar level to that of the main study in both the maintenance and switch groups and was comparable between groups.
- The efficacy of Cimzia (certolizumab) for the treatment of AS was established in 1 randomized, double-blind, placebo-controlled study (n = 325) in which a significantly greater proportion of patients achieved ASAS 20 response with certolizumab 200 mg every 2 weeks and certolizumab 400 mg every 4 weeks compared to placebo at 12 weeks (*Landewe et at 2014*). Patient-reported outcomes measured by the SF-36, health-related quality of life (HRQoL), and reports of pain, fatigue and sleep were significantly improved with certolizumab in both dose groups (*Sieper et al 2015a*). A Phase 3, randomized, placebo-controlled trial found that 62.5% of patients on certolizumab maintained ASAS 20 response to week 96 in a population of patients with axial spondyloarthritis which includes AS (*Sieper et al 2015b*).
- The efficacy and safety of Cosentyx (secukinumab) were evaluated in the double-blind, placebo-controlled, randomized MEASURE 1 and 2 studies (*Baeten et al 2015*). MEASURE 1 enrolled 371 patients and MEASURE 2 enrolled 219 patients with active AS with radiologic evidence treated with NSAIDs. Patients were treated with secukinumab 75 or 150 mg SQ every 4 weeks (following IV loading doses) or placebo. The primary outcome, ASAS 20 response at week 16, was significantly higher in the secukinumab 75 mg (60%) and 150 mg (61%) groups compared to placebo (29%, $p < 0.001$ for each dose) for MEASURE 1. For MEASURE 2 at week 16, ASAS 20 responses were seen in 61% of the secukinumab 150 mg group, 41% of the 75 mg group, and 28% of the placebo

group (p < 0.001 for secukinumab 150 mg vs placebo; p = 0.10 for secukinumab 75 mg vs placebo). Common AEs reported included nasopharyngitis, headache, diarrhea, and upper respiratory tract infections. Improvements were observed from week 1 and sustained through week 52. In a long-term extension of MEASURE 1, ASAS 20 response rates were 73.7% with secukinumab 150 mg and 68.0% with 75 mg at week 104 and in MEASURE 2, ASAS 20 response rates were 71.5% with both doses at week 104 (*Braun et al 2017, Marzo-Ortega et al 2017*). In a 3-year extension of MEASURE-1, ASAS 20/40 response rates were 80.2%/61.6% for secukinumab 150 mg and 75.5%/50.0% for secukinumab 75 mg at week 156 (*Baraliakos et al 2017*).

- In 2 systematic reviews of TNF blockers for the treatment of AS, patients taking Simponi (golimumab), Enbrel (etanercept), Remicade (infliximab), and Humira (adalimumab) were more likely to achieve ASAS 20 or ASAS 40 responses compared with patients from control groups. The RR of reaching ASAS 20 after 12 or 14 weeks was 2.21 (95% CI, 1.91 to 2.56) (*Machado et al 2013*). After 24 weeks, golimumab, etanercept, infliximab, and adalimumab were more likely to achieve ASAS 40 compared to placebo (*Maxwell et al 2015*). A systematic review and network meta-analysis evaluated biologic agents for the treatment of AS, including adalimumab, etanercept, golimumab, infliximab, Cosentyx (secukinumab), and Actemra (tocilizumab; not FDA-approved for AS) (*Chen et al 2016*). A total of 14 studies were included. Infliximab was ranked best and secukinumab second best for achievement of ASAS 20 response; however, differences among agents were not statistically significant with the exception of infliximab 5 mg compared to tocilizumab (OR, 4.81; 95% credible interval [CrI], 1.43 to 17.04). Safety endpoints were not included in this analysis.

Crohn's disease (CD)

- In a trial evaluating Remicade (infliximab) for induction of remission, significantly more patients achieved remission at 4 weeks with infliximab compared to placebo (p < 0.005)(*Targan et al 1997*). In a placebo-controlled trial, significantly more patients treated with infliximab 5 and 10 mg/kg had a reduction greater than or equal to 50% in the number of fistulas compared to patients treated with placebo (p = 0.002 and p = 0.02, respectively)(*Present et al 1999*). In an open-label trial evaluating the use of infliximab in pediatric CD patients, 88.4% responded to the initial induction regimen, and 58.6% were in clinical remission at week 10 (*Hyams et al 2007*).
- The safety and efficacy of Entyvio (vedolizumab) was demonstrated in 2 trials for CD in patients who responded inadequately to immunomodulator therapy, TNF blockers, and/or corticosteroids. In 1 trial, a higher percentage of Entyvio-treated patients achieved clinical response and remission at week 52 compared to placebo. However, in the second trial, Entyvio did not achieve a statistically significant clinical response or clinical remission over placebo at week 6 (*Sandborn et al 2013, Sands et al 2014*).
- A meta-analysis evaluating Cimzia (certolizumab) use over 12 to 26 weeks for the treatment of CD demonstrated that the agent was associated with an increased rate of induction of clinical response (RR, 1.36; p = 0.004) and remission (RR, 1.95; p < 0.0001) over placebo. However, risk of infection was higher with certolizumab use (*Shao et al 2009*).
- Additionally, Humira (adalimumab), Cimzia (certolizumab) and Remicade (infliximab) demonstrated the ability to achieve clinical response (RR, 2.69; p < 0.00001; RR, 1.74; p < 0.0001 and RR, 1.66; p = 0.0046, respectively) and maintain clinical remission (RR, 1.68; p = 0.000072 with certolizumab and RR, 2.5; p = 0.000019 with infliximab; adalimumab, data not reported) over placebo in patients with CD. Adalimumab and infliximab also had a steroid-sparing effect (*Behm et al 2008*). Other systematic reviews have further demonstrated the efficacy of these agents in CD (*Singh et al 2014, Fu et al 2017*).
- In a systematic review of patients with CD who had failed a trial with Remicade (infliximab), the administration of Humira (adalimumab) was associated with remission rates of 19 to 68% at 1 year. Serious cases of sepsis, cellulitis, and fungal pneumonia occurred in 0 to 19% of patients in up to 4 years of treatment (*Ma et al 2009*).
- A systematic review of 8 randomized clinical trials with TYSABRI (natalizumab) or Entyvio (vedolizumab) for the management of CD evaluated the rates of failure of remission induction (*Chandar et al 2015*). Fewer failures of remission induction were reported with natalizumab and vedolizumab compared to placebo (RR 0.87; 95% CI, 0.84 to 0.91; I^2=0%). The summary effect sizes were similar for both natalizumab (RR 0.86; 95% CI, 0.80 to 0.93) and vedolizumab (RR 0.87; 95% CI, 0.79 to 0.95). No significant difference was detected between the 2 active treatments (p = 0.95). No significant differences between natalizumab and vedolizumab were observed for rates of serious AEs, infections (including serious infections), and treatment discontinuation. Rates of infusion reactions in induction trials were more common with natalizumab over vedolizumab (p = 0.007). Progressive multifocal leukoencephalopathy (PML) has been reported with natalizumab but has not been reported with vedolizumab.
- The use of Stelara (ustekinumab) for the treatment of CD was evaluated in the UNITI-1, UNITI-2, and IM-UNITI studies (*Feagan et al 2016*). All were Phase 3, double-blind, placebo-controlled trials.
    - UNITI-1 (n = 741) was an 8-week induction trial that compared single IV doses of ustekinumab 130 mg IV, weight-based ustekinumab (~6 mg/kg), and placebo in patients with nonresponse or intolerance to ≥ 1 TNF inhibitors. The primary endpoint was clinical response at week 6, which was defined as a decrease from

baseline in the CDAI of ≥100 points or a CDAI score of < 150. A clinical response was achieved by 34.4%, 33.7%, and 21.5% of patients in the ustekinumab 130 mg, weight-based ustekinumab, and placebo groups, respectively (p = 0.002 for 130 mg dose vs placebo; p = 0.003 for weight-based dose vs placebo). Benefits were also demonstrated on all major secondary endpoints, which included clinical response at week 8, clinical remission (CDAI < 150) at week 8, and CDAI decrease of ≥70 points at weeks 3 and 6.

- UNITI-2 (n = 628) had a similar design to UNITI-1, but was conducted in patients with treatment failure or intolerance to immunosuppressants or glucocorticoids (with no requirement for prior TNF inhibitor use). In this trial, a clinical response was achieved by 51.7%, 55.5%, and 28.7% of patients in the ustekinumab 130 mg, weight-based ustekinumab, and placebo groups, respectively (p < 0.001 for both doses vs placebo). Benefits were also demonstrated on all major secondary endpoints.
- IM-UNITI was a 44-week maintenance trial that enrolled patients completing UNITI-1 and UNITI-2. Of 1,281 enrolled patients, there were 397 randomized patients (primary population); these were patients who had had a clinical response to ustekinumab induction therapy and were subsequently randomized to ustekinumab 90 mg SQ every 8 or 12 weeks or placebo. The primary endpoint, clinical remission at week 44, was achieved by 53.1%, 48.8%, and 35.9% of patients in the ustekinumab every 8 week, ustekinumab every 12 week, and placebo groups, respectively (p = 0.005 for every 8 week regimen vs placebo; p = 0.04 for every 12 week regimen vs placebo). Numerical and/or statistically significant differences for ustekinumab vs placebo were observed on key secondary endpoints including clinical response, maintenance of remission, and glucocorticoid-free remission.

Hidradenitis suppurativa (HS)

- Two 36-week, Phase 3, double-blind, multicenter, placebo-controlled, randomized trials, PIONEER I and II, evaluated Humira (adalimumab) for the treatment of HS (*Kimball et al 2016*). A total of 633 adults (307 in PIONEER I and 326 in PIONEER II) with moderate to severe HS were enrolled. The study consisted of 2 treatment periods; in the first period, patients were randomized to placebo or weekly adalimumab for 12 weeks; in the second period, patients initially assigned to placebo received weekly adalimumab (PIONEER I) or placebo (PIONEER II) for 24 weeks and patients initially assigned to adalimumab were re-randomized to placebo, weekly adalimumab, or every-other-week adalimumab. The adalimumab dosage regimen was 160 mg at week 0, followed by 80 mg at week 2, followed by 40 mg doses starting at week 4.
  - The primary endpoint was HS clinical response (HiSCR) at week 12, defined as at least 50% reduction in total abscess and inflammatory nodule count with no increase in abscess count and no increase in draining fistula count compared to baseline. HiSCR rates at week 12 were significantly higher for the groups receiving adalimumab than for the placebo groups: 41.8% vs 26.0% in PIONEER I (p = 0.003) and 58.9% vs 27.6% in PIONEER II (p < 0.001).
  - Among patients with a clinical response at week 12, response rates in all treatment groups subsequently declined over time. During period 2, there were no significant differences in clinical response rates in either trial between patients randomly assigned to adalimumab at either a weekly dose or an every-other-week dose and those assigned to placebo, regardless of whether the patients had a response at week 12. For patients who received placebo in period 1, 41.4% of those assigned to adalimumab weekly in period 2 (PIONEER I) and 15.9% of those reassigned to placebo in period 2 (PIONEER II) had a clinical response at week 36.
  - The authors noted that the magnitude of improvement with adalimumab treatment was modest compared with adalimumab treatment in other disease states, and patients were unlikely to achieve complete symptom resolution.

Juvenile idiopathic arthritis (JIA)

- In a trial of pediatric patients (6 to 17 years of age) with JIA (extended oligoarticular, polyarticular, or systemic without systemic manifestations), the patients treated with placebo had significantly more flares than the patients treated with Orencia (abatacept) (p = 0.0003). The time to flare was significantly different favoring abatacept (p = 0.0002) (*Ruperto et al 2008*).
- Humira (adalimumab) was studied in a group of patients (4 to 17 years of age) with active polyarticular JIA who had previously received treatment with NSAIDs. Patients were stratified according to MTX use and received 24 mg/m^2 (maximum of 40 mg) of adalimumab every other week for 16 weeks. The patients with an American College of Rheumatology Pediatric 30 (ACR Pedi 30) response at week 16 were randomly assigned to receive adalimumab or placebo in a double-blind method every other week for up to 32 weeks. The authors found that 74% of patients not receiving MTX and 94% of those receiving MTX had an ACR Pedi 30 at week 16. Among those not receiving MTX, flares occurred in 43% receiving adalimumab and 71% receiving placebo (p = 0.03). In the patients receiving MTX, flares occurred in 37 and 65% in the adalimumab and placebo groups, respectively (p = 0.02). ACR Pedi scores were

significantly greater with adalimumab than placebo and were sustained after 104 weeks of treatment (*Lovell et al 2008*).

- A double-blind, multicenter, randomized controlled trial compared Humira (adalimumab) and placebo in 46 children ages 6 to 18 years with enthesitis-related arthritis (*Burgos-Vargas et al 2015*). Patients were TNF inhibitor naïve. At week 12, the percentage change from baseline in the number of active joints with arthritis was significantly reduced with adalimumab compared to placebo (-62.6% vs -11.6%, p = 0.039). A total of 7 patients (3 placebo; 4 adalimumab) escaped the study early during the double-blind phase and moved to open-label adalimumab therapy. Analysis excluding these patients produced similar results (adalimumab, -83.3 vs placebo -32.1; p = 0.018). At week 52, adalimumab-treated patients had a mean reduction in active joint count from baseline of 88.7%. A total of 93.5% of patients achieved complete resolution of their swollen joints with a mean of 41 days of adalimumab therapy.
- In a trial involving 69 pediatric patients with active polyarticular JIA despite treatment with NSAIDs and MTX, Enbrel (etanercept) was associated with a significant reduction in flares compared to placebo (28% vs 81%; p = 0.003) (*Lovell et al 2000*). Ninety-four percent of patients who remained in an open-label 4 year extension trial met ACR Pedi 30; C-reactive protein (CRP) levels, articular severity scores, and patient pain assessment scores all decreased. There were 5 cases of serious AEs related to etanercept therapy after 4 years (*Lovell et al 2006*).
- The approval of Actemra (tocilizumab) for the indication of SJIA was based on a randomized, placebo-controlled trial (n = 112). Children age 2 to 17 years of age with active SJIA and inadequate response to NSAIDs and corticosteroids were included in the study. The primary endpoint was ACR 30 and absence of fever at week 12. At week 12, the proportion of patients achieving ACR 30 and absence of fever was significantly greater in the tocilizumab-treated patients compared to the placebo treated patients (85% vs 24%; p < 0.0001)(*De Benedetti et al 2012*). The double-blind, randomized CHERISH study evaluated tocilizumab for JIA flares in patients ages 2 to 17 years with JIA with an inadequate response or intolerance to MTX (*Brunner et al 2015*). Tocilizumab-treated patients experienced significantly fewer JIA flares at week 40 compared to patients treated with placebo (25.6% vs 48.1%; p < 0.0024).
- In 2 trials in patients with SJIA, Ilaris (canakinumab) was more effective at reducing flares than placebo. It also allowed for glucocorticoid dose tapering or discontinuation. More patients treated with canakinumab experienced infections than patients treated with placebo (*Ruperto et al 2012*).
- A meta-analysis of trials evaluating biologics for the treatment of SJIA included 5 trials; 1 each for Kineret (anakinra), Ilaris (canakinumab), and Actemra (tocilizumab), and 2 for rilonacept (not FDA-approved for JIA and not included in this review) (*Tarp et al 2016*). The primary endpoint, the proportion of patients achieving a modified ACR Pedi 30 response, was superior to placebo for all agents, but did not differ significantly among anakinra, canakinumab, and tocilizumab. However, comparisons were based on low-quality, indirect evidence and no firm conclusions can be drawn on their relative efficacy. No differences among drugs for serious AEs were demonstrated.

Plaque psoriasis (PsO)

- In a randomized, double-blind, double-dummy trial, Humira (adalimumab) was compared to MTX and placebo in patients with moderate to severe PsO despite treatment with topical agents. The primary outcome was the proportion of patients that achieved Psoriasis Area and Severity Index (PASI) 75 at 16 weeks. Significantly more patients in the adalimumab group achieved the primary endpoint compared to patients in the MTX (p < 0.001) and placebo (p < 0.001) groups, respectively (*Saurat et al 2008*).
- More than 2,200 patients were enrolled in 2 published, pivotal, phase III trials that served as the primary basis for the FDA approval of Stelara (ustekinumab) in PsO. PHOENIX 1 and PHOENIX 2 enrolled patients with moderate to severe PsO to randomly receive ustekinumab 45 mg, 90 mg or placebo at weeks 0, 4, and every 12 weeks thereafter (*Leonardi et al 2008, Papp et al 2008, Langley et al 2015*). In PHOENIX 1, patients who were initially randomized to ustekinumab at week 0 and achieved long-term response (at least PASI 75 at weeks 28 and 40) were re-randomized at week 40 to maintenance ustekinumab or withdrawal from treatment. Patients in the 45 mg ustekinumab and 90 mg ustekinumab groups had higher proportion of patients achieving PASI 75 compared to patients in the placebo group at week 12 (p < 0.0001 for both). PASI 75 response was better maintained to at least 1 year in those receiving maintenance ustekinumab than in those withdrawn from treatment at week 40 (p < 0.0001) (*Leonardi et al 2008*). In PHOENIX 2, the primary endpoint (the proportion of patients achieving a PASI 75 response at week 12) was achieved in significantly more patients receiving ustekinumab 45 and 90 mg compared to patients receiving placebo (p < 0.0001). Partial responders were re-randomized at week 28 to continue dosing every 12 weeks or escalate to dosing every 8 weeks. More partial responders at week 28 who received 90 mg every 8 weeks achieved PASI 75 at week 52 than did those who continued to receive the same dose every 12 weeks. There was no such response to changes in dosing intensity in partial responders treated with 45 mg. AEs were similar between groups (*Papp et al 2008*). A total of 70% (849 of 1212) of ustekinumab-treated patients completed therapy through week 244. At week 244, the proportions of patients initially randomized to ustekinumab 45 mg and 90 mg who achieved PASI 75 were 76.5% and 78.6%, respectively. A total of 50.0% and 55.5% of patients, respectively, achieved PASI 90 (*Langley et al 2015*).

- In a study comparing Enbrel (etanercept) and Stelara (ustekinumab), a greater proportion of PsO patients achieved the primary outcome (PASI 75 at week 12) with ustekinumab 45 (67.5%) and 90 mg (73.8%) compared to etanercept 50 mg (56.8%; p = 0.01 vs ustekinumab 45 mg; p < 0.001 vs ustekinumab 90 mg). In this trial, etanercept therapy was associated with a greater risk of injection site erythema (14.7% vs 0.7% of all ustekinumab patients) (*Griffiths et al 2010).*
- Approval of Otezla (apremilast) for moderate to severe PsO was based on results from the ESTEEM trials. In the trials, 1,257 patients with moderate to severe PsO were randomized 2:1 to apremilast 30 mg twice daily (with a titration period) or placebo. The primary endpoint was the number of patients with a 75% improvement on the PASI 75. In ESTEEM 1, significantly more patients receiving apremilast achieved PASI 75 compared to placebo (33.1% vs 5.3%; p < 0.0001) at 16 weeks. In ESTEEM 2, significantly more patients receiving apremilast also achieved PASI 75 compared to placebo (28.8% vs 5.8%; p < 0.0001) at 16 weeks (*Papp et al 2015, Paul et al 2015a*).
    - Additional analyses of the ESTEEM trials have been published. In 1 analysis (*Thaçi et al 2016*), the impact of apremilast on health-related quality of life, general function, and mental health was evaluated using patient-reported outcome assessments. The study demonstrated improvement with apremilast vs placebo, including improvements on the dermatology life quality index (DLQI) and SF-36 mental component summary (MCS) that exceeded minimal clinically important differences. In another analysis (*Rich et al 2016*), effects of apremilast on difficult-to-treat nail and scalp psoriasis were evaluated. At baseline in ESTEEM 1 and ESTEEM 2, respectively, 66.1% and 64.7% of patients had nail psoriasis and 66.7% and 65.5% had moderate to very severe scalp psoriasis. At week 16, apremilast produced greater improvements in Nail Psoriasis Severity Index (NAPSI) score vs placebo; greater NAPSI-50 response (50% reduction from baseline in target nail NAPSI score) vs placebo; and greater response on the Scalp Physician Global Assessment (ScPGA) vs placebo. Improvements were generally maintained over 52 weeks in patients with a PASI response at week 32.
- Cosentyx (secukinumab) was evaluated in 2 large, phase 3, double-blind trials in patients with moderate to severe PsO. The co-primary endpoints were the proportions of patients achieving PASI 75 and the proportions of patients with clear or almost clear skin (score 0 or 1) on the modified investigator's global assessment (IGA) at 12 weeks.
    - In ERASURE (n = 738), 81.6%, 71.6%, and 4.5% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, and placebo, respectively, and 65.3%, 51.2%, and 2.4% achieved a score of 0 or 1 on the IGA (*Langley et al 2014*).
    - In FIXTURE (n = 1306), 77.1%, 67%, 44%, and 4.9% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, Enbrel (etanercept) at FDA-recommended dosing, and placebo, respectively, and 62.5%, 51.1%, 27.2%, and 2.8% achieved a score of 0 or 1 on the IGA (*Langley et al 2014*).
- Two smaller, phase 3, double-blind, placebo-controlled trials evaluated Cosentyx (secukinumab) given by prefilled syringe (FEATURE) or auto-injector/pen (JUNCTURE). Again, co-primary endpoints were the proportions of patients achieving PASI 75 and obtaining a score of 0 or 1 on the modified IGA at 12 weeks.
    - In FEATURE (n = 177), 75.9%, 69.5%, and 0% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, and placebo, respectively, and 69%, 52.5%, and 0% achieved a score of 0 or 1 on the IGA (*Blauvelt et al 2015*).
    - In JUNCTURE (n = 182), 86.7%, 71.7%, and 3.3% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, and placebo, respectively, and 73.3%, 53.3%, and 0% achieved a score of 0 or 1 on the IGA (*Paul et al 2015b*).
- Secondary endpoints, including the proportions of patients demonstrating a reduction of 90% or more on the PASI (PASI 90), a reduction of 100% (PASI 100), and change in the DLQI further support the efficacy of Cosentyx (secukinumab) (*Blauvelt et al 2015, Langley et al 2014, Paul et al 2015b*).
- In the CLEAR study, Cosentyx (secukinumab) 300 mg SQ every 4 weeks and Stelara (ustekinumab) 45 mg or 90 mg SQ (based on body weight) every 12 weeks were compared for safety and efficacy in a double-blind, randomized controlled trial in 676 patients with moderate to severe PsO (*Thaçi et al 2015*). The primary endpoint, proportion of patients achieving PASI 90 at week 16, was significantly higher with secukinumab compared to ustekinumab (79% vs 57.6%; p < 0.0001). Achievement of PASI 100 response at week 16 was also significantly higher with secukinumab over ustekinumab (44.3% vs 28.4%; p < 0.0001). Infections and infestations were reported in 29.3% of secukinumab- and 25.3% of ustekinumab-treated patients. Most infections were not serious and were managed without discontinuation. The most commonly reported AEs included headache and nasopharyngitis. Serious AEs were reported in 3% of each group.
- A meta-analysis of 7 Phase 3 clinical trials demonstrated the efficacy of Cosentyx (secukinumab) vs placebo and vs Enbrel (etanercept) in patients with PsO (*Ryoo et al 2016*). The ORs for achieving PASI 75 and for achieving IGA 0 or 1 were both 3.7 for secukinumab vs etanercept. Secukinumab 300 mg was significantly more effective than 150 mg. Secukinumab was well-tolerated throughout the 1-year trials.

- The use of Taltz (ixekizumab) for the treatment of PsO was evaluated in the UNCOVER-1, UNCOVER-2, and UNCOVER-3 trials. All were Phase 3, double-blind, randomized trials.
    - UNCOVER-1 (n = 1296) compared ixekizumab 160 mg loading dose then 80 mg every 2 weeks, ixekizumab 160 mg loading dose then 80 mg every 4 weeks, and placebo (*Gordon et al 2016, Taltz product dossier 2016*). Co-primary endpoints were the proportion of patients achieving PASI 75 and the proportion of patients achieving a physician's global assessment (PGA) score of 0 or 1 (clear or almost clear) at week 12. In the ixekizumab every 2 week, ixekizumab every 4 week, and placebo groups, PASI 75 was achieved by 89.1%, 82.6%, and 3.9% of patients, respectively ($p < 0.001$ for both doses vs placebo), and PGA 0 or 1 was achieved by 81.8%, 76.4%, and 3.2% of patients, respectively ($p < 0.001$ for both doses vs placebo). Improvements for ixekizumab vs placebo were also seen in secondary endpoints including PASI 90, PASI 100, PGA 0, and change in DLQI.
    - UNCOVER-2 (n = 1224) compared ixekizumab 160 mg loading dose then 80 mg every 2 weeks, ixekizumab 160 mg then 80 mg every 4 weeks, etanercept 50 mg twice weekly, and placebo (*Griffiths et al 2015*). Co-primary endpoints were the proportion of patients achieving PASI 75 and the proportion of patients achieving a PGA 0 or 1 at week 12. The proportions of patients achieving PASI 75 were 89.7%, 77.5%, 41.6%, and 2.4% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively ($p < 0.0001$ for all active treatments vs placebo and for both ixekizumab arms vs etanercept). The proportions of patients achieving PGA 0 or 1 were 83.2%, 72.9%, 36%, and 2.4% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively ($p < 0.0001$ for all active treatments vs placebo and for both ixekizumab arms vs etanercept). Improvements were also greater for ixekizumab vs placebo, etanercept vs placebo, and ixekizumab vs etanercept for all secondary endpoints including PGA 0, PASI 90, PASI 100, and DLQI.
    - UNCOVER-3 (n = 1346) had the same treatment groups and primary and secondary endpoints as UNCOVER-2 (*Griffiths et al 2015*). The proportions of patients achieving PASI 75 were 87.3%, 84.2%, 53.4%, and 7.3% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively ($p < 0.0001$ for all active treatments vs placebo and for both ixekizumab arms vs etanercept). The proportions of patients achieving PGA 0 or 1 were 80.5%, 75.4%, 41.6%, and 6.7% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively ($p < 0.0001$ for all active treatments vs placebo and for both ixekizumab arms vs etanercept). Improvements were also greater for ixekizumab vs placebo, etanercept vs placebo, and ixekizumab vs etanercept for all secondary endpoints including PGA 0, PASI 90, PASI 100, and DLQI.
    - Results through week 60 for UNCOVER-1, UNCOVER-2, and UNCOVER-3 have been reported (*Gordon et al 2016*). At week 12 in UNCOVER-1 and UNCOVER-2, patients responding to ixekizumab (PGA 0 or 1) were re-randomized to receive ixekizumab 80 mg every 4 weeks, ixekizumab 80 mg every 12 weeks, or placebo through week 60. Among the patients who were randomly reassigned at week 12 to receive 80 mg of ixekizumab every 4 weeks (the approved maintenance dosing), 80 mg of ixekizumab every 12 weeks, or placebo, a PGA score of 0 or 1 was maintained by 73.8%, 39.0%, and 7.0% of the patients, respectively, and high rates were maintained or attained for additional measures such as PASI 75, PASI 90, and PASI 100 (pooled data for UNCOVER-1 and UNCOVER-2). At week 12 in UNCOVER-3, patients entered a long-term extension period in which they received ixekizumab 80 mg every 4 weeks through week 60. At week 60, at least 73% had a PGA score of 0 or 1 and at least 80% had a PASI 75 response. In addition, most patients had maintained or attained PASI 90 or PASI 100 at week 60.
- The IXORA-S study (n = 676) was a head-to-head study that compared Taltz (ixekizumab) (160 mg LD, then 80 mg every 2 weeks for 12 weeks, then 80 mg every 4 weeks) to Stelara (ustekinumab) (45 mg or 90 mg weight-based dosing per label) (*Reich et al 2017[b]).* The primary endpoint, PASI 90 response at week 12, was achieved by 72.8% and 42.2% of patients in the ixekizumab and ustekinumab groups, respectively ($p < 0.001$); superior efficacy of ixekizumab was maintained through week 24. Response rates for PASI 75, PASI 100, and PGA 0 or 1 also favored ixekizumab over ustekinumab (adjusted $p < 0.05$).
- The use of Siliq (brodalumab) for the treatment of PsO was evaluated in the AMAGINE-1, AMAGINE-2, and AMAGINE-3 trials. All were Phase 3, double-blind, randomized trials.
    - AMAGINE-1 (n = 661) compared brodalumab 210 mg, brodalumab 140 mg, and placebo; each treatment was given at weeks 0, 1, and 2, followed by every 2 weeks to week 12 (*Papp et al 2016*). This 12-week induction phase was followed by a withdrawal/retreatment phase through week 52: patients receiving brodalumab who achieved PGA 0 or 1 (PGA success) were re-randomized to the placebo or induction dose, and patients randomized to brodalumab with PGA ≥ 2 and those initially receiving placebo received brodalumab 210 mg every 2 weeks. Patients in the withdrawal phase who had disease recurrence (PGA ≥ 3) between weeks 16 and 52 were retreated with their induction doses of brodalumab. Co-primary endpoints were the proportion of

patients achieving PASI 75 and the proportion of patients achieving PGA success at week 12. PASI 75 was achieved by 83% (95% CI, 78 to 88), 60% (95% CI, 54 to 67), and 3% (95% CI, 1 to 6) of patients in the brodalumab 210 mg, brodalumab 140 mg, and placebo groups, respectively; PGA success was achieved by 76% (95% CI, 70 to 81), 54% (95% CI, 47 to 61), and 1% (95% CI, 0 to 4), respectively ($p < 0.001$ for all comparisons of brodalumab vs placebo). Differences in key secondary endpoints at week 12 also favored brodalumab vs placebo, including PASI 90, PASI 100, and PGA 0. In the randomized withdrawal phase, high response rates were maintained in those who continued brodalumab, while most patients re-randomized to placebo experienced return of disease (but were able to recapture disease control with retreatment).

- AMAGINE-2 (n = 1831) and AMAGINE-3 (n = 1881) were identical in design and compared brodalumab 210 mg, brodalumab 140 mg, Stelara (ustekinumab), and placebo (*Lebwohl et al 2015*). Brodalumab was given at weeks 0, 1, and 2, followed by every 2 weeks to week 12. Ustekinumab was given in weight-based doses per its FDA-approved labeling. At week 12, patients receiving brodalumab were re-randomized to receive brodalumab at a dose of 210 mg every 2 weeks or 140 mg every 2, 4, or 8 weeks; patients receiving ustekinumab continued ustekinumab; and patients receiving placebo were switched to brodalumab 210 mg every 2 weeks; maintenance continued though week 52. The primary endpoints included a comparison of both brodalumab doses vs placebo with regard to the proportion of patients achieving PASI 75 and the proportion of patients achieving PGA success (PGA 0 or 1) at week 12, as well as a comparison of brodalumab 210 mg vs ustekinumab with regard to the proportion of patients achieving PASI 100 at week 12.
  - In AMAGINE-2, the proportion of patients achieving PASI 75 was 86% (95% CI, 83 to 89), 67% (95% CI, 63 to 70), 70% (95% CI, 65 to 75), and 8% (95% CI, 5 to 12) in the brodalumab 210 mg, brodalumab 140 mg, ustekinumab, and placebo groups, respectively, and the proportion of patients achieving PGA success was 79% (95% CI, 75 to 82), 58% (95% CI, 54 to 62), 61% (95% CI, 55 to 67), and 4% (95% CI, 2 to 7), respectively ($p < 0.001$ for all comparisons of brodalumab vs placebo). The proportion of patients achieving PASI 100 was 44% (95% CI, 41 to 49), 26% (95% CI, 22 to 29), 22% (95% CI, 17 to 27), and 1% (95% CI, 0 to 2), respectively ($p < 0.001$ for both brodalumab doses vs placebo and for brodalumab 210 mg vs ustekinumab; $p = 0.08$ for brodalumab 140 mg vs ustekinumab).
  - In AMAGINE-3, the proportion of patients achieving PASI 75 was 85% (95% CI, 82 to 88), 69% (95% CI, 65 to 73), 69% (95% CI, 64 to 74), and 6% (95% CI, 4 to 9) in the brodalumab 210 mg, brodalumab 140 mg, ustekinumab, and placebo groups, respectively, and the proportion of patients achieving PGA success was 80% (95% CI, 76 to 83), 60% (95% CI, 56 to 64), 57% (95% CI, 52 to 63), and 4% (95% CI, 2 to 7), respectively ($p < 0.001$ for all comparisons of brodalumab vs placebo). The proportion of patients achieving PASI 100 was 37% (95% CI, 33 to 41), 27% (95% CI, 24 to 31), 19% (95% CI, 14 to 23), and 0.3% (95% CI, 0 to 2), respectively ($p < 0.001$ for both brodalumab doses vs placebo and for brodalumab 210 mg vs ustekinumab; $p = 0.007$ for brodalumab 140 mg vs ustekinumab).
  - In both studies, the 2 brodalumab doses were superior to placebo with regard to all key secondary endpoints. Patients receiving brodalumab 210 mg throughout the induction and maintenance phases demonstrated an increase in PASI response rates through week 12 and a stabilization during weeks 16 to 52. Based on PGA success rates, maintenance with brodalumab 210 mg or 140 mg every 2 weeks was superior to the use of the less frequent maintenance regimens, and the 210 mg regimen was superior to the 140 mg regimen.

- The use of Tremfya (guselkumab) for the treatment of moderate to severe PsO was evaluated in the VOYAGE 1, VOYAGE 2, and NAVIGATE trials. All were phase 3, double-blind, randomized trials.
  - Patients in both VOYAGE 1 and VOYAGE 2 were initially assigned to receive guselkumab (100 mg at weeks 0 and 4, then every 8 weeks), placebo, or Humira (adalimumab) (80 mg at week 0, 40 mg at week 1, then every 2 weeks). Patients in the placebo group were switched to guselkumab at week 16. The coprimary endpoints included the proportion of patients achieving an IGA score of 0 or 1 at week 16 as well as the proportion of patients achieving a PASI 90 response at week 16 in the guselkumab group compared with placebo. Comparisons between guselkumab and adalimumab were assessed as secondary endpoints at weeks 16, 24, and 48. To evaluate maintenance and durability of response in VOYAGE 2, subjects randomized to guselkumab at week 0 and who were PASI 90 responders at week 28 were re-randomized to either continue treatment with guselkumab every 8 weeks or be withdrawn from therapy (ie, receive placebo).
    - In VOYAGE 1 (n = 837), IGA 0 or 1 was achieved in more patients treated with guselkumab (85.1%) compared to placebo (6.9%) at week 16 ($p < 0.001$), and a higher percentage of patients achieved PASI 90 with guselkumab (73.3%) compared to placebo (2.9%; $p<0.001$) (*Blauvelt et al 2017*). Additionally, IGA 0 or 1 was achieved in more patients with guselkumab vs adalimumab at week 16

(85.1% vs 65.9%), week 24 (84.2% vs. 61.7%), and week 48 (80.5% vs 55.4%; p < 0.001). PASI 90 score was also achieved in a higher percentage of patients with guselkumab vs adalimumab at week 16 (73.3% vs 49.7%), week 24 (80.2% vs 53%), and week 48 (76.3% vs 47.9%; p < 0.001).
        - In VOYAGE 2 (n = 992), IGA 0 or 1 and PASI 90 were achieved by a higher proportion of patients who received guselkumab (84.1% and 70%) vs placebo (8.5% and 2.4%) (p < 0.001 for both comparisons). At week 16, IGA score of 0 or 1 and PASI 90 were achieved in more patients with guselkumab (84.1% and 70%) vs adalimumab (67.7% and 46.8%) (p < 0.001). PASI 90 was achieved in 88.6% of patients who continued on guselkumab vs 36.8% of patients who were rerandomized to placebo at week 48. In patients who were nonresponders to adalimumab and switched to guselkumab, PASI 90 was achieved by 66.1% of patients.
    - In NAVIGATE (n = 871), patients were assigned to open-label ustekinumab 45 or 90 mg at weeks 0 and 4 (*Langley et al 2017*). Patients with IGA 0 or 1 at week 16 were continued on ustekinumab, while patients with an inadequate response to ustekinumab at week 16 (IGA ≥ 2) were randomized to guselkumab 100 mg or ustekinumab. Patients treated with guselkumab had a higher mean number of visits with IGA of 0 or 1 and ≥ 2-grade improvement (relative to week 16) compared to randomized ustekinumab from week 28 to 40 (1.5 vs 0.7; p < 0.001). A higher proportion of patients achieved IGA of 0 or 1 with ≥ 2 grade improvement at week 28 with guselkumab (31.1%) vs randomized ustekinumab (14.3%; p = 0.001); at week 52, 36.2% of guselkumab-treated patients achieved this response vs 17.3% of the ustekinumab-treated patients. The proportion of patients with PASI 90 response at week 28 was 48.1% for the guselkumab group vs 22.6% for the ustekinumab group (p ≤ 0.001).
- The approval of Ilumya (tildrakizumab-asmn) was based on 2 randomized, double-blind, multicenter, phase 3 trials: reSURFACE1 (772 patients) and reSURFACE2 (1,090 patients). Enrolled adult patients with moderate-to-severe chronic plaque psoriasis received tildrakizumab-asmn 200 mg, tildrakizumab-asmn 100 mg, or placebo in both studies; reSURFACE 2 also included an Enbrel (etanercept) arm. Only the tildrakizumab-asmn 100 mg dose was approved by the FDA. The coprimary endpoints included the proportion of patients achieving PASI 75 and PGA response (score of 0 or 1 with ≥ 2 reduction from baseline) at week 12 (*Reich et al 2017*).
    - In reSURFACE 1, PASI 75 response was achieved by 64% and 6% of the tildrakizumab-asmn 100 mg and placebo arms at week 12, respectively; a PGA response was achieved by 58% vs 7% of the tildrakizumab-asmn 100 mg and placebo groups, respectively (p < 0.0001 for both comparisons).
    - In reSURFACE 2, PASI 75 response was achieved by 61% and 6% of the tildrakizumab-asmn 100 mg and placebo arms, respectively; a PGA response was achieved by 55% vs 4% of the tildrakizumab-asmn 100 mg and placebo groups, respectively (p < 0.0001 for both comparisons). A higher proportion of patients in the tildrakizumaz 100 mg group achieved PASI 75 vs etanercept (61% vs 48%, respectively; p = 0.001), but the rates of PGA responses did not differ significantly between groups (55% vs 48%, respectively; p = 0.0663).
- For most immunomodulators that are FDA-approved for the treatment of PsO, the indication is limited to adults. In 2016, Enbrel (etanercept) received FDA approval for treatment of PsO in pediatric patients age ≥ 4 years. Limited information from published trials is also available on the use of Stelara (ustekinumab) in adolescent patients (age 12 to 17 years).
    - A 48-week, double-blind, placebo-controlled trial (n = 211) evaluated the use of etanercept in patients 4 to 17 years of age with moderate-to-severe PsO (*Paller et al 2008*). Patients received etanercept 0.8 mg SQ once weekly or placebo for 12 weeks, followed by 24 weeks of open-label etanercept; 138 patients underwent a second randomization to placebo or etanercept at week 36 to investigate effects of withdrawal and retreatment. The primary endpoint, PASI 75 at week 12, was achieved by 57% and 11% of patients receiving etanercept and placebo, respectively. A significantly higher proportion of patients in the etanercept group than in the placebo group achieved PASI 90 (27% vs 7%) and a PGA of 0 or 1 (53% vs 13%) at week 12 (p < 0.001). During the withdrawal period from week 36 to week 48, response was lost by 29 of 69 patients (42%) assigned to placebo at the second randomization. Four serious AEs (including 3 infections) occurred in 3 patients during treatment with open-label etanercept; all resolved without sequelae. The authors concluded that etanercept significantly reduced disease severity in this population. Results of a 5-year, open-label extension study (n = 182) demonstrated that etanercept was generally well tolerated and efficacy was maintained in those who remained in the study for up to 264 weeks (69 of 181 patients) (*Paller et al 2016*).
    - A 52-week, double-blind, placebo-controlled trial (n = 110) evaluated the use of ustekinumab in patients 12 to 17 years of age with moderate-to-severe PsO (*Landells et al 2015*). Patients received a weight-based standard dose (SD), a half-strength dose (HSD), or placebo. The primary endpoint, the proportion of patients achieving a PGA 0 or 1 at week 12, was significantly greater in the SD (69.4%) and HSD (67.6%) groups vs placebo (5.4%) (p < 0.001 for both doses vs placebo). The proportions of patients achieving PASI 75 at this time point were 80.6%, 78.4%, and 10.8% in the SD, HSD, and placebo groups, respectively (p < 0.001 for

both doses vs placebo), and the proportions of patients achieving PASI 90 were 61.1%, 54.1%, and 5.4% in the SD, HSD, and placebo groups, respectively (p < 0.001 for both doses vs placebo). In both groups, the proportions of patients achieving these endpoints were maintained from week 12 through week 52. The authors concluded that ustekinumab appears to be a viable treatment option for moderate-to-severe PsO in the adolescent population. The standard dose provided a response comparable to that in adults with no unexpected AEs through 1 year of treatment.

- Combination therapy is commonly utilized, such as with different topical therapies, systemic plus topical therapies, and combinations of certain systemic therapies with phototherapy (*Feldman 2015*). Combinations of different systemic therapies have not been adequately studied; however, there are some data to show that combined therapy with Enbrel (etanercept) plus MTX may be beneficial for therapy-resistant patients (*Busard et al 2014; Gottlieb et al 2012*).
- In a meta-analysis evaluating the efficacy and tolerability of biologic and nonbiologic systemic treatments for moderate to severe PsO, Humira (adalimumab) use was associated with a risk difference of 64% compared to placebo in achieving a PASI 75 response (p < 0.00001) while Enbrel (etanercept) 25 and 50 mg twice weekly were associated with a risk difference of 30 and 44% compared to placebo (p < 0.00001 for both strengths vs placebo). The Remicade (infliximab) group had the greatest response with a risk difference of 77% compared to the placebo group (p < 0.0001). The withdrawal rate was 0.5% with adalimumab, 0.4 to 0.5% with etanercept and 1.3% with infliximab (*Schmitt et al 2008*).
- Another meta-analysis evaluated the efficacy and safety of long-term treatments (≥24 weeks) for moderate-to-severe PsO (*Nast et al 2015a*). A total of 25 randomized trials (n = 11,279) were included. Compared to placebo, RRs for achievement of PASI 75 were 13.07 (95% CI, 8.60 to 19.87) for Remicade (infliximab), 11.97 (95% CI, 8.83 to 16.23) for Cosentyx (secukinumab), 11.39 (95% CI, 8.94 to 14.51) for Stelara (ustekinumab), 8.92 (95% CI, 6.33 to 12.57) for Humira (adalimumab), 8.39 (95% CI, 6.74 to 10.45) for Enbrel (etanercept), and 5.83 (95% CI, 2.58 to 13.17) for Otezla (apremilast). Head-to-head studies demonstrated better efficacy for secukinumab and infliximab vs etanercept, and for infliximab vs MTX. The biologics and apremilast also had superior efficacy vs placebo for endpoints of PASI 90 and PGA 0 or 1. The investigators stated that based on available evidence, infliximab, secukinumab, and ustekinumab are the most efficacious long-term treatments, but noted that additional head-to-head comparisons and studies on safety and patient-related outcomes are desirable.
- In a meta-analysis of 41 RCTs that used hierarchical clustering to rate efficacy and tolerability, Humira (adalimumab), Cosentyx (secukinumab), and Stelara (ustekinumab) were characterized by high efficacy and tolerability, Remicade (infliximab) and Taltz (ixekizumab) were characterized by high efficacy and poorer tolerability, and Enbrel (etanercept), MTX, and placebo were characterized by poorer efficacy and moderate tolerability in patients with PsO (*Jabbar-Lopez et al 2017*).
- A Cochrane review evaluated biologics in patients with moderate to severe PsO in 109 studies (*Sbidian E et al 2017*) between 12 and 16 weeks after randomization. Agents included in the review were Humira (adalimumab), Enbrel (etanercept), Cimzia (certolizumab), Stelara (ustekinumab), Cosentyx (secukinumab), Taltz (ixekizumab), Siliq (brodalumab), Remicade (infliximab), and Tremfya (guselkumab). The network meta-analysis showed that all of the biologics were significantly more effective in achieving PASI 90 compared to placebo. Cosentyx (secukinumab), Taltz (ixekizumab), and Siliq (brodalumab) were significantly more effective than Remicade (infliximab), Humira (adalimumab), and Enbrel (etanercept), but not Cimzia (certolizumab). Stelara (ustekinumab) was superior to Enbrel (etanercept). There was no significant difference amongst the agents in the risk of serious adverse effects.

Psoriatic arthritis (PsA)

- In 2 trials, PsA patients receiving Humira (adalimumab) 40 mg every other week achieved an ACR 20 at a higher rate than with placebo. Thirty-nine percent in the active treatment group vs 16% in the placebo group achieved this endpoint by week 12 (p = 0.012) in a trial (n = 100); while 58 and 14% of patients, respectively, achieved this endpoint in a second trial (p < 0.001) (*Genovese et al 2007, Mease et al 2005*). Adalimumab use was also associated with an improvement in structural damage, as measured by the mTSS, compared to those receiving placebo (-0.2 vs 1; p < 0.001) (*Mease et al 2005*).
- In a 12-week trial in adult patients with PsA despite NSAID therapy, 87% of Enbrel (etanercept) treated patients met PsA response criteria, compared to 23% of those on placebo (p < 0.0001). A PASI 75 improvement and ACR 20 response were detected in 26 and 73% of etanercept-treated patients vs 0 (p = 0.0154) and 13% (p < 0.0001) of placebo-treated patients (*Mease et al 2000*). In a second trial, the mean annualized rate of change in the mTSS with Enbrel (etanercept) was -0.03 unit, compared to 1 unit with placebo (p < 0.0001). At 24 weeks, 23% of etanercept patients eligible for PsO evaluation achieved at least a PASI 75, compared to 3% of placebo patients (p = 0.001). Additionally, HAQ scores were significantly improved with etanercept (54%) over placebo (6%; p < 0.0001). Injection site reaction occurred at a greater rate with etanercept than placebo (36% vs 9%; p < 0.001) (*Mease et al 2004*).

- The FDA approval of Simponi (golimumab) for PsA was based on the GO-REVEAL study, a multicenter, randomized, double-blind, placebo-controlled trial in adult patients with moderate to severely active PsA despite NSAID or DMARD therapy (n = 405). Golimumab with or without MTX compared to placebo with or without MTX, resulted in significant improvement in signs and symptoms as demonstrated by the percentage of patients achieving a ACR 20 response at week 14. The ACR responses observed in the golimumab-treated groups were similar in patients receiving and not receiving concomitant MTX therapy (*Kavanaugh et al 2009*).
    - Subcutaneous golimumab for patients with active PsA demonstrated safety and efficacy over 5 years in the long-term extension of the GO-REVEAL study. Approximately one-half of patients took MTX concurrently. ACR 20 response rates at year 5 were 62.8 to 69.9% for golimumab SQ 50 or 100 mg every 4 weeks (*Kavanaugh et al 2014b*).
    - Post-hoc analyses of the 5-year GO-REVEAL results evaluated the relationship between achieving minimal disease activity (MDA; defined as the presence of ≥5 of 7 PsA outcomes measures [≤1 swollen joint, ≤1 tender joint, PASI ≤1, patient pain score ≤15, patient global disease activity score ≤20, HAQ disability index [HAQ DI] ≤0.5, and ≤1 tender enthesis point]) and long-term radiographic outcomes including radiographic progression. Among golimumab-treated patients, achieving long-term MDA was associated with better long-term functional improvement, patient global assessment, and radiographic outcomes. Radiographic benefit was more pronounced in patients using MTX at baseline. The authors conclude that in patients with active PsA, aiming for MDA as part of a treat-to-target strategy may provide long-term functional and radiographic benefits (*Kavanaugh et al 2016*).
- In another trial, more Remicade (infliximab) treated patients achieved ACR 20 at weeks 12 and 24 compared to placebo treated patients ($p < 0.001$) (*Antoni et al 2005*).
- The efficacy of Cimzia (certolizumab) in the treatment of PsA was established in 1 multicenter, double-blind, placebo controlled trial (n = 409). Patients were randomized to receive placebo, Cimzia 200 mg every 2 weeks, or Cimzia 400 mg every 4 weeks. At week 12, ACR 20 response was significantly greater in both active treatment groups compared to placebo (*Mease et al 2014*).
- The FDA-approval of Stelara (ustekinumab) for PsA was based on the results of 2 randomized, double-blind, placebo-controlled trials in adult patients with active PsA despite NSAID or DMARD therapy (PSUMMIT 1 and PSUMMIT 2). In PSUMMIT 1 (n = 615), a greater proportion of patients treated with ustekinumab 45 mg or 90 mg alone or in combination with MTX achieved ACR 20 response at week 24 compared to placebo (42.4% and 49.5% vs 22.8%; $p < 0.0001$ for both comparisons); responses were maintained at week 52 (*McInnes et al 2013*). Similar results were observed in the PSUMMIT 2 trial (n = 312) with 43.8% of ustekinumab-treated patients and 20.2% of placebo-treated patients achieving an ACR 20 response ($p < 0.001$) (*Ritchlin et al 2014*).
    - In PSUMMIT-1, patients taking placebo or ustekinumab 45 mg could adjust therapy at week 16 if they had an inadequate response, and all remaining patients in the placebo group at week 24 were crossed over to receive treatment with ustekinumab 45 mg (*McInnes et al 2013*). At week 100 (*Kavanaugh et al 2015a*), the ACR 20 responses were 63.6%, 56.7%, and 62.7% in the 90 mg, 45 mg, and placebo crossover groups, respectively. ACR 50 and ACR 70 responses followed a similar pattern and ranged from 37.3% to 46% and 18.6% to 24.7%, respectively. At week 100, the proportions of patients achieving PASI 75 were 71.3%, 72.5%, and 63.9% in the 90 mg, 45 mg, and placebo crossover groups, respectively. Improvements in physical function and health-related quality of life (HRQoL) were sustained over time, with median decreases in HAQ-DI scores from baseline to week 100 of 0.38, 0.25, and 0.38 in the 90 mg, 45 mg, and placebo crossover groups, respectively.
- Cosentyx (secukinumab) gained FDA approval for the treatment of PsA based on 2 multicenter, double-blind, placebo-controlled randomized controlled trials – FUTURE 1 and FUTURE 2 *(Mease et al 2015, McInnes et al 2015*). The FUTURE 1 study randomized patients to secukinumab 75 mg or 150 mg every 4 weeks (following IV loading doses) or placebo and evaluated ACR 20 at week 24. In the FUTURE 2 study, patients were randomized to secukinumab 75 mg, 150 mg, or 300 mg SQ every 4 weeks (following SQ loading doses given at weeks 0, 1, 2, 3, and 4) or placebo and evaluated at week 24 for ACR 20 response.
    - In FUTURE 1 at week 24, both the secukinumab 75 mg and 150 mg doses demonstrated significantly higher ACR 20 responses vs placebo (50.5% and 50.0% vs 17.3%, respectively; $p < 0.0001$ vs placebo).
    - All pre-specified endpoints including dactylitis, enthesitis, SF-36 PCS, HAQ-DI, DAS28-CRP, ACR 50, PASI 75, PASI 90, and mTSS score were achieved by week 24 and reached statistical significance.
    - At week 104 in a long-term extension study of FUTURE 1, ACR 20 was achieved in 66.8% of patients with secukinumab 150 mg and 58.6% of patients with secukinumab 75 mg (*Kavanaugh et al 2017*).
    - In FUTURE 2 at week 24, ACR 20 response rates were significantly greater with secukinumab than with placebo: 54.0%, 51.0%, and 29.3% vs 15.3% with secukinumab 300 mg, 150 mg, and 75 mg vs placebo, respectively ($p < 0.0001$ for secukinumab 300 mg and 150 mg; $p < 0.05$ for 75 mg vs placebo).

  - Improvements were seen with secukinumab 300 mg and 150 mg with regard to PASI 75/90 scores, DAS28-CRP, SF-36 PCS, HAQ-DI, dactylitis, and enthesitis. Efficacy was observed in both TNF-naïve patients and in patients with prior TNF inadequate response or intolerance.
- The efficacy of Otezla (apremilast) was demonstrated in 3 placebo-controlled trials in patients with PsA. At week 16, significantly more patients in the Otezla groups had ≥ 20% improvement in symptoms, as defined by ACR response criteria (*Cutolo et al 2013, Edwards et al 2016, Kavanaugh et al 2014a*). Clinical improvements observed at 16 weeks were sustained at 52 weeks (*Edwards et al 2016, Kavanaugh et al 2015b*).
- Orencia (abatacept) gained FDA approval for the treatment of PsA based on 2 double-blind, placebo-controlled clinical trials in patients with an inadequate response or intolerance to DMARD therapy (*Mease et al 2011, Mease et al 2017*). In a phase 2 dose-finding trial (n = 170), patients received abatacept 3 mg/kg, 10 mg/kg, or 30/10 mg/kg (2 doses of 30 mg/kg then 10 mg/kg) on days 1, 15, 29 and then every 28 days (*Mease et al 2011*). Compared to placebo (19%), the proportion of patients achieving ACR 20 was significantly higher with abatacept 10 mg/kg (48%; p = 0.006) and 30/10 mg/kg (42%; p = 0.022) but not 3 mg/kg (33%). A phase 3 trial (n = 424) randomized patients to abatacept 125 mg weekly or placebo (*Mease et al 2017*). At week 24, the proportion of patients with ACR 20 response was significantly higher with abatacept (39.4%) vs placebo (22.3%; p < 0.001).
- A small, single-center randomized trial (N = 100) compared Remicade (infliximab), Enbrel (etanercept), and Humira (adalimumab) in patients with PsA who had had an inadequate response to DMARDs (*Atteno et al 2010*). The investigators found that each of the agents effectively controlled the signs and symptoms of PsA, and ACR response rates were similar among agents. Patients receiving infliximab and adalimumab showed the greatest improvement in PASI scores, whereas patients receiving etanercept showed the greatest improvement on the tender joint count and HAQ. Limitations of this trial were lack of blinding and lack of a placebo group.
- A meta-analysis based on both direct and indirect comparisons evaluated the efficacy and safety of Humira (adalimumab), Enbrel (etanercept), Remicade (infliximab), and Simponi (golimumab) over 24 weeks for the treatment of PsA (*Fénix et al 2013*). The investigators found no differences among products for the primary endpoint of ACR 50 or secondary endpoints of ACR 20 and ACR 70, except that etanercept was associated with a lower ACR 70 response. However, low sample sizes limited the power of the analysis.
- A meta-analysis of 9 randomized controlled trials and 6 observational studies evaluated Humira (adalimumab), Enbrel (etanercept), Simponi (golimumab), or placebo in the achievement of ACR 20, ACR 50, and ACR 70 endpoints in patients with moderate to severe PsA (*Lemos et al 2014*). Patients who used adalimumab, etanercept and golimumab were more likely to achieve ACR 20 and ACR 50 after 12 or 24 weeks of treatment. In long-term analysis (after all participants used anti-TNF for at least 24 weeks), there was no difference in ACR 20 and ACR 50 between the anti-TNF and control groups, but patients originally randomized to anti-TNF were more likely to achieve ACR 70.
- A meta-analysis of 8 studies evaluated Cosentyx (secukinumab), Taltz (ixekizumab), Siliq (brodalumab), and Stelara (ustekinumab) in the achievement of ACR 20, ACR 50, and ACR 70 endpoints in patients with PsA (*Bilal et al 2018*). Patients who used these agents were more likely to achieve ACR 20, ACR 50, and ACR70 after 24 weeks of treatment. Another network meta-analysis of 6 studies evaluated Cosentyx (secukinumab), Taltz (ixekizumab), and Stelara (ustekinumab) over 24 weeks in patients with active PsA (*Wu et al 2018*). The investigators found that all agents improved ACR20 and ACR50 at week 24 compared to placebo. A different network meta-analysis of 8 studies evaluated Orencia (abatacept), Otezla (apremilast), Stelara (ustekinumab), and Cosentyx (secukinumab) in the achievement of ACR 20 and ACR 50 in adults with moderate to severe PsA (*Kawalec et al 2018*). The investigators found a significant difference in ACR20 response rate between Cosentyx (secukinumab) 150 mg and Otezla (apremilast) 20 mg (RR, 2.55; 95% CI, 1.24 to 5.23) and Cosentyx (secukinumab) 300 mg and Otezla (apremilast) 20 mg (RR, 3.57; 95% CI, 1.48 to 8.64) or Otezla (apremilast) 30 mg (RR, 2.84; 95% CI, 1.18 to 6.86).
- Two indirect comparison meta-analyses sought to compare the efficacy of biologics for the treatment of PsA in patients with an inadequate response to prior therapies.
  - An analysis of 12 randomized trials compared various biologics in patients having an inadequate response to NSAIDs or traditional DMARDs (*Ungprasert et al 2016a*). The investigators determined that patients receiving older TNF inhibitors (evaluated as a group: Enbrel [etanercept], Remicade [infliximab], Humira [adalimumab], and Simponi [golimumab]) had a statistically significantly higher chance of achieving ACR 20 compared to patients receiving Cimzia (certolizumab), Otezla (apremilast), or Stelara (ustekinumab). Patients receiving Cosentyx (secukinumab) also had a higher chance of achieving ACR 20 compared to certolizumab, ustekinumab, and apremilast, but the relative risk did not always reach statistical significance. There was no statistically significant difference in this endpoint between secukinumab and the older TNF inhibitors, or between apremilast, ustekinumab, and certolizumab.
  - An analysis of 5 randomized trials compared various non-TNF inhibitor biologics (Orencia [abatacept], secukinumab, ustekinumab, and apremilast) in patients having an inadequate response or intolerance to TNF

inhibitors (*Ungprasert et al 2016b*). The investigators found no difference for any between-agent comparison in the likelihood of achieving an ACR 20 response.
    - These meta-analyses had limitations, notably being based on a small number of trials, and should be interpreted with caution.

Ulcerative colitis (UC)

- Two trials (ACT 1 and ACT 2) evaluated Remicade (infliximab) compared to placebo for the treatment of UC. In both trials, clinical response at week 8 was significantly higher in infliximab 5 and 10 mg/kg treated patients compared to placebo treated patients (all $p < 0.001$). A significantly higher clinical response rate in both infliximab groups was maintained throughout the duration of the studies (*Rutgeerts et al 2005*). A randomized open-label trial evaluated infliximab at different dosing intervals for the treatment of pediatric UC. At week 8, 73.3% of patients met the primary endpoint of clinical response (95% CI, 62.1 to 84.5%) (*Hyams et al 2012*).
- In the ULTRA 2 study, significantly more patients taking Humira (adalimumab) 160 mg at week 0, 80 mg at week 2, and then 40 mg every other week for 52 weeks achieved clinical remission and clinical response vs patients taking placebo (*Sandborn et al 2012*). These long term results confirm the findings of ULTRA 1. This 8-week induction trial demonstrated that adalimumab in same dosage as ULTRA 2 was effective for inducing clinical remission (*Reinisch et al 2011*). In ULTRA 1, significant differences between the adalimumab and placebo groups were only achieved for 2 of the secondary end points at week 8, i.e., rectal bleeding and PGA subscores. Conversely, in ULTRA 2, significantly greater proportions of adalimumab-treated patients achieved almost all secondary end points at week 8. This may have been because of the high placebo response rates in ULTRA 1. A meta-analysis of 3 randomized trials comparing adalimumab to placebo demonstrated that adalimumab increased the proportion of patients with clinical responses, clinical remission, mucosal healing, and inflammatory bowel disease questionnaire responses in the induction and maintenance phases. It also increased the proportion of patients with steroid-free remission in the maintenance phase (*Zhang et al 2016*).
- Simponi (golimumab) was studied in 1,064 patients with moderate to severe UC. Patients receiving golimumab 200 mg then 100 mg or golimumab 400 mg then 200 mg at weeks 0 and 2 were compared to patients receiving placebo. At week 6, significantly greater proportions of patients in the golimumab 200/100 mg and golimumab 400/200 mg groups (51.8%, and 55%, respectively) were in clinical response than patients assigned to placebo (29.7%; $p < 0.0001$ for both comparisons) (*Sandborn et al 2014b*). In a study enrolling patients who responded in a prior study with golimumab, the proportion of patients who maintained a clinical response through week 54 was greater for patients treated with golimumab 100 mg and 50 mg compared to placebo (49.7 and 47 vs 31.2%; $p < 0.001$ and $p = 0.01$, respectively) (*Sandborn et al 2014a*).
- The safety and efficacy of Entyvio (vedolizumab) was evaluated in a trial for UC in patients who responded inadequately to previous therapy. A higher percentage of Entyvio-treated patients achieved or maintained clinical response and remission over placebo at weeks 6 and 52, as measured by stool frequency, rectal bleeding, endoscopic findings, and PGA (*Feagan et al 2013*). A systematic review and meta-analysis (n = 606; 4 trials) demonstrated that vedolizumab was superior to placebo for clinical response (RR, 0.82; 95% CI, 0.75 to 0.91), induction of remission (RR, 0.86; 95% CI, 0.80 to 0.91), and endoscopic remission (RR, 0.82; 95% CI, 0.75 to 0.91) (*Bickston et al 2014, Mosli et al 2015*).
- A network meta-analysis of 12 trials of biologic-naïve patients with moderate-severe UC ranked infliximab and vedolizumab highest for induction of clinical remission and mucosal healing among tofacitinib, vedolizumab, golimumab, adalimumab, and infliximab (*Singh et al 2018*). Among patients with prior exposure to anti-TNF agents (4 trials), the results ranked tofacitinib the highest for induction of clinical remission and mucosal healing.

Uveitis (UV)

- The safety and efficacy of Humira (adalimumab) were assessed in adult patients with non-infectious intermediate, posterior, and panuveitis in 2 randomized, double-masked, placebo-controlled studies, VISUAL I and VISUAL II.
    - VISUAL I (n = 217) enrolled adults with active noninfectious intermediate UV, posterior UV, or panuveitis despite having received prednisone treatment for ≥2 weeks (*Jaffe et al 2016*). Patients were randomized to adalimumab (80 mg loading dose then 40 mg every 2 weeks) or placebo; all patients also received a prednisone burst followed by tapering of prednisone over 15 weeks. The primary endpoint was the time to treatment failure (TTF) at or after week 6. TTF was a multicomponent outcome that was based on assessment of new inflammatory lesions, visual acuity, anterior chamber cell grade, and vitreous haze grade. The median TTF was 24 weeks in the adalimumab group and 13 weeks in the placebo group. Patients receiving adalimumab were less likely than those in the placebo group to have treatment failure (hazard ratio, 0.50; 95% CI, 0.36 to 0.70; $p < 0.001$).
    - VISUAL II (n = 226) had a similar design to VISUAL I; however, VISUAL II enrolled patients with inactive UV on corticosteroids rather than active disease (*Nguyen et al 2016a*). Patients were randomized to adalimumab

(80 mg loading dose then 40 mg every 2 weeks) or placebo; all patients tapered prednisone by week 19. TTF was significantly improved in the adalimumab group compared with the placebo group (median not estimable [>18 months] vs 8.3 months; hazard ratio, 0.57, 95% CI, 0.39 to 0.84; p = 0.004). Treatment failure occurred in 61 (55%) of 111 patients in the placebo group compared with 45 (39%) of 115 patients in the adalimumab group.

Multiple indications

- The efficacy of infliximab-dyyb (European Union formulation) in patients (n = 481) with CD, UC, RA, PsA, spondyloarthritis, and PsO who were treated with the originator infliximab (European Union formulation) for ≥ 6 months was assessed in the NOR-SWITCH trial (*Jørgensen et al 2017*). Twenty-five percent of patients in the infliximab originator group experienced disease worsening compared to 30% of patients in the infliximab-dyyb group (TD, -4.4%; 95% CI, -12.7% to 3.9%; noninferiority margin, 15%). The authors concluded that infliximab-dyyb was noninferior to originator infliximab.

CAPS, CRS, FMF, GCA, HIDS/MKD, and TRAPs

- The efficacy of Kineret (anakinra) for NOMID was evaluated in a prospective, open-label, uncontrolled study in 43 patients treated for up to 60 months. The study demonstrated improvements in all disease symptoms comprising the disease-specific Diary Symptom Sum Score (DSSS), as well as in serum markers of inflammation. A subset of patients (n = 11) who went through a withdrawal phase experienced worsening of disease symptoms and inflammatory markers, which promptly responded to reinstitution of treatment (*Kineret prescribing information 2016*). A cohort study of 26 patients followed for 3 to 5 years demonstrated sustained improvement in disease activity and inflammatory markers (*Sibley et al 2012*).
- The efficacy and safety of Ilaris (canakinumab) has been evaluated for the treatment of CAPS, TRAPS, HIDS/MKD, and FMF.
    - Efficacy and safety in CAPS were evaluated in a trial in patients aged 9 to 74 years with the MWS phenotype and in a trial in patients aged 4 to 74 years with both MWS and FCAS phenotypes. Most of the trial periods were open-label. Trials demonstrated improvements based on physician's assessments of disease activity and assessments of skin disease, CRP, and serum amyloid A (*Ilaris prescribing information 2016*). Published data supports the use of canakinumab for these various CAPS phenotypes (*Koné-Paut et al 2011, Kuemmerle-Deschner et al 2011, Lachmann et al 2009*).
    - Efficacy and safety in TRAPS, HIDS/MKD, and FMF were evaluated in a study in which patients having a disease flare during a screening period were randomized into a 16-week double-blind, placebo-controlled period. For the primary efficacy endpoint, canakinumab was superior to placebo in the proportion of TRAPS, HIDS/MKD, and FMF patients who resolved their index disease flare at day 15 and had no new flare for the duration of the double-blind period. Resolution of the flare was defined as a PGA score <2 (minimal or no disease) and CRP within normal range (or reduction ≥70% from baseline) (*Ilaris prescribing information 2016*).
- The efficacy and safety of Actemra (tocilizumab) has been evaluated for treatment of GCA and CRS.
    - Efficacy and safety of tocilizumab in GCA were evaluated in a double-blind, placebo-controlled phase 3 trial (GiACTA) in patients ≥ 50 years old with active GCA and a history of elevated ESR (*Stone et al 2017*). Patients received tocilizumab every week or every other week with a 26-week prednisone taper, or received placebo with a 26-week or 52-week prednisone taper. Patients who received tocilizumab every week and every other week experienced higher sustained remission rates at week 52 compared to placebo (p < 0.01).
    - The efficacy of tocilizumab in CRS was based on the result of a retrospective analysis of pooled outcome data from clinical trials of chimeric antigen receptor (CAR) T-cell therapies for hematological cancers (*Actemra prescribing information 2017*). Patients aged 3 to 23 years received tocilizumab with or without high-dose corticosteroids for severe or life-threatening CRS. Sixty-nine percent of patients treated with tocilizumab achieved a response. In a second study using a separate study population, CRS resolution within 14 days was confirmed.

Treatment Guidelines

- RA:
    - In patients with moderate or high disease activity despite DMARD monotherapy, the ACR recommends the use of combination DMARDs, a TNF inhibitor, or a non-TNF inhibitor biologic (tocilizumab, abatacept, or rituximab); tofacitinib is another option in patients with established RA, mainly in patients failing or intolerant to biologic DMARDs. If disease activity remains moderate or high despite use of a TNF inhibitor, a non-TNF biologic is recommended over another TNF inhibitor or tofacitinib. Anakinra was excluded from the ACR guideline because of its low use and lack of new data (*Singh et al 2016c*).

- EULAR guidelines are similar to ACR guidelines. These guidelines state that if the treatment target is not reached with a conventional DMARD strategy in a patient with poor prognostic factors, addition of a biologic DMARD or a targeted synthetic DMARD (eg, tofacitinib) should be considered, with current practice being a biologic DMARD. Biologic and targeted synthetic DMARDs should be combined with a conventional DMARD, but in patients who cannot use a conventional DMARD concomitantly, a targeted synthetic DMARD or an IL-6 inhibitor (eg, tocilizumab) may have some advantages compared with other biologic DMARDs. The guideline notes that if a TNF inhibitor has failed, patients may receive another TNF inhibitor or an agent with another mode of action. An effective biologic should not be switched to another biologic for non-medical reasons (*Smolen et al 2017*).
- The ACR released a position statement on biosimilars, which stated that the decision to substitute a biosimilar product for a reference drug should only be made by the prescriber. The ACR does not endorse switching stable patients to a different medication (including a biosimilar) of the same class for cost saving reasons without advance consent from the prescriber and knowledge of the patient (*ACR 2016*). Similarly, the Task Force on the Use of Biosimilars to Treat Rheumatological Disorders recommends that both healthcare providers and patients should take part in the decision-making process for switching amongst biosimilars (*Kay et al 2018*).
- EULAR has released guidelines for use of antirheumatic drugs in pregnancy, which state that etanercept and certolizumab are among possible treatment options for patients requiring therapy (*Götestam Skorpen et al 2016*).

- JIA:
  - The American College of Rheumatology (ACR) published recommendations for the treatment of JIA in 2011, followed by an update in 2013 focusing on the management of SJIA (and tuberculosis screening) (*Beukelman et al 2011, Ringold et al 2013*).
    - According to the 2011 guideline, recommendations for JIA treatment vary based on factors such as disease characteristics and activity, current medication, and prognostic features. For patients with a history of arthritis in ≥ 5 joints (which includes extended oligoarthritis, polyarthritis, and some related subtypes), a TNF inhibitor is generally recommended in patients with continued disease activity after receiving an adequate trial of a conventional DMARD. In patients with a history of ≥ 5 affected joints failing a TNF inhibitor, treatment approaches may include switching to a different TNF inhibitor or abatacept (*Beukelman et al 2011*).
    - According to the 2013 update, the inflammatory process in SJIA is likely different from that of other JIA categories, with IL-1 and IL-6 playing a central role. In patients with SJIA and active systemic features, recommendations vary based on the active joint count and the physician global assessment. Anakinra is 1 of the recommended first-line therapies; canakinumab, tocilizumab, and TNF-inhibitors are among the second-line therapies. In patients with SJIA and no active systemic features, treatments vary based on the active joint count. Abatacept, anakinra, tocilizumab, and TNF inhibitors are among the second-line treatments for these patients (*Ringold et al 2013*).

- UC:
  - For the treatment of UC, sulfasalazine is recommended by the American College of Gastroenterology (ACG) as first-line treatment of active disease. Balsalazide, mesalamine, olsalazine and sulfasalazine are recommended for maintenance of remission and reduction of relapses. If these therapies fail, infliximab should be considered (*Kornbluth et al 2010*). Note that other immunomodulators were not indicated for UC when these guidelines were written; an update is currently in process.

- CD:
  - The ACG states that the anti-TNF monoclonal antibodies adalimumab, certolizumab, and infliximab are effective in the treatment of moderate to severely active CD in patients who are resistant to corticosteroids or are refractory to thiopurines or methotrexate. These agents can be considered for treating perianal fistulas, and infliximab can also treat enterocutaneous and rectovaginal fistulas in CD. Adalimumab, certolizumab, and infliximab are effective for the maintenance of anti-TNF induced remission; due to the potential for immunogenicity and loss of response, combination with azathioprine/6-mercaptopurine or methotrexate should be considered. The combination of infliximab with an immunomodulator (thiopurine) is more effective than monotherapy with individual agents in patients with moderate to severe CD and who are naïve to both agents. Infliximab can also treat fuliminant CD. Vedolizumab with or without an immunomodulator can be used for induction and maintenance of remission in patients with moderate to severe CD. Patients are candidates for ustekinumab therapy, including for the maintenance of remission, if they have moderate to severe CD and have failed corticosteroids, thiopurines, methotrexate, or anti-TNF inhibitors. The guideline

acknowledges the effectiveness of biosimilar infliximab and biosimilar adalimumab for the management of moderate to severe CD (*Lichtenstein et al 2018*).
    - The American Gastroenterological Association (AGA) recommends using anti-TNF drugs to induce remission in patients with moderately severe CD (*Terdiman et al 2013*). The AGA supports the use of TNF inhibitors and/or thiopurines as pharmacologic prophylaxis in patients with surgically-induced CD remission (*Nguyen et al 2017*).
    - An AGA Institute clinical decision tool for CD notes the importance of controlling both symptoms and the underlying inflammation, and makes recommendations for treatments (budesonide, azathioprine, 6-mercaptopurine, prednisone, MTX, a TNF inhibitor, or certain combinations) based on the patient's risk level (*Sandborn 2014*).
    - The European Crohn's and Colitis Organisation (ECCO) recommends TNF inhibitors for patients with CD who have relapsed or are refractory to corticosteroids, depending on disease location and severity, and states that early TNF inhibitor therapy should be initiated in patients with high disease activity and features indicating a poor prognosis. Furthermore, the ECCO guideline states that all currently available TNF inhibitors seem to have similar efficacy in luminal CD and similar AE profiles; therefore the choice depends on availability, route of administration, patient preference, and cost. Vedolizumab is noted to be an appropriate alternative to TNF inhibitors for some patients (*Gomollón et al 2017*).
- Pregnancy in inflammatory bowel disease:
    - Consensus statements for the management of inflammatory bowel disease in pregnancy, coordinated by the Canadian Association of Gastroenterology, state that TNF inhibitor treatment does not appear to be associated with unfavorable pregnancy outcomes and should generally be continued during pregnancy. Because of the low risk of transfer across the placenta, certolizumab may be preferred in women who initiate TNF inhibitor therapy during pregnancy (*Nguyen et al 2016b*).
- PsO and PsA:
    - Consensus guidelines from the National Psoriasis Foundation Medical Board state that treatment of PsO includes topical agents; oral therapies such as acitretin, cyclosporine, and MTX; and biologic therapies (*Hsu et al 2012*).
    - Guidelines from the American Academy of Dermatology state that for the management of PsO, topical agents including corticosteroids are used adjunctively to either ultraviolet light or systemic medications for resistant lesions in patients with more severe disease (*Menter et al 2008, Menter et al 2009a, Menter et al 2009b, Menter et al 2010, Menter et al 2011*). Biologic agents are routinely used when ≥ 1 traditional systemic agents are not tolerated, fail to produce an adequate response, or are unable to be used due to patient comorbidities. First-line agents for PsO (> 5% BSA) with concurrent PsA include adalimumab, etanercept, golimumab, infliximab, MTX, or a combination of a TNF blocker and MTX.
    - Guidelines for PsO from the European Dermatology Forum, European Association for Dermatology and Venereology, and International Psoriasis Council (European S3 guidelines) state that adalimumab, etanercept, infliximab, and ustekinumab are recommended as second-line medications for induction and long-term treatment if phototherapy and conventional systemic agents were inadequate, contraindicated, or not tolerated (*Nast et al 2015b*). In patients with PsA and active joint involvement despite use of NSAIDs and a potential poor prognosis due to polyarthritis, increased inflammatory markers and erosive changes, it is recommended to start synthetic DMARDs early to prevent progression of disease and erosive joint destruction. For inadequately responding patients with PsA after at least 1 synthetic DMARD, biologic DMARDS are recommended in combination with synthetic DMARDs or as monotherapy.
    - The American Academy of Dermatology recommends that moderate to severe PsA that is more extensive or aggressive in nature or that significantly impacts quality of life should be treated with MTX, TNF-blockers, or both (*Gottleib et al 2008, Menter et al 2009b, Menter et al 2011*).
    - EULAR 2015 PsA guidelines recommend TNF inhibitors in patients with peripheral arthritis and an inadequate response to at least 1 synthetic DMARD, such as MTX. For patients with peripheral arthritis and an inadequate response to at least 1 synthetic DMARD, in whom a TNF inhibitor is not appropriate, biologics targeting IL-12/23 or IL-17 pathways may be considered. Apremilast is considered a treatment option in patients with peripheral arthritis and an inadequate response to at least 1 synthetic DMARD, in whom biologics are not appropriate (*Gossec et al 2016, Ramiro et al 2016*).
    - The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommendations for PsA vary based on whether the arthritis is peripheral or axial and based on prior therapies, and may include DMARDS, NSAIDs, simple analgesics, a TNF inhibitor, an IL-12/23 inhibitor, or a PDE-4 inhibitor (*Coates et al 2016).*
- AS:

- Joint recommendations for the management of axial spondyloarthritis are available from ASAS and EULAR. (Ankylosing spondylitis [AS] is synonymous with radiographic axial spondyloarthritis; these guidelines also include non-radiographic axial spondyloarthritis). The guidelines state that NSAIDs should be used first-line in patients with pain and stiffness; other analgesics might be considered if NSAIDs have failed or are contraindicated or poorly tolerated. Glucocorticoid injections may be considered but patients with axial disease should not receive long-term systemic glucocorticoids. Sulfasalazine may be considered in patients with peripheral arthritis, but patients with purely axial disease should normally not be treated with conventional DMARDs. Biologic DMARDs should be considered in patients with persistently high disease activity despite conventional treatments, and current practice is to start with a TNF inhibitor. If a TNF inhibitor fails, switching to another TNF inhibitor or to an IL-17 inhibitor should be considered (*van der Heijde et al 2017*).
- The 2015 ACR, Spondylitis Association of America, and Spondyloarthritis Research and Treatment Network guidelines strongly recommend TNF inhibitors for patients who have active disease despite NSAIDs. No particular TNF inhibitor is preferred over another, except in patients with concomitant inflammatory bowel disease or recurrent iritis, in whom infliximab or adalimumab would be preferred over etanercept (*Ward et al 2016).*

- Ocular inflammatory disorders:
  - Expert panel recommendations for the use of TNF inhibitors in patients with ocular inflammatory disorders are available from the American Uveitis Society (*Levy-Clarke et al 2014*). Infliximab and adalimumab can be considered as first-line immunomodulatory agents for the treatment of ocular manifestations of Behçet's disease and as second-line immunomodulatory agents for the treatment of UV associated with juvenile arthritis. They also can be considered as potential second-line immunomodulatory agents for the treatment of severe ocular inflammatory conditions including posterior UV, panuveitis, severe UV associated with seronegative spondyloarthropathy, and selected patients with scleritis. Etanercept seems to be associated with lower rates of treatment success in these conditions.
- Additional indications:
  - Based upon guidelines from the European Dermatology Forum, adalimumab is recommended among first-line therapies for HS, and infliximab may be considered a second-line option (*Gulliver et al 2016, Zouboulis et al 2015*).
  - For the treatment of FMF, EULAR recommendations state that treatment with colchicine should begin as soon as FMF is diagnosed. Biologic treatment, such as anti-IL-1 therapy, is indicated in patients not responding to the maximum tolerated dose of colchicine. TNF inhibitors have also been used in colchicine-resistant patients, with good responses seen in observational studies (*Ozen et al 2016*).
  - No recent guidelines were identified for CAPS, CRS, GCA, HIDS/MKD, or TRAPS.

SAFETY SUMMARY

- Contraindications:
  - Actemra (tocilizumab), Cimzia (certolizumab), Cosentyx (secukinumab), Entyvio (vedolizumab), Ilaris (canakinumab), Ilumya (tildrakizumab-asmn), Inflectra (infliximab-dyyb), Kevzara (sarilumab), Kineret (anakinra), Otezla (apremilast), Remicade (infliximab), Renflexis (infliximab-abda), Stelara (ustekinumab), and Taltz (ixekizumab) use in patients with hypersensitivity to any component of the product.
  - Siliq in patients with Crohn's disease because Siliq may cause worsening of disease.
  - Enbrel (etanercept) in patients with sepsis.
  - Kineret (anakinra) in patients with hypersensitivity to *E coli*-derived proteins.
  - Remicade (infliximab), Inflectra (infliximab-dyyb), and Renflexis (infliximab-abda) in patients with hypersensitivity to murine proteins; and doses >5 mg/kg in patients with moderate to severe heart failure.
- Boxed Warnings:
  - Actemra (tocilizumab), Cimzia (certolizumab), Enbrel (etanercept), Humira (adalimumab), Inflectra (infliximab-dyyb), Kevzara (sarilumab), Olumiant (baricitinib), Remicade (infliximab), Renflexis (infliximab-abda), Simponi / Simponi Aria (golimumab), and Xeljanz / Xeljanz XR (tofacitinib) all have warnings for serious infections such as active tuberculosis, which may present with pulmonary or extrapulmonary disease; invasive fungal infections; and bacterial, viral, and other infections due to opportunistic pathogens.
  - In addition, Cimzia (certolizumab), Enbrel (etanercept), Humira (adalimumab), Inflectra (infliximab-dyyb), Olumiant (baricitinib), Remicade (infliximab), Renflexis (infliximab-abda), Simponi / Simponi Aria (golimumab), and Xeljanz (tofacitinib) all have warnings for increased risk of malignancies.
  - Rituxan (rituximab) can cause fatal infusion reactions, hepatitis B activation, severe mucocutaneous reactions, and progressive multifocal leukoencephalopathy (PML).

  - Siliq has a boxed warning that suicidal ideation and behavior, including completed suicides, have occurred in patients treated with Siliq. The prescriber should weigh potential risks and benefits in patients with a history of depression and/or suicidal ideation or behavior, and patients should seek medical attention if these conditions arise or worsen during treatment.
  - Olumiant (baricitinib) has a boxed warning for thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis.
- Warnings/Precautions (applying to some or all of the agents in the class):
  - Reactivation of HBV or other viral infections
  - Serious infections including tuberculosis
  - New onset or exacerbation of central nervous system demyelinating disease and peripheral demyelinating disease
  - Pancytopenia
  - Worsening and new onset congestive heart failure
  - Hypersensitivity reactions
  - Lupus-like syndrome
  - Malignancy and lymphoproliferative disorders
  - Avoiding live vaccinations
  - Noninfectious pneumonia with Stelara (ustekinumab)
  - Increased lipid parameters and liver function tests with Actemra (tocilizumab), Xeljanz / Xeljanz XR (tofacitinib) and Kevzara (sarilumab)
  - Increased incidence of CD and UC with Cosentyx (secukinumab) and Taltz (ixekizumab); risk of new-onset CD or exacerbation of CD with Siliq (brodalumab)
  - Diarrhea, nausea, and vomiting with Otezla (apremilast)
  - Depression with Otezla (apremilast)
  - Gastrointestinal perforations with Xeljanz / Xeljanz XR (tofacitinib), Olumiant (baricitinib), Actemra (tocilizumab), Kevzara (sarilumab), and Rituxan (rituximab)
  - PML with Entyvio (vedolizumab)
  - Thrombosis with Olumiant (baricitinib)
  - Consult prescribing information for other drug-specific warnings/precautions
- Adverse Reactions:
  - Infusion site reactions, diarrhea, nausea/vomiting, abdominal pain, infections, hypertension and headache.
  - Consult prescribing information for other drug-specific AEs
- Risks of Long-Term Treatment: As it becomes accepted practice to treat patients with these conditions for long-term, it is imperative to assess the long-term safety of these products. Because these agents suppress the immune system, serious infections and malignancies are a concern. Several long-term efficacy and safety studies support several agents in this class. The extension studies were performed in an open-label manner and were subject to attrition bias.
  - Rheumatoid Arthritis
    - Safety of adalimumab for RA has been supported in a 5-year study in RA and a 10-year study in patients with early RA (*Keystone et al 2014a, Burmester et al 2014b*). In the 5-year extension study, overall rates of serious AEs and serious infections were 13.8 events per 100 patient-years and 2.8 events per 100 patient-years, respectively. The rate of serious events was highest in the first 6 months and then declined. No new safety signals were reported in the 10-year study.
    - Certolizumab plus MTX had a consistent safety profile over 5 years in patients with RA (*Keystone et al 2014b*). The most frequently reported AEs included urinary tract infections (rate of 7.9 per 100 patient-years), nasopharyngitis (rate of 7.3 per 100 patient-years), and upper respiratory infections (rate of 7.3 per 100 patient-years). Serious AE rates were 5.9 events per 100 patient-years for serious infections and 1.2 events per 100 patient-years for malignancies.
    - Abatacept has been evaluated in 2 long-term extension studies. Abatacept IV plus MTX demonstrated a similar safety profile between the 7 year follow-up and a 52-week double-blind study (*Westhovens et al 2014*). Serious AEs reported in both the double-blind and long-term follow-up studies were the following: serious infections (17.6 events per 100 patient-years), malignancies (3.2 events per 100 patient-years), and autoimmune events (1.2 events per 100 patient-years). In a 5-year extension trial, rates of serious infections, malignancies, and autoimmune events were 2.8, 1.5, and 0.99 events per 100 patient-years exposure, respectively. Efficacy was demonstrated by ACR 20 with response rates of 82.3% and 83.6% of patients at year 1 and year 5, respectively.
    - Data from 5 RCTs of Actemra (tocilizumab), their open-label extension trials, and a drug interaction study were analyzed for measures of safety. A total of 4,009 patients with moderate to severe RA

received at least 1 dose of tocilizumab. Mean duration of tocilizumab treatment was 3.07 years (up to 4.6 years); total duration of observation was 12,293 patient-years (PY). The most common AEs and serious AEs were infections. A longer-term safety profile from this analysis matches previous observations. No new safety signals were identified (*Genovese et al 2013*).

- A Cochrane review showed no evidence of a statistically significant difference in the rate of withdrawal because of AEs in the Enbrel (etanercept) plus DMARD group and the DMARD alone group at 6 months, 12 months, and 2 years. At 3 years, withdrawals were significantly reduced in the etanercept 25 mg plus DMARD group compared with the DMARD alone group (RR, 0.7; 95% CI, 0.5 to 1). There was no evidence of statistically significant differences in the rates of breast cancer at 12 months, fever at 6 months, flu-like syndrome at 6 months and 2 years, infection at 6 months and 2 years, malignancy at 12 months and 2 years, pneumonia at 12 months, and serious infection at 12 months and 2 years between the etanercept plus DMARD group and the DMARD group (*Lethaby et al 2013*).
- A systematic review analyzed 66 randomized controlled trials and 22 long-term extension studies evaluating biologics and tofacitinib for the rate of serious infections in patients with moderate to severe active RA (*Strand et al 2015b*). The estimated incidence rates (unique patients with events/100 patient-years) of serious infections were 3.04 (95% CI, 2.49 to 3.72) for abatacept, 3.72 (95% CI, 2.99 to 4.62) for rituximab, 5.45 (95% CI, 4.26 to 6.96) for tocilizumab, 4.90 (95% CI, 4.41 to 5.44) for TNF inhibitors, and 3.02 (95% CI, 2.25 to 4.05) for tofacitinib 5 mg and 3.00 (95% CI, 2.24 to 4.02) for tofacitinib 10 mg. Authors concluded that the rates of serious infections with tofacitinib in RA patients are within the range of those reported for biologic DMARDs.
- A meta-analysis analyzed 50 randomized controlled trials and long-term extension studies evaluating biologic DMARDs and tofacitinib to compare the risks of malignancies in patients with RA (*Maneiro et al 2017*). The overall risk of malignancies was 1.01 (95% CI, 0.72 to 1.42) for all TNF antagonists, 1.12 (95% CI, 0.33 to 3.81) for abatacept, 0.54 (95% CI, 0.20 to 1.50) for rituximab, 0.70 (95% CI, 0.20 to 2.41) for tocilizumab, and 2.39 (95% CI, 0.50 to 11.5) for tofacitinib. The authors concluded that treatment with biologic DMARDs or tofacitinib does not increase the risk of malignancies.

o PsO

- A total of 3,117 patients treated with at least 1 dose of Stelara (ustekinumab) for moderate to severe PsO were evaluated for long-term safety. At least 4 years of ustekinumab exposure was seen in 1,482 patients (including 838 patients with ≥ 5 years of exposure). The most commonly reported AEs were nasopharyngitis, upper respiratory tract infection, headache and arthralgia. Infections, malignancies and cardiac disorders were the most commonly reported serious AEs. Twenty deaths were reported through year 5. The causes of death were considered related to cardiovascular events (n = 5), malignancy (n = 5), infection (n = 3) and other causes (n = 7). The observed mortality rate among ustekinumab-treated patients was consistent with that expected in the general U.S. population (SMR = 0.36; 95% CI, 0.22 to 0.55). From year 1 to year 5, rates of overall AEs, and AEs leading to discontinuation generally decreased. Serious AE rates demonstrated year-to-year variability with no increasing trend. The results of this long-term study of AEs are similar to reports of shorter-term studies (*Papp et al 2013*).
- In a 5-year extension study, a total of 2510 patients on etanercept for the treatment of PsO were evaluated for long-term safety and efficacy (*Kimball et al 2015*). Serious AEs were reported as a cumulative incidence of the entire 5-year observation period. The following incidences were reported: serious infections (6.5%, 95% CI, 5.4 to 7.7%); malignancies excluding nonmelanoma skin cancer (3.2%, 95% CI, 2.3 to 4.1%); nonmelanoma skin cancer (3.6%, 95% CI, 2.7 to 4.1%); coronary artery disease (2.8%, 95% CI, 2 to 3.6%); PsO worsening (0.7%, 95% CI, 0.3 to 1.2%); CNS demyelinating disorder (0.2%, 95%CI, 0 to 0.4%); lymphoma and tuberculosis each (0.1%, 95% CI, 0 to 0.3%); and opportunistic infection and lupus each (0.1%, 95%CI, 0 to 0.2%). A total of 51% of patients reported clear/almost clear rating at month 6 and remained stable through 5 years.
- In a ≥ 156-week extension study, a total of 1,184 patients treated with apremilast in ESTEEM 1 and 2 were evaluated for long-term safety and tolerability (*Crowley et al 2017*). Serious AEs (≥ 2 patients) were coronary artery disease (n = 6), acute myocardial infarction (n = 4), osteoarthritis (n = 4), and nephrolithiasis (n = 4). The exposure-adjusted incidence rate for major cardiac events was 0.5/100 patients years, for malignancies was 1.2/100 patient years, for serious infections was 0.9/100 patient-years, and for suicide attempts was 0.1/100 patient-years.
- A multicenter registry called Psoriasis Longitudinal Assessment and Registry (PSOLAR) evaluated the risk of serious infections in patients with PsO (*Kalb et al 2015*). Patients were followed for up to 8

years with a total of 11,466 patients with PsO enrolled, 74.3% of whom were from the U.S. A total of 22,311 patient-years of data were collected. Ustekinumab, infliximab, adalimumab, and etanercept as well as traditional DMARDs were included in the data analysis. During the follow-up period, 323 serious infections were reported. The rates of serious infections per 100 patient-years were 0.83 (secukinumab), 1.47 (etanercept), 1.97 (adalimumab), and 2.49 (infliximab). The most commonly reported serious infection was cellulitis. Risk factors for serious infections were increasing age, diabetes mellitus, smoking, and history of significant infections prior to registry entry. Exposure to infliximab (hazard ratio, 2.51; 95% CI, 1.45 to 4.33; p < 0.001) and adalimumab (hazard ratio, 2.13; 95% CI, 1.33 to 3.41; p = 0.002) during the registry were independently associated with the risk of serious infections whereas use of ustekinumab or etanercept were not.

- PsA
  - Subcutaneous golimumab for patients with active PsA demonstrated safety and efficacy over 5 years in the long-term extension of the randomized, placebo-controlled GO-REVEAL study (*Kavanaugh et al 2014b*). Approximately one-half of patients also took MTX concurrently. No new safety signals were observed.
- AS
  - A meta-analysis of 25 randomized controlled studies with 2,403 patients with AS or non-radiographic axial spondyloarthritis treated with agents such as adalimumab, certolizumab, etanercept, golimumab, infliximab, sarilumab, tocilizumab, and secukinumab showed no significant increase in the risk of serious infections with biologic agents compared to controls (OR, 1.42; 95% CI, 0.58 to 3.47) (*Wang et al 2018*).
  - Another meta-analysis of 14 randomized controlled trials with 2,032 patients with AS that were treated with adalimumab, certolizumab, etanercept, golimumab, or infliximab revealed no significant difference between TNF inhibitors and placebo for overall serious adverse events (OR, 1.34; 95% CI, 0.87 to 2.05), risk of serious infections (OR, 1.59; 95% CI, 0.63 to 4.01), risk of malignancy (OR, 0.98; 95% CI, 0.25 to 3.85), and discontinuation due to adverse events (OR, 1.55; 95% CI, 0.95 to 2.54) (*Hou et al 2018*).
- Multiple indications
  - One study looked at 23,458 patients who were treated with Humira (adalimumab) for RA, JIA, AS, PsA, PsO and CD. Patients received adalimumab for up to 12 years. No new safety signals were observed from this analysis. Rates of malignancies and infections were similar to the general population and also similar to rates reported in other shorter-term trials for anti-TNF therapies (*Burmester et al 2013b*).
  - Pooled data from 5 Phase 3 trials of SQ golimumab over at least 3 years demonstrated a safety profile consistent with other TNF inhibitors (*Kay et al 2015*). A total of 1,179 patients with RA, PsA or AS were treated for at least 156 weeks. Rates of AEs up to week 160 for placebo, golimumab 50 mg and golimumab 100 mg, respectively, were as follows: 0.28, 0.30, 0.41 for death; 5.31, 3.03, 5.09 for serious infection; 0, 0.17, 0.35 for tuberculosis; 0, 0.13, 0.24 for opportunistic infection; 0, 0, 0.12 for demyelination; and 0, 0.04, 0.18 for lymphoma.
  - A total of 18 multicenter, placebo-controlled, randomized controlled trials evaluated the safety profile of certolizumab pegol monotherapy or in combination with DMARDs in RA, CD, AS, PsA and PsO (*Capogrosso Sansone et al 2015).* All but 1 trial was conducted in a double-blind manner. The overall pooled risk ratios for all doses of certolizumab pegol were reported as follows: AEs (defined as AE reported but not evaluated for causality) 1.09 (95% CI, 1.04 to 1.14), serious AEs 1.50 (95% CI, 1.21 to 1.86), ADRs (defined as an AE possibly related to drug treatment by investigators) 1.20 (95% CI, 1.13 to 1.45), infectious AEs 1.28 (95% CI, 1.13 to 1.45), infectious serious AEs 2.17 (95% CI, 1.36 to 3.47), upper respiratory tract infections 1.34 (95% CI, 1.15 to 1.57), neoplasms 1.04 (95% CI, 0.49 to 2.22), and tuberculosis 2.47 (95% CI, 0.64 to 9.56). Rare AEs may not have been captured by the studies due to limiting the reporting of most AEs to those occurring in > 3 to 5%.
  - Several recent meta-analyses evaluated the safety of TNF inhibitors.
    - An analysis of TNF inhibitors in RA, PsA, and AS included data from 71 randomized trials (follow-up 1 to 36 months) and 7 open-label extension studies (follow-up 6 to 48 months) (*Minozzi et al 2016*). The data demonstrated that use of TNF inhibitors increases the risk of infectious AEs. Overall, there was a 20% increase of any infections, a 40% increase of serious infections, and a 250% increase of tuberculosis. The tuberculosis incidence rate was higher with infliximab and adalimumab compared to etanercept. There was little data on the incidence of opportunistic infections.

- An analysis of TNF inhibitors in RA, PsA, and AS included data from 32 randomized trials (follow-up 2 to 36 months) and 6 open-label extension trials (follow-up 6 to 48 months) (*Bonovas et al 2016*). Synthesis of the data did not demonstrate that the use of TNF inhibitors significantly affects cancer risk during this length of treatment. However, few malignancy events were observed and evidence may be insufficient to make definitive conclusions, particularly regarding longer-term risks.

- Drug interactions
  - Do not give with live (including attenuated) vaccines; additionally, non-live vaccines may not elicit a sufficient immune response.
  - Do not give 2 immunomodulators together.
  - For Xeljanz / Xeljanz XR (tofacitinib), adjust dose with potent inhibitors of cytochrome P450 (CYP) 3A4 and medications that result in both moderate inhibition of CYP3A4 and potent inhibition of CYP2C19. Coadministration with potent CYP3A4 inducers and potent immunosuppressive drugs is not recommended.
- Risk Evaluation and Mitigation Strategy (REMS)
  - Siliq (brodalumab) is available only through the Siliq REMS program. The goal of the program is to mitigate the risk of suicidal ideation and behavior, including completed suicides, which occurred in clinical trials. Key requirements of the REMS program include:
    - Prescribers must be certified with the program.
    - Patients must sign a patient-prescriber agreement form.
    - Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive the product.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
Actemra (tocilizumab)	Vials: 80 mg/4 mL; 200 mg/10 mL; 400 mg/20 mL Prefilled syringe: 162 mg/0.9 mL	**RA:** IV: 4 mg/kg IV every 4 weeks. May increase to 8 mg/kg IV every 4 weeks. Maximum dose = 800 mg. SQ: <100 kg, administer 162 mg SQ every other week, followed by an increase to every week based on clinical response; >100 kg, 162 mg administered SQ every week. **PJIA:** <30 kg, 10 mg/kg IV every 4 weeks; ≥30 kg, 8 mg/kg IV every 4 weeks. <30 kg, 162 mg SQ every 3 weeks; ≥30 kg, 162 mg SQ every 2 weeks. **SJIA:** <30 kg, 12 mg/kg IV every 2 weeks; ≥30 kg, 8 mg/kg IV every 2 weeks. **GCA:** 162 mg SQ every week with tapering glucocorticoids. May give every other week depending on clinical considerations. **CRS:** <30 kg, 12 mg/kg IV; ≥30 kg, 8 mg/kg IV; maximum, 800 mg per infusion.	**RA:** Can give with MTX or other DMARDs. **PJIA and SJIA:** Can give with MTX. **GCA:** Can use alone after discontinuation of glucocorticoids. **CRS:** Can give with corticosteroids. May repeat up to 3 additional doses if no clinical improvement, with at least 8 hours between doses. **RA, PJIA, and SJIA, and GCA**: Adjust dose for liver enzyme abnormalities, low platelet count and low ANC.	Give as a single 60-minute intravenous infusion. <30 kg, use a 50 mL infusion bag. ≥30 kg, use a 100 mL infusion bag. Before infusion, allow bag to come to room temperature. Do not administer with other drugs. Patients can self-inject with the prefilled syringe. Rotate injection sites.
Cimzia (certolizumab)	Powder for reconstitution: 200 mg Prefilled syringe: 200 mg/mL	**CD:** 400 mg SQ initially and at weeks 2 and 4. Maintenance dose is 400 mg every 4 weeks. **RA, PsA:** 400 mg SQ initially and at weeks 2 and 4. Then 200 mg every 2 weeks. Can consider a maintenance dose of 400 mg every 4 weeks. **PsO:** 400 mg SQ every other week or 400 mg SQ initially and at weeks 2 and 4,	Patients can self-inject with the prefilled syringe.	When a 400 mg dose is required, give as 2 200 mg SQ injections in separate sites in the thigh or abdomen.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		followed by 200 mg every other week **AS:** 400 mg SQ initially and at weeks 2 and 4. Maintenance dose is 200 mg every 2 weeks or 400 mg every 4 weeks.		
Cosentyx (secukinumab)	Sensoready pen: 150 mg/1 mL Prefilled syringe: 150 mg/1 mL Vial: 150 mg lyophilized powder	**PsO:** 300 mg by SQ injection at weeks 0, 1, 2, 3 and 4, followed by 300 mg every 4 weeks **PsA, AS:** With a loading dose (not required): 150 mg at weeks 0, 1, 2, 3, and 4, followed by 150 mg every 4 weeks; without loading dose: 150 mg every 4 weeks	**PsO:** For some patients, a dose of 150 mg may be acceptable. **PsA:** For PsA patients with coexistent moderate to severe PsO, dosing for PsO should be followed. If active PsA continues, consider 300 mg dose.	Each 300 mg dose is given as 2 subcutaneous injections of 150 mg. Patients may self-administer with the pen or prefilled syringe. The vial is for healthcare professional use only.
Enbrel (etanercept)	Prefilled syringe: 25 mg and 50 mg Prefilled SureClick autoinjector: 50 mg Multiple-use vial: 25 mg lyophilized powder Solution Cartridge: 50 mg	**RA, AS, PsA:** 50 mg SQ weekly **PsO (adults):** 50 mg SQ twice weekly for 3 months, then 50 mg weekly **PJIA and PsO (pediatrics):** ≥63 kg, 50 mg SQ weekly; <63 kg, 0.8 mg/kg SQ weekly	**RA, AS, PsA:** MTX, NSAIDs, glucocorticoids, salicylates, or analgesics may be continued **JIA:** NSAIDs glucocorticoids, or analgesics may be continued	Patients may be taught to self-inject. May bring to room temperature prior to injecting.
Entyvio (vedolizumab)	Lyophilized cake for injection in 300 mg single-dose vial	**CD and UC:** 300 mg administered by intravenous infusion at time 0, 2, and 6 weeks, and then every 8weeks thereafter. Discontinue therapy if there is no evidence of therapeutic benefit by week 14.	All immunizations should be to date according to current guidelines prior to initial dose.	Entyvio should be reconstituted at room temperature and prepared by a trained medical professional. It should be used as soon as possible after reconstitution and dilution.
Humira (adalimumab)	Prefilled syringe: 10 mg/0.1 mL 10 mg/0.2 mL 20 mg/0.2 mL 20 mg/0.4 mL	**RA, AS, PsA**: 40 mg SQ every other week. For RA, may increase to 40 mg every week if not on MTX.	**RA, AS, PsA:** MTX, other non-biologic DMARDS, glucocorticoids, NSAIDs, and/or	Patients may be taught to self-inject. Injections should occur at separate sites in the thigh or abdomen. Rotate injection sites.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
	40 mg/0.4 mL 40 mg/0.8 mL 80 mg/0.8 mL Single-use pen: 80 mg/0.8 mL 40 mg/0.8 mL 40 mg/0.4 mL Single-use vial: 40 mg/0.8 mL	**PJIA:** 10 kg to <15 kg: 10 mg SQ every other week; 15 kg to <30 kg: 20 mg SQ every other week; ≥30 kg, 40 mg SQ every other week **CD, HS and UC:** 160 mg SQ on Day 1 (given in 1 day or split over 2 consecutive days), followed by 80 mg SQ 2 weeks later (Day 15). Two weeks later (Day 29) begin a maintenance dose of 40 mg SQ every other week. **PsO and UV:** initial dose of 80 mg SQ, followed by 40 mg SQ every other week starting 1 week after the initial dose. **CD in pediatric patients ≥ 6 years and older:** 17 kg to < 40 kg: 80 mg on day 1 (given as two 40 mg injections) and 40 mg 2 weeks later (on day 15); maintenance dose is 20 mg every other week starting at week 4. ≥40 kg: 160 mg on day (given in 1 day or split over 2 consecutive days) and 80 mg 2 weeks later (on day 15); maintenance dose is 40 mg every other week starting at week 4.	analgesics may be continued. **JIA:** NSAIDs, MTX, analgesics, and/or glucocorticoids, may be continued. **CD and UC:** aminosalicylates and/or corticosteroids may be continued. Azathioprine, 6-MP or MTX may be continued if necessary. Needle cover of the syringe contains dry rubber (latex).	May bring to room temperature prior to injecting.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
Ilaris (canakinumab)	Vial: 150 mg (lyophilized powder and injection solution formulations)	**SJIA:** ≥7.5 kg, 4 mg/kg SQ every 4 weeks (maximum dose of 300 mg). **CAPS**: ≥15 to ≤40 kg, 2 mg/kg SQ; >40 kg, 150 mg SQ; frequency every 8 weeks **TRAPS, HIDS/MKD, and FMF**: ≤40 kg, 2 mg/kg SQ; >40 kg, 150 mg SQ; frequency every 4 weeks	For CAPS: children 15 to 40 kg with an inadequate response can be increased to 3 mg/kg For TRAPS, HIDS/MKD, and FMF: If the clinical response is inadequate, the dose may be increased to 4 mg/kg (weight ≤40 kg) or 300 mg (weight >40 kg)	Do not inject into scar tissue.
Ilumya (tildrakizumab-asmn)	Prefilled syringe: 100 mg/mL	**PsO:** 100 mg SQ at weeks 0 and 4, and then every 12 weeks		Should be administered only by a healthcare provider. Bring to room temperature (30 minutes) prior to injecting.
Inflectra (infliximab-dyyb)	Vial: 100 mg	**CD (≥6 years old), PsA, PsO and UC**: 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks. In adults with CD who lose response, can increase dose to 10 mg/kg. **RA:** 3 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks. Can increase to 10 mg/kg or give every 4 weeks. **AS:** 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 weeks.	**RA:** give with MTX **CD:** If no response by week 14, consider discontinuation.	Premedication to help stop infusion reactions can include antihistamines (anti-H1 ± anti-H2), acetaminophen and/or corticosteroids. Use 250 mL 0.9% sodium chloride for infusion. Infuse over 2 hours. Do not administer with other drugs.
Kevzara (sarilumab)	Prefilled syringe: 150 mg/1.14 mL 200 mg/1.14 mL	**RA:** 200 mg SQ every 2 weeks.	**RA:** give with or without MTX or other conventional DMARDs	Patients may be taught to self-inject. Bring to room temperature (30 minutes [pre-filled

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
	Prefilled pen: 150 mg/1.14 mL 200 mg/1.14 mL		Reduce dose for neutropenia, thrombocytopenia, and elevated liver enzymes.	syringe] or 60 minutes [pre-filled pen]) prior to injecting. Rotate injection sites.
Kineret (anakinra)	Prefilled syringe: 100 mg/0.67 mL	**RA:** 100 mg SQ once daily. **CAPS (NOMID):** 1 to 2 mg/kg SQ once daily. Maximum dose is 8 mg/kg/day.	**NOMID**: dose can be given once or twice daily.	Patients may be taught to self-inject. A new syringe must be used for each dose.
Olumiant (baricitinib)	Tablet: 2 mg	**RA:** 2 mg once daily	Avoid use in combination with other JAK inhibitiors, biologic DMARDs, or potent immunosuppressants such as azathioprine and cyclosporine	May be taken with or without food.
Orencia (abatacept)	Vial: 250 mg Prefilled syringe: 50 mg/0.4 mL 87.5 mg/0.7 mL 125 mg/1 mL ClickJect autoinjector: 125 mg/mL	**RA:** IV: <60kg, 500 mg IV; 60 to 100 kg, 750 mg IV; >100 kg, 1,000 mg IV initially, then 2 and 4 weeks after the first infusion and every 4 weeks thereafter SQ: 125 mg SQ once weekly initiated with or without an IV loading dose. With IV loading dose, use single IV infusion as per body weight listed above, followed by the first 125 mg SQ injection within a day of the IV infusion and then once weekly. **PJIA:** IV: 6 to 17 years and <75 kg: 10 mg/kg IV initially, then 2 and 4 weeks after the first infusion and every 4 weeks thereafter. >75 kg, follow adult RA IV schedule; maximum dose = 1,000 kg. SQ: 2 to 17 years, 10 to <25 kg, 50 mg once weekly; 25 to < 50 kg,		IV infusion should be over 30 minutes. Use 100 mL bag for IV infusion. Do not administer with other drugs. Patients may be taught to self-inject the SQ dose. For SQ, injection sites should be rotated.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		87.5 mg once weekly, ≥ 50 kg, 125 mg once weekly. **PsA:** IV: follow adult RA IV schedule. SQ: 125 mg once weekly without IV dose.		
Otezla (apremilast)	Tablet: 10 mg, 20 mg, and 30 mg	**PsA, PsO:** Day 1: 10 mg in the morning Day 2: 10 mg in the morning and in the evening Day 3: 10 mg in the morning and 20 mg in evening Day 4: 20 mg in the morning and evening Day 5: 20 mg in the morning and 30 mg in the evening Day 6 and thereafter: 30 mg twice daily	Titrate according to the labeling when initiating therapy to reduce gastrointestinal symptoms. Dosage should be reduced to 30 mg once daily in patients with severe renal impairment (CrCl <30 mL/min as estimated by the Cockcroft-Gault equation). For initial dosing in these patients, use only the morning titration schedule listed above (evening doses should be excluded).	May be taken with or without food. Do not crush, split, or chew the tablets.
Remicade (infliximab)	Vial: 100 mg	**CD (≥6 years old), PsA, PsO and UC (≥6 years old)**: 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks. In adults with CD who lose response, can increase dose to 10 mg/kg. **RA:** 3 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks. Can increase to 10 mg/kg or give every 4 weeks. **AS:** 5 mg/kg IV at	**RA:** give with MTX **CD:** If no response by week 14, consider discontinuation.	Premedication to help stop infusion reactions can include antihistamines (anti-H1 ± anti-H2), acetaminophen and/or corticosteroids. Use 250 mL 0.9% sodium chloride for infusion. Infuse over 2 hours. Do not administer with other drugs.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 weeks.		
Renflexis	Vial: 100 mg	**CD (≥6 years old), PsA, PsO and UC**: 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks. In adults with CD who lose response, can increase dose to 10 mg/kg. **RA:** 3 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks. Can increase to 10 mg/kg or give every 4 weeks. **AS:** 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 weeks.	**RA:** give with MTX **CD:** If no response by week 14, consider discontinuation.	Premedication to help stop infusion reactions can include antihistamines (anti-H1 ± anti-H2), acetaminophen and/or corticosteroids. Use 250 mL 0.9% sodium chloride for infusion. Infuse over 2 hours. Do not administer with other drugs.
Rituxan (rituximab)	Vial: 100 mg 500 mg	**RA:** 1,000 mg IV every 2 weeks times 2 doses. Additional doses should be given every 24 weeks or based on clinical evaluation but no sooner than 16 weeks.	Give with MTX.	Give methyl-prednisolone 100 mg IV 30 minutes prior to each infusion to reduce the incidence and severity of infusion reactions.
Siliq (brodalumab)	Prefilled syringe: 210 mg/1.5 mL	**PsO:** 210 mg SQ at weeks 0, 1, and 2 followed by every 2 weeks	**PsO**: If an adequate response has not been achieved after 12 to 16 weeks, consider discontinuation	Patients may self-inject when appropriate and after proper training. The syringe should be allowed to reach room temperature before injecting.
Simponi/ Simponi Aria (golimumab)	SmartJect® autoinjector: 50 mg and 100 mg Prefilled syringe: 50 mg and 100 mg Aria, Vial: 50 mg/4 mL	**RA, PsA, and AS**: 50 mg SQ once monthly **UC:** 200 mg SQ at week 0; then 100 mg at week 2; then 100 mg every 4 weeks. **Aria (RA, PsA, and AS)**: 2 mg/kg IV at	**RA:** give with MTX **PsA and AS**: may give with or without MTX or other DMARDs. Needle cover of the syringe	Patients may be taught to self-inject the SQ dose. For SQ, injection sites should be rotated. For SQ, bring to room temperature for 30 minutes prior to injecting.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		weeks 0 and 4, then every 8 weeks.	contains dry rubber (latex). **Aria (RA)**: give with MTX (**PsA, AS)**: give with or without MTX or other non-biologic DMARDs. Corticosteroids, NSAIDs, and/or analgesics may be continued. Efficacy and safety of switching between IV and SQ formulations have not been established.	**Aria**: IV infusion should be over 30 minutes. Dilute with 0.9% sodium chloride or 0.45% sodium chloride for a final volume of 100 mL. Do not administer with other drugs.
Stelara (ustekinumab)	Prefilled syringe: 45 mg and 90 mg Vial: 130 mg	**PsO, PsA**: ≤100 kg, 45 mg SQ initially and 4 weeks later, followed by 45 mg every 12 weeks. >100 kg, 90 mg SQ initially and 4 weeks later, followed by 90 mg every 12 weeks. **PsO (adolescents):** <60 kg, 0.75 mg/kg (injection volume based on weight) 60 to 100 kg, 45 mg >100 kg, 90 mg **CD**: Initial single IV dose: ≤55 kg, 260 mg; >55 kg to ≤85 kg, 390 mg; >85 kg, 520 mg; followed by 90 mg SQ every 8 weeks (irrespective of body weight)	Needle cover of the syringe contains dry rubber (latex).	Patients may be taught to self-inject using the prefilled syringes. Stelara for IV infusion must be diluted, prepared and infused by a healthcare professional; it is diluted in 0.9% sodium chloride and infused over at least 1 hour. Rotate injection sites.
Tremfya (guselkumab)	Prefilled syringe: 100 mg	**PsO:** 100 mg by SQ injection at week 0, week 4, and then every 8 weeks		Patients may be taught to self-inject. Bring to room temperature (30 minutes) prior to injecting.
Taltz (ixekizumab)	Prefilled syringe: 80 mg Autoinjector: 80 mg	**PsO:** 160 mg by SQ injection at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks		Patients may be taught to self-inject with either the prefilled syringe or the autoinjector. Bring to room temperature

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		PsA: 160 mg by SQ injection at week 0, followed by 80 mg every 4 weeks NOTE: For patients with PsA with coexistent moderate-to-severe PsO, use dosing regimen for PsO.		prior to injecting. Rotate injection sites.
Xeljanz / Xeljanz XR (tofacitinib)	Tablet: 5 mg, 10 mg Extended release Tablet: 11 mg	**RA:** 5 mg PO twice daily or 11 mg PO once daily **PsA:** 5 mg PO twice daily, used in combination with non-biologic DMARDs; 11 mg once daily used in combination with nonbiologic DMARDs **UC (Xeljanz):** 10 mg PO twice daily for at least 8 weeks, then 5 or 10 mg twice daily. Discontinue 10 mg twice daily dose after 16 weeks if no response	Patients may switch from Xeljanz 5 mg twice daily to Xeljanz XR 11 mg once daily the day following the last dose of Xeljanz 5 mg. Use as monotherapy or in combination with MTX or other nonbiologic DMARDs. Use of Xeljanz in combination DMARDs or with potent immunosuppres-sants such as azathioprine and cyclosporine is not recommended. Dose interruption is recommended for management of lymphopenia (< 500 cells/mm^3), neutropenia (ANC < 500 cells/mm^3) and anemia. Dose adjustment needed for hepatic and renal impairment and patients taking CYP450 inhibitors.	May take with or without food. Swallow Xeljanz XR tablets whole; do not crush, split, or chew.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations

ANC=absolute neutrophil count; AS=ankylosing spondylitis; CRS=cytokine release syndrome; DMARD=disease-modifying anti-rheumatic drug; GCA=giant cell arteritis; HS=hidradenitis suppurative; IV=intravenous infusion; JAK=Janus kinase; JIA=juvenile idiopathic arthritis; MTX=methotrexate; NOMID=neonatal-onset multisystem inflammatory disease; NSAID=non-steroidal anti-inflammatory drug; PJIA=polyarticular juvenile idiopathic arthritis; PO=orally; PsA=psoriatic arthritis; PsO=plaque psoriasis; RA=rheumatoid arthritis; SJIA=systemic juvenile idiopathic arthritis; SQ=subcutaneously; UC=ulcerative colitis.

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
Actemra (tocilizumab)	Frequency of serious infection greater in ≥65 years. Use caution.	Not studied in children <2 years. Safety and efficacy only established in SJIA, PJIA, and CRS.	No dose adjustment in mild or moderate impairment. Not studied in severe impair-ment.	Not studied in patients with impairment.	Unclassified† Limited data in pregnant women not sufficient to determine risks. Unknown whether excreted in breast milk; risks and benefits should be considered.
Cimzia (certolizumab)	The number of subjects ≥65 years in clinical trials was not sufficient to determine whether they responded differently from younger subjects. Use caution.	Safety and effectiveness have not been established.	No data	No data	Unclassified† Limited data from ongoing pregnancy registry not sufficient to inform risks. Minimal exrection in breast milk; risks and benefits should be considered.
Cosentyx (secukinumab)	The number of subjects ≥65 years in clinical trials was not sufficient to determine whether they responded differently from younger subjects.	Safety and efficacy have not been established.	No data	No data	Unclassified† Data on use in pregnant women insufficient to inform risks. Unknown whether excreted in breast milk; use with caution.
Entyvio (vedolizumab)	The number of patients ≥65 years in clinical trials was insufficient to determine differences.	Safety and efficacy have not been established.	Safety and efficacy have not been established.	Safety and efficacy have not been established.	Pregnancy category B* Unknown whether excreted in breast milk; use with caution.
Enbrel (etanercept)	Use caution.	Not studied in children <2 years with PJIA	No data	No data	Unclassified† Available studies do not reliably support

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
		or <4 years with PsO.			association with major birth defects. Present in low levels in breast milk; consider risks and benefits.
Humira (adalimumab)	Frequency of serious infection and malignancies is greater in ≥65 years. Use caution.	Only studied in PJIA (ages 2 years and older) and CD (6 years and older).	No data	No data	Unclassified† Present in low levels in breast milk; consider risks and benefits.
Ilaris (canakinumab)	The number of patients ≥65 years in clinical trials was insufficient to determine differences.	Not studied in children <2 years (SJIA, TRAPS, HIDS/ MKD, and FMF) or <4 years (CAPS).	No data	No data	Unclassified† Limited data from postmarketing reports not sufficient to inform risks. Unknown whether excreted in breast milk; consider risks and benefits.
Ilumya (tildrakizumab-asmn)	The number of patients ≥65 years in clinical trials was insufficient to determine differences.	Safety and efficacy have not been established.	No data	No data	Unclassified† Data on use in pregnant women insufficient to inform risks. Unknown whether excreted in breast milk; consider risks and benefits.
Inflectra (infliximab-dyyb)	Frequency of serious infection is greater in ≥65 years. Use caution.	Not recom-mended in <6 years in children with CD.	No data	No data	Pregnancy category B* Unknown whether excreted in breast milk; discontinue nursing or discontinue the drug.
Kevzara (sarilumab)	Frequency of serious infection is greater in ≥ 65 years. Use caution.	Safety and efficacy not established.	Dosage adjustment not required in mild to moderate renal impairment. Kevzara has not been studied in	No data.	Unclassified† Data on use in pregnant women insufficient to inform risks. Unknown whether excreted in breast

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
			severe renal impairment.		milk; consider risks and benefits.
Kineret (anakinra)	Use caution.	For NOMID, has been used in all ages. Not possible to give a dose <20 mg.	CrCl<30 mL/min: give dose every other day	No data	Unclassified† Data on use in pregnant women insufficient to inform risks. Unknown whether excreted in breast milk; use caution.
Olumiant (baricitinib)	No overall differences were observed in the safety and efficacy profiles of elderly patients.	Safety and efficacy have not been established.	Use not recommended in patients with estimated glomerular filtration rate < 60 mL/min/1.73 m^2	No dose adjustment for mild or moderate impairment; not recommended in patients with severe hepatic impairment	Unclassified† Data on use in pregnant women insufficient to inform risks. Unknown whether excreted in breast milk; use caution.
Orencia (abatacept)	Frequency of serious infection and malignancies is greater in ≥65 years. Use caution.	Not recom-mended in <2 years. IV dosing has not been studied in patients < 6 years old. ClickJect autoinjector subcutaneous injection has not been studied in patients < 18 years.	No data	No data	Unclassified† Data on use in pregnant women insufficient to inform risks. Unknown whether excreted in breast milk.
Otezla (apremilast)	No overall differences were observed in the safety profile of elderly patients.	Safety and efficacy have not been established.	The dose of Otezla should be reduced to 30 mg once daily in patients with severe renal impairment (CrCl<30 mL/min).	No dosage adjustment necessary.	Pregnancy category C* Unknown whether excreted in breast milk; use caution.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
Remicade (infliximab)	Frequency of serious infection is greater in ≥65 years. Use caution.	Not recommended in <6 years in children with CD or UC.	No data	No data	Pregnancy category B* Unknown whether excreted in breast milk; discontinue nursing or discontinue the drug.
Renflexis (infliximab-abda)	Frequency of serious infection is greater in ≥ 65 years. Use caution.	Not recommended in < 6 years in children with CD.	No data	No data	Unclassified† Available data do not report clear association with adverse outcomes. Unknown whether excreted in breast milk; consider risks and benefits.
Rituxan (rituximab)	Rates of serious infections, malignancies, and cardiovascular events were higher in older patients.	Safety and effectiveness have not been established.	No data	No data	Unclassified† May potentially cause B-cell lymphocytopenia due to in-utero exposure. Unknown whether excreted in breast milk; risks and benefits should be weighed before use.
Siliq (brodalumab)	No differences in safety or efficacy were observed between older and younger patients, but the number of patients ≥65 years was insufficient to determine any differences in response.	Safety and effectiveness in <18 years have not been established.	No data	No data	Unclassified† There are no human data in pregnant women to inform risks. Unknown whether excreted in breast milk; risks and benefits should be weighed before use.
Simponi/ Simponi Aria (golimumab)	SQ: No differences in AEs observed between older and younger patients. Use caution. IV Aria: Use caution.	Effectiveness in <18 years has not been established (Simponi). Safety and effectiveness in < 18 years have	No data	No data	Pregnancy category B* (Aria) Unclassified† No adequate and well-controlled trials in pregnant women. (Simponi).

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
		not been established (Aria).			Unknown whether excreted in breast milk. Discontinue nursing or discontinue the drug (Aria). Consider risks and benefits (Simponi).
Stelara (ustekinumab)	No differences observed between older and younger patients. Use caution.	Safety and effectiveness have not been established.	No data	No data	Unclassified† Limited data in pregnant women are insufficient to inform risks. Unknown whether excreted in breast milk; systemic exposure to breasted infant expected to be low; consider risks and benefits.
Taltz (ixekizumab)	No differences observed between older and younger patients; however, the number of patients ≥65 years was not sufficient to determine differences.	Safety and effectiveness have not been established.	No data	No data	Unclassified† There are no available data in pregnant women to inform risks. Unknown whether excreted in breast milk; consider risks and benefits.
Tremfya (guselkumab)	No differences observed between older and younger patients; however, the number of patients ≥ 65 years was not sufficient to determine differences.	Safety and efficacy have not been established.	No data	No data	Unclassified† No available data in pregnant women to inform risks. Unknown whether excreted in breast milk; consider risks and benefits.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
Xeljanz / Xeljanz XR (tofacitinib)	Frequency of serious infection is greater in ≥65 years. Use caution.	Safety and effectiveness have not been established.	Reduce dose to 5 mg daily in moderate to severe impairment.	Reduce dose to 5 mg daily in moderate hepatic impairment. Not recommended in severe hepatic impairment.	Unclassified† No adequate and well-controlled studies in pregnancy are available. Unknown whether excreted in breast milk; discontinue nursing or discontinue the drug.

CrCl=creatinine clearance; CRS=cytokine release syndrome; NOMID= Neonatal-Onset Multisystem Inflammatory Disease; PJIA=polyarticular juvenile idiopathic arthritis; SJIA=systemic juvenile idiopathic arthritis

*Pregnancy Category B = No evidence of risk in humans, but there remains a remote possibility. Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women.

Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

†In accordance with the FDA's Pregnancy and Lactation Labeling Rule (PLLR), this product is not currently assigned a Pregnancy Category. Consult product prescribing information for details.

CONCLUSION

- Immunomodulators for a variety of conditions associated with inflammation are available. Mechanisms of action and indications vary among the products. Products in this class have clinical trial data supporting efficacy for their FDA-approved indications.
- Limited head-to-head clinical trials between the agents have been completed.
    - In patients with RA, abatacept and infliximab showed comparable efficacy at 6 months, but abatacept demonstrated greater efficacy after 1 year on some endpoints such as DAS28-ESR, EULAR response, LDAS, and ACR 20 responses (*Schiff et al 2008*).
    - In patients with RA, abatacept and adalimumab were comparable for ACR 20 and ACR 50 responses over 2 years in a single-blind study (*Schiff et al 2014*).
    - In patients with RA and an inadequate response or intolerance to MTX, sarilumab significantly improved change from baseline in DAS28-ESR over adalimumab (*Burmester et al 2017*). DAS28-ESR remission, ACR 20/50/70 response rates, and improvements in HAQ-DI scores were also more likely with sarilumab.
    - Patients with severe arthritis who could not take MTX were randomized to monotherapy with tocilizumab or adalimumab for 24 weeks in a randomized, double-blind study (*Gabay et al 2013*). The patients in the tocilizumab group had a significantly greater improvement in DAS28 at week 24 than patients in the adalimumab group.
    - In biologic-naïve patients with RA and an inadequate response to DMARDs, initial treatment with rituximab was demonstrated to have non-inferior efficacy to initial TNF inhibitor treatment (*Porter et al 2016*).
    - A randomized, open-label trial evaluated biologic treatments in patients with RA who had had an inadequate response to a TNF inhibitor. In this population, a non-TNF biologic (tocilizumab, rituximab, or abatacept) was more effective in achieving a good or moderate disease activity response at 24 weeks than use of a second TNF inhibitor. However, a second TNF inhibitor was also often effective in producing clinical improvement (*Gottenberg et al 2016*). Another recent randomized trial did not demonstrate clinical efficacy differences between abatacept, rituximab, and use of a second TNF inhibitor in this patient population *(Manders et al 2015*).
    - Secukinumab and ustekinumab were compared for safety and efficacy in the CLEAR study, a double-blind, randomized controlled trial in 676 patients with moderate to severe PsO (*Thaçi et al 2015*). The proportion of patients achieving PASI 90 at week 16 was significantly higher with secukinumab compared to ustekinumab (79% vs 57.6%; $p < 0.0001$).
    - In the IXORA-S study, the proportion of patients achieving PASI 90 at week 12 was significantly higher with ixekizumab compared to ustekinumab (72.8% vs 42.2%, respectively; $p < 0.001$) (*Reich et al 2017 [b]).*

  - A greater proportion of PsO patients achieved the primary outcome, PASI 75 at week 12, with ustekinumab 45 mg (67.5%) and 90 mg (73.8%) compared to etanercept 50 mg (56.8%; p = 0.01 vs ustekinumab 45 mg; p < 0.001 vs ustekinumab 90 mg). In this trial, etanercept therapy was associated with a greater risk of injection site erythema than ustekinumab (14.7% vs 0.7%) (*Griffiths et al 2010*).
  - In the FIXTURE study in patient with moderate to severe PsO, 77.1%, 67%, 44%, and 4.9% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, etanercept at FDA-recommended dosing, and placebo, respectively (*Langley et al 2014*).
  - In the UNCOVER-2 and UNCOVER-3 studies, the proportions of patients achieving PASI 75 and achieving PGA 0 or 1 were higher in patients treated with ixekizumab compared to those treated with etanercept.
  - In the AMAGINE-2 and AMAGINE-3 studies, the proportions of patients achieving PASI 100 were higher in patients treated with brodalumab compared to those treated with ustekinumab (*Lebwohl et al 2015*).
  - In the VOYAGE 1 and VOYAGE 2 studies, the proportions of patients with moderate to severe PsO achieving IGA 0 or 1 and PASI 90 were higher with guselkumab compared to those treated with adalimumab *(Blauvelt et al 2017, Reich et al 2017[a]*).
  - No meaningful differences were shown in the treatment of RA and PsA in comparisons of infliximab and infliximab-dyyb conducted to establish biosimilarity between these agents (*Park et al 2013, Park et al 2016, Park et al 2017, Yoo et al 2013, Yoo et al 2016, Yoo et al 2017*). Similarly, no meaningful differences between infliximab and infliximab-abda were found in treatment of RA in clinical studies to establish biosimilarity (*Choe et al 2017, Shin et al 2015*).
  - In patients with CD, UC, RA, PsA, spondyloarthritis, and PsO who were treated with the originator infliximab for ≥ 6 months, infliximab-dyyb was noninferior to infliximab originator group for disease worsening (*Jørgensen et al 2017*).
  - More comparative studies are needed.
- For RA, patients not responding to initial DMARD treatment may be treated with combination DMARDs, TNF inhibitors, non-TNF inhibitor biologics, and/or tofacitinib (*Singh et al 2016c; Smolen et al 2017*). EULAR has released guidelines for use of antirheumatic drugs in pregnancy, which state that the TNF inhibitors etanercept and certolizumab are among possible treatment options for patients requiring therapy (*Götestam Skorpen et al 2016*).
- For the management of PsO, biologic agents are routinely used when ≥ 1 traditional systemic agents are not tolerated, fail to product an adequate response, or are unable to be used due to patient comorbidities (*Gottleib et al 2008, Menter et al 2008, Menter et al 2009a, Menter et al 2009b, Menter et al 2010, Menter et al 2011, Nast et al 2015b*). EULAR 2015 PsA guidelines recommend TNF inhibitors in patients with peripheral arthritis and an inadequate response to at least 1 synthetic DMARD, such as MTX (*Gossec et al 2016, Ramiro et al 2016*). For patients with peripheral arthritis and an inadequate response to at least 1 synthetic DMARD, in whom a TNF inhibitor is not appropriate, biologics targeting IL-12/23 or IL-17 pathways may be considered. Apremilast is considered a treatment option in patients with peripheral arthritis and an inadequate response to at least 1 synthetic DMARD, in whom biologics are not appropriate. Guidelines from GRAPPA recommend various biologics for the treatment of PsO and PsA based on patient-specific factors, including TNF inhibitors, IL-17 and IL-12/23 inhibitors, and PDE-4 inhibitors (*Coates et al 2016*).
- In patients with JIA and involvement of ≥ 5 joints, the ACR recommends the use of a TNF inhibitor after an adequate trial of a conventional DMARD (*Beukelman et al 2011*). The ACR updated guideline for SJIA notes that IL-1 and IL-6 play a central role in the inflammatory process for this condition, and recommend agents such as anakinra, canakinumab, tocilizumab, abatacept, and TNF inhibitors among either first- or second-line treatments (*Ringold et al 2013*).
- According to the ACG, for the treatment of UC, infliximab should be considered after failure of first-line non-biologic agents (*Kornbluth et al 2010*). Other immunomodulators were not indicated for UC when these guidelines were written.
- The ACG states that the anti-TNF monoclonal antibodies adalimumab, certolizumab, and infliximab are effective in the treatment of moderate to severely active CD in patients who are resistant to corticosteroids or are refractory to thiopurines or methotrexate. These agents can be considered for treating perianal fistulas, and infliximab can also treat enterocutaneous and rectovaginal fistulas in CD. Adalimumab, certolizumab, and infliximab are effective for the maintenance of anti-TNF induced remission as monotherapy or in combination with azathioprine/6-mercaptopurine or methotrexate. The combination of infliximab with an immunomodulator (thiopurine) is more effective than monotherapy with individual agents in patients with moderate to severe CD and who are naïve to both agents. Infliximab can also treat fuliminant CD. Vedolizumab with or without an immunomodulator can be used for induction and maintenance of remission in patients with moderate to severe CD. Patients are candidates for ustekinumab therapy, including for the maintenance of remission, if they have moderate to severe CD and have failed corticosteroids, thiopurines, methotrexate, or anti-TNF inhibitors. The guideline acknowledges the effectiveness of

biosimilar infliximab and biosimilar adalimumab for the management of moderate to severe CD (*Lichtenstein et al 2018*). The AGA recommends using anti-TNF drugs to induce remission in patients with moderately severe CD (*Terdiman et al 2013*). ECCO recommends TNF inhibitors for patients with CD who have relapsed or are refractory to corticosteroids, depending on disease location and severity, and states that early TNF inhibitor therapy should be initiated in patients with high disease activity and features indicating a poor prognosis; vedolizumab is an alternative for some patients (*Gomollón et al 2017*).

- Consensus statements for the management of inflammatory bowel disease in pregnancy, coordinated by the Canadian Association of Gastroenterology, state that TNF inhibitor treatment does not appear to be associated with unfavorable pregnancy outcomes and should generally be continued during pregnancy (*Nguyen et al 2016b*).
- Based upon guidelines from the European Dermatology Forum, adalimumab is recommended among first-line therapies for HS, with infliximab a potential second-line option (*Gulliver et al 2016, Zouboulis et al 2015*).
- Joint guidelines from ASAS and EULAR state that biologic DMARDs should be considered in patients with AS and persistently high disease activity despite conventional treatments (*van der Heijde et al 2017*). The 2015 ACR, Spondylitis Association of America, and Spondyloarthritis Research and Treatment Network guidelines strongly recommend TNF inhibitors for patients who have active disease despite NSAIDs; no TNF inhibitor is preferred over another for AS for most patients (*Ward et al 2016*).
- Infliximab and adalimumab are recommended over etanercept for various ocular inflammatory disorders (*Levy-Clarke et al 2016*).
- Caution is warranted with these biologic agents due to severe infections and malignancies that can occur with their use. Tocilizumab, TNF inhibitors, and tofacitinib have boxed warnings regarding a risk of serious infections. TNF inhibitors and tofacitinib also have boxed warnings regarding an increased risk of malignancies. Brodalumab has a boxed warning regarding the risk of suicidal ideation and behavior.
- Warnings, precautions, and AE profiles vary in this class.
- All of the biologic agents with the exception of apremilast and tofacitinib are given by subcutaneous injection and/or intravenous infusion. Administration schedule varies among the injectable agents in the class. Apremilast and tofacitinib are given orally.
- Selection of an agent for a patient is determined by approved indications, response, administration method, tolerability, AE profile, and cost of the agent.

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Anthem Short-Acting Opioid Analgesics for Acute Pain Duration of Use

Override(s)	Approval Duration
Quantity Limit	1 year

Medications	Quantity Limit
Butalbital-APAP-Caffeine-Codeine – All oral formulations of the following: Butalbital/acetaminophen/caffeine/codeine Acetaminophen/caffeine/dihydrocodeine **Butalbital-ASA-caffeine-codeine – All oral formulations of the following:** Butalbital/aspirin/caffeine/codeine **Codeine sulfate - All oral formulations of codeine sulfate** **Hydrocodone-Acetaminophen tablets (2.5mg-325mg, 5mg-300mg, 5mg-325mg, 7.5mg-300mg, 7.5mg-325mg, 10mg-300mg, 10mg-325mg)** **Hydrocodone-Acetaminophen oral solution (2.5mg-108mg/5mL, 5mg-163mg/7.5mL, 5mg-217mg/10mL, 7.5-325/15mL, 10mg-300mg/15mL, 10mg-325mg/15mL)** **Hydrocodone-Ibuprofen – All oral formulations of hydrocodone/ibuprofen** **Hydromorphone – All oral tablet and liquid formulations of immediate release hydromorphone** **Meperidine - All oral formulations of meperidine** **Morphine sulfate IR tabs and solution – All oral tablet and liquid formulations of immediate release morphine sulfate** **Nucynta (tapentadol) – All oral formulations of immediate release Nucynta**	7 days' supply per fill; 14 day's supply per 30 days

Oxymorphone - All oral formulations of immediate release oxymorphone **Oxycodone – All oral formulations of immediate release oxycodone** **Oxycodone-Acetaminophen tablets (2.5mg-300mg, 2.5mg-325mg, 5mg-300mg, 5mg-325mg, 7.5mg-300mg, 7.5mg-325mg, 10mg-300mg, 10mg-325mg)** **Oxycodone-Acetaminophen oral solution (5mg-325mg/5mL)** **Oxycodone-Aspirin tablets (4.8355mg-325mg)** **Oxycodone-Ibuprofen tablets (5mg-400mg)** **Pentazocine-naloxone - All oral formulations of pentazocine/naloxone** **Acetaminophen-Cod #2 tablets (acetaminophen-codeine 300mg-15mg)** **Tylenol with codeine #3 tablets (acetaminophen-codeine 300mg-30mg)** **Acetaminophen-codeine oral solution, suspension 120-12mg/5mL, 300/12.5mL** **Tylenol With Codeine #4 Tablets (acetaminophen-codeine 300mg-60mg)** **Ultram, Tramadol HCl, Ultracet, Tramadol HCl-Acetaminophen – All oral formulations**	

APPROVAL CRITERIA

Requests for greater than 7 days' supply per fill and greater than 14 days' supply per 30 days of short-acting opioid analgesics may be approved for the following:

I. Individual is currently utilizing opioid therapy on a consistent basis for chronic pain; **OR**

II. Individual has a diagnosis of cancer related pain and/or is actively undergoing cancer treatment (provide diagnosis); **OR**
III. Individual has a terminal condition and is receiving palliative/end-of-life care (provide diagnosis); **OR**
IV. Individual has a diagnosis of sickle cell anemia.

NOTE: Individuals currently receiving opioids on a consistent basis is defined as prescribed use for 90 out of the past 110 days.

Tramadol containing agents may be subject to the following age requirements via prior authorization:

I. Individual is 18 years of age or older; **OR**
II. Individual is 12 years of age or older and treating for pain conditions other than postsurgical removal of tonsils and/or adenoids. (FDA Safety Announcement 2017)

Codeine containing agents may be subject to the following age requirements via prior authorization:

I. Individual is 12 years of age or older. (FDA Safety Announcement 2017)

NOTE: An FDA Safety advisory released on 4-20-2017 noted that the label for codeine containing agents would be updated to include a contraindication for use in treating pain or cough in children younger than 12 years. This is due to serious risks, including slowed or difficult breathing and death, which appear to be a greater risk in children younger than 12 years (https://www.fda.gov/drugs/drugsafety/ucm549679.htm).

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2017. URL: http://www.clinicalpharmacology.com. Updated periodically.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.

DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2017; Updated periodically.

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Clinical Pharmacy Program Guidelines for Short-Acting Opioid Products- Health Plan of Nevada Medicaid

Program	Prior Authorization/Medical Necessity – Short-Acting Opioid Products- Nevada Medicaid
Medication	**Short-Acting Opioids:** **Includes both brand and generic versions of the listed products unless otherwise noted:** All salt forms, single and combination ingredient products, and all brand and generic formulations of the following: butorphanol tartrate nasal spray, codeine, morphine, hydrocodone, hydromorphone, oxycodone, oxymorphone, pentazocine, tramadol, tapentadol, meperidine, levorphanol tartrate, dihydrocodeine, opium **Short-Acting Opioids – Cough and cold products:** **Includes both brand and generic versions of the listed products unless otherwise noted:** Products containing codeine or hydrocodone in combinations with one or more of the following: homatropine, chlorpheniramine, guaifenesin, pyrilamine, brompheniramine, phenylephrine, triprolidine, dexchlorpheniramine, promethazine, pseudoephedrine.
Markets in Scope	Nevada

(i) Background:

The CDC and the American Academy of Neurology recommends the following best practices in the prescription of opioids:

- Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain.
- Before starting opioid therapy, treatment goals should be established with patients that include realistic goals for pain and function and should consider how therapy will be discontinued if benefits do not outweigh risks. Track pain and function at every visit (at least every 3 months) using a brief, validated instrument. Continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
- When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended release/long-acting opioids.
- Document the daily morphine equivalent dose (MED) in mg/day from all sources of opioids. Access the state prescription drug monitoring program (PDMP) data at

treatment initiation and periodically during treatment. Currently all states except for Missouri have a PDMP.

- To avoid increased risk of respiratory depression, long-acting opioids should not be prescribed concurrently with benzodiazepines. Screen for past and current substance abuse and for severe depression, anxiety, and PTSD prior to initiation.
- Use random urine drug screening prior to initiation and periodically during treatment with a frequency according to risk.
- Use a patient treatment agreement, signed by both the patient and prescriber that addresses risks of use and responsibilities of the patient.
- Methadone should not be the first choice for a long-acting opioid. Only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients should consider prescribing methadone for pain.
- CDC recommends avoiding escalating doses above 50-90 mg/day MED unless sustained meaningful improvement in pain and function is attained, and not without consultation with a pain management specialist. A list of MED for the long-acting opioids is available in Table 1.
- The American Academy of Neurology recommends avoiding escalating doses above 80-120 mg/day MED unless sustained meaningful improvement in pain and function is attained, and not without consultation with a pain management specialist. A list of MED for the long-acting opioids is available in Table 1.
- Clinicians should evaluate benefits and harms of continued therapy at least every 3 months. If benefits do not outweigh harms, opioids should be tapered and discontinued. Evaluation should include assessment of substance use disorder/opioid dependence. Validated scales (such as the DAST-10) are available at www.drugabuse.gov.

Table 1. CDC Recommended Opioid Maximum Morphine Equivalents per Day*

Active Ingredient	FDA Label Max Daily Doses	90 MED Equivalent (mg/day) (non treatment naïve)
Morphine	None	90mg
Hydromorphone	None	22.5mg
Hydrocodone	None	90mg
Tapentadol	600mg IR products	225mg
Oxymorphone	None	30mg
Oxycodone	None	60mg
Codeine	360mg	600mg
Pentazocine	None	243mg
Tramadol	400mg IR products	900mg
Meperidine	600mg	900mg

Butorphanol	None	12.86mg
Opium	4 suppositories/day Deodorized tincture: 24mg/day Camphorated tincture: 16mg/day	90mg

*Doses are not considered equianalgesic and table does not represent a dose conversion chart.

Max MED is the maximum dose per day based on morphine equivalent dose allowed without consultation or prescription by a pain specialist. Max MED is based upon the CDC guidelines and adjusted for currently available product strengths. Fentanyl is dosed in mcg/hr rather than mg/day.

Opioid (codeine or hydrocodone) containing cough and cold products are FDA labeled for use in adults 18 years of age and older. Use of prescription opioid cough and cold medicines containing codeine or hydrocodone should be limited in children younger than 18 years old due to serious risks associated with use.

Coverage Criteria:

(ii) Short-Acting Opioids: Criteria for Opioid Naïve Members, including Non-Preferred Reviews and Quantity Limits

NOTE: An opioid-naïve member is defined as not having filled an opioid in the past 60 days.

Patients 20 years and older will be limited to a 7 day supply and less than 50 MED/day for their initial short-acting opioid fill

Patients under the age of 20 years will be limited to a 3 day supply and less than 50 MED/day for their initial short-acting opioid fill.

NOTE: This section does NOT apply to cough and cold products.

A. Short-Acting Opioids

1. Opioid naïve members (defined as not having filled an opioid in the past 60 days) may receive greater than the supply limit and/or greater than 50 MED based on **ALL** of the following:

   a. If the request is for greater than the supply limit **ONE** of the following:

      (1) Cancer diagnosis
      (2) End of life care, including hospice care
      (3) Palliative care
      (4) Sickle cell anemia
      (5) **Both** of the following:
         (a) **ONE** of the following:

i. Traumatic injury
ii. Post-surgical procedures, excluding dental procedures
iii. Prescriber attests that the patient has received an opioid within the past 60 days

-AND-

(b) Prescriber attests to **both** of the following:
i. The information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided.
ii. If requested for traumatic injury or post-surgical procedure, prescriber attests that based on injury or surgical procedure performed the member requires greater than a 7 day supply for patients 20 years and older or greater than a 3 day supply for patients under the age of 20 years of short-acting opioid to adequately control pain.

-AND-

b. If the request is for 50 MED or greater **ONE** of the following:
NOTE: If the request exceeds 90 MED, please skip Section b-Requests for 50 MED or greater and proceed to Section IV-Morphine Equivalent Dosing (MED) Reviews

(1) Diagnosis of cancer, end of life pain (including hospice care), palliative care or sickle cell anemia
(2) Patient new to the plan is currently exceeding 50 MED and prescriber attests patient has been on a short-acting opioid in the past 60 days.
(3) All of the following:
(a) Document **all** of the following:
i. The diagnosis associated with the need for pain management with opioids.
ii. If used in patients with medical comorbidities or if used concurrently with a benzodiazepine or other drugs that could potentially cause drug-drug interactions, the prescriber has acknowledged that they have completed an assessment of increased risk for respiratory depression.
iii. The prescriber has acknowledged that they have completed an addiction risk and risk of overdose assessment.
iv. Prescriber attests the member requires more than 50 MED per day to adequately control pain.

-AND-

c. If the request is for a non-preferred medication the patient must have a history of failure, contraindication or intolerance to a trial of at least three preferred short-acting opioids.

Authorization for cancer, end of life, palliative care, or sickle cell pain will be issued for 12 months. All other approvals will be issued for the requested duration, not to exceed one month.

(iii) Short-Acting Opioids: Criteria for Opioid Experienced Members: Non-Preferred Reviews

NOTE: This section does NOT apply to cough and cold products.

A. If the request is for a non-preferred medication the patient must have a history of failure, contraindication or intolerance to a trial of at least three preferred short-acting opioids.

Authorization will be issued for 12 months.

(iv) Morphine Equivalent Dosing (MED) Reviews: For Requests Exceeding the 180MED Cumulative Threshold.
NOTE: This section does NOT apply to cough and cold products.

A. Criteria for Morphine Equivalent Dosing (MED) Reviews:

1. **Cancer/Hospice/End of Life Related Pain**

   a. Doses exceeding the cumulative MED of 180 mg will be approved up to the requested amount for ALL opioid products if the member has cancer pain or an end of life diagnosis (hospice care).

   Authorization will be issued for 12 months for cancer pain/hospice/end of life related pain. The authorization should be entered for an MED of 9999 so as to prevent future disruptions in therapy if the patient's dose is increased.

2. **Non-cancer/non-hospice/non-end of life related pain (Initial Authorization)**

   a. If the dose exceeds the maximum cumulative MED of 90mg, must meet ALL of the following:

      (1) Prescriber attests to ALL of the following:
      - The information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare

may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided.

- Treatment goals are defined, including estimated duration of treatment.
- Treatment plan includes the use of a non-opioid analgesic and/or non-pharmacologic intervention
- Patient has been screened for substance abuse/opioid dependence
- If used in patients with medical comorbidities or if used concurrently with a benzodiazepine or other drugs that could potentially cause drug-drug interactions, the prescriber has acknowledged that they have completed an assessment of increased risk for respiratory depression.

-AND-

(2) BOTH of the following:
(a) Patient has tried and failed non-opioid pain medication (document drug name and date of trial)
(b) Opioid medication doses of less than 90 MED have been tried and did not adequately control pain (document drug regimen or MED and dates of therapy)

Authorization will be issued for 6 months for non-cancer/non-hospice/non-end of life related pain up to the current requested MED plus 90 MED.

If the member has been established on the requested MED dose for at least 30 days and does not meet the medical necessity authorization criteria requirements, a denial should be issued and a maximum 60-day authorization may be authorized one time for the requested MED dose.

3. **Non-cancer/non-hospice/non-end of life related pain (Reauthorization)**

a. If the dose exceeds the maximum cumulative MED of 180mg, must meet **ALL** of the following:

(1) Prescriber attests to ALL of the following:
- The information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare

may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided.

- Treatment goals are defined, including estimated duration of treatment.
- Treatment plan includes the use of a non-opioid analgesic and/or non-pharmacologic intervention
- Patient has been screened for substance abuse/opioid dependence
- If used in patients with medical comorbidities or if used concurrently with a benzodiazepine or other drugs that could potentially cause drug-drug interactions, the prescriber has acknowledged that they have completed an assessment of increased risk for respiratory depression.

-AND-

(2) Identify rationale for not tapering and discontinuing opioid (Document rationale)

-AND-

(3) Patient demonstrates meaningful improvement in pain and function (Document improvement in function or pain score improvement).

Authorization will be issued for 6 months for non-cancer/non-hospice/non-end of life related pain up to the current requested MED plus 90 MED.

If the member has been established on the requested MED dose for at least 30 days and does not meet the medical necessity authorization criteria requirements, a denial should be issued and a maximum 60-day authorization may be authorized one time for the requested MED dose.

(v) Cough and Cold Products
Quantity Limit Rules:

- **120mL/fill**

- **360mL/30 days**

A. Criteria for Morphine Equivalent Dosing (MED) Reviews

1. Doses exceeding the cumulative MED of 90 mg will be approved up to the requested amount if the prescriber attests they are aware of patient's current opioid therapy and MED dose and feels the treatment with the requested product is medically necessary.

   Authorization will be issued for up to 30 days for cough and cold related treatment. The authorization should be entered for the MED requested.

B. Criteria for Reviews for Members Under the Age of 18 Years

1. **Opioid containing cough and cold products** will be approved based on **all** of the following criteria:

   a. Prescriber attests they are aware of FDA labeled contraindications regarding use of opioid containing cough and cold products in patients less than 18 years of age and feels the treatment with the requested product is medically necessary. (Document rationale for use)

   -AND-

   b. Patient does not have a comorbid condition that may impact respiratory depression (e.g., asthma or other chronic lung disease, sleep apnea, body mass index > 30)

   -AND-

   c. Patient has tried and failed at least one non-opioid containing cough and cold remedy

   Authorization will be issued for 30 days.

C. Criteria for Requests Exceeding the Quantity Limit

1. Requests exceeding the quantity limit will be approved based on **both** of the following:
   a. Doses exceeding the quantity limit will be approved up to the requested amount if the prescriber attests that a larger quantity is medically necessary.

   -AND-

   b. The requested dose is within FDA maximum dose per day, where an FDA maximum dose per day exists.

   Authorization will be issued for up to 30 days. The authorization should be entered for the quantity requested.

D. Criteria for Non-Preferred Reviews

1. If the request is for a non-preferred medication the patient must have a history of failure, contraindication or intolerance to a trial of at least three preferred cough and cold products.

Authorization will be issued for 30 days.

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Program	Prior Authorization - Short-Acting Opioid Pain Medications-Nevada
Change Control	
Date	Change
10/2017	Created Nevada specific criteria since they will not be going live with the MED edit on 10/1.
1/1/2018	Added MED section- Nevada MED limit is 180. Separated short- and long-acting opioids into individual policies. Added maximum dosage for tapentadol. Updated background.
3/2018	Added criteria for members new to therapy (days supply and MED limit). Removed efficient medication dosing question and FDA max dosing questions from quantity limit section to accommodate operational edits for new to therapy limits. Expanded attestation for the MED section: treatment goals, treatment plan, screening for substance abuse/opioid dependence, and medical comorbidities questions combined into an attestation and documentation requirements removed.
5/2018	Added criteria for opioid containing cough and cold products for members who are under the age of 18 and for patients exceeding the quantity limit. Removed prescriber check. Go-live 7/1/2018.

5/2018 v2	Updated MED language to include confirmation that less than 180 MED is not adequate.
8/2018	Separated MED into initial and reauthorization. Removed statements from the MED attestation that would have been evaluated in the authorization for the drug itself. Updated auth duration language.
9/2018	Added criteria for new to therapy programs for members under 20 years of age. Go-live 10/1/18.

Clinical Policy: Age Limit Override (Codeine, Tramadol, Hydrocodone)

Reference Number: CP.PMN.138
Effective Date: 03.13.18
Last Review Date: 05.18
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Prior authorization is required for the following medications in the respective age groups due to FDA labeling of these medications:

- Codeine-containing medications indicated for pain are contraindicated in pediatric patients younger than age 12 years;
- Tramadol-containing medications are not indicated for pain in patients younger than age 18 years (use is contraindicated in patients less than 18 years to treat post-tonsillectomy and post-adenoidectomy pain);
- Codeine- and hydrocodone-containing medications indicated for cough and cold are not indicated for use in pediatric patients younger than age 18 years.

FDA Approved Indication(s)

Codeine- and tramadol-containing medications are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate, including discomfort associated with acute painful musculoskeletal conditions and management of the symptom complex of tension (or muscle contraction) headache.

Codeine- and hydrocodone-containing medications are indicated for relief of cough, nasal congestion, and other upper respiratory symptoms associated with allergies or cold.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that codeine-, tramadol-, and hydrocodone-containing opioids are **medically necessary** for the following reasons:

I. Initial Approval Criteria

A. Pain (must meet all):

***In addition to meeting these criteria, requests for all opioids are subject to the criteria outlined in the opioid analgesic policy for the relevant line of business.*

1. Prescribed for pain management;
2. Prescribed agent is FDA-approved for pain management;
3. Member meets one of the following (a or b):
   a. Failure of at least two non-opioid ancillary treatments (e.g., non-steroidal anti-inflammatory drugs [NSAIDs], acetaminophen, anticonvulsants, antidepressants)

at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

b. Prescribed by or in consultation with an oncologist, hematologist, hospice provider, or pain specialist for cancer, palliative care, or sickle cell disease;

4. Failure of at least two age-appropriate opioid analgesics (e.g., morphine, oxycodone), unless contraindicated or clinically significant adverse effects are experienced;
5. Use is not for pain post-tonsillectomy or post-adenoidectomy;
6. Dose does not exceed health plan's approved quantity limit.

Approval duration:
Non-cancer pain - 7 days
Cancer, sickle cell, or palliative care - 12 months

B. Cough (must meet all):

1. Diagnosis of cough due to viral or bacterial infection;
2. Prescribed agent is FDA-approved for the treatment of cough;
3. Failure of at least two of the following agents at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: dextromethorphan, benzonatate, guaifenesin;
4. Member is concurrently receiving appropriate therapy for the underlying cause of the cough (e.g., antihistamines, decongestants, bronchodilators, oral and/or inhaled corticosteroids, antibiotics);
5. Dose does not exceed the FDA-approved maximum recommended dose.

Approval duration: 14 days

C. Other diagnoses/indications
Not applicable.

II. Continued Therapy

A. Cancer, Sickle Cell, or Palliative Care Pain (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed health plan's approved quantity limit.

Approval duration: 12 months

B. All Other Indications in Section I (must meet all)**:**
Continued therapy for cough, or non-cancer, -sickle cell or -palliative care pain will not be authorized as the underlying causes of cough and pain must be treated with appropriate therapy.

C. Other diagnoses/indications:
Not applicable.

III. Diagnoses/Indications for which coverage is NOT authorized:

Not applicable

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NSAIDs: non-steroidal anti-inflammatory drugs

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Analgesic agents		
acetaminophen (Tylenol®)	**Analgesia** Weight-based pediatric dosing 10 – 15 mg/kg/dose PO Q4 – 6 hr PRN Age 6 to 11 years 325 mg PO Q4 – 6 hr PRN Age 12 years or older Immediate-release: 650 mg PO Q4 – 6 hr PRN or 1000 mg PO Q6 hr PRN Extended-release: 1300 mg PO Q8 hr PRN	75 mg/kg/day not to exceed 4 g/day
carbamazepine (Tegretol®)	**Neuropathic pain*** Initial: 50 – 100 mg PO BID Maintenance: 100 – 200 mg PO Q4 – 6 hr	1,200 mg/day
cyclobenzaprine (Fexmid®)	**Muscle spasm** Age 15 years or older 5 – 10 mg PO TID	30 mg/day
duloxetine (Cymbalta®)	**Chronic musculoskeletal pain** 30 mg PO QD for 1 week, then 60 mg PO QD	60 mg/day
gabapentin (Neurontin®)	**Neuropathic pain*** 1,200 – 3,600 mg/day PO in 3 divided doses	3,600 mg/day
ibuprofen (Advil®, Motrin®)	**Analgesia** Age 6 months to less than 12 years 4 – 10 mg/kg/dose PO Q6 – 8 hr PRN Age 12 to 17 years 400 mg PO Q4 – 6 hr PRN	40 mg/kg/day not to exceed 2,400 mg/day
oxycodone (Roxicodone®, OxyContin®)	**Moderate-to-severe pain** (immediate-release tablets) 0.1 – 0.2 mg/kg/dose (moderate pain) or 0.2 mg/kg/dose (severe pain) PO **Severe pain** (extended-release tablets) Age 11 months or older	N/A

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Initial dose PO based on conversion from current opioid regimen dose	
morphine sulfate immediate-release	**Acute pain** Age 6 months or younger 0.08 – 0.1 mg/kg/dose PO Q3 – 4 hr Age greater than 6 months Weight < 50 kg: 0.2 – 0.5 mg/kg/dose PO Q3 – 4 hr PRN Weight ≥ 50 kg: 15 – 20 mg/kg PO Q3 – 4 hr PRN	N/A
dextromethorphan (Delsym®, Robitussin®)	**Cough (suppressant)** Age 4 to 6 years (syrup) Immediate-release: 2.5 – 7.5 mg PO Q4 – 8 hr PRN Extended-release: 15 mg PO BID PRN Age 6 to less than 12 years Immediate-release: 5 – 10 mg PO Q4 hr PRN or 15 mg PO Q6 – 8 hr PRN Extended-release: 30 mg PO BID PRN Age 12 years or older Immediate-release: 10 – 20 mg PO Q4 hr PRN or 20 – 30 mg PO Q6 – 8 hr PRN	Age 4 to 6 years: 30 mg/day Age 6 to 12 years: 60 mg/day Age ≥ 12 years: 120 mg/day
guaifenesin (Mucinex®)	**Cough (expectorant)** Age 2 to less than 4 years Liquid: 50 – 100 mg PO Q4 hr PRN Age 4 to less than 6 years 50 – 100 mg PO Q4 hr PRN Age 6 to less than 12 years 100 – 200 mg PO Q4 hr PRN Age 12 years or older 200 – 400 mg PO Q4 hr PRN	Age 2 to < 6 years: 600 mg/day Age 6 to < 12 years: 1,200 mg/day Age ≥ 12 years: 2,400 mg/day
benzonatate (Tessalon Perles®)	**Cough** Age greater than 10 years 100 – 200 mg PO TID PRN	600 mg/day
albuterol nebulizer	**Bronchospasm** Age 2 to less than 12 years Weight 10 – 15 kg: 0.63 – 1.25 mg PO TID or QID PRN	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Weight > 15 kg: 0.63 – 2.5 mg PO TID or QID PRN Age 12 years or older 2.5 mg PO TID or QID PRN	
albuterol metered dose inhaler (ProAir®, Proventil®, Ventolin®)	**Bronchospasm** 2 inhalations Q4 – 6 hr PRN	Varies
diphenhydramine (Benadryl®)	**Cough** Age 12 years or older 25 mg PO Q4 hr PRN	150 mg/day
oxymetazoline (Afrin® Nasal Spray)	**Nasal congestion** Age 6 years or older 2 – 3 sprays in each nostril BID for ≤ 3 days	Max 3 days use
phenylephrine (Afrin® Childrens)	**Nasal congestion** Age 2 to less than 6 years 0.125% solution: 2 – 3 sprays in each nostril for no more than Q4 hrs for ≤ 3 days Age 6 to less than 12 years 0.25% solution: 2 – 3 sprays in each nostril for no more than Q4 hrs for ≤ 3 days Age 12 years or greater 0.25% to 1% solution: 2 – 3 sprays in each nostril for no more than Q4 hrs for ≤ 3 days	Max 3 days use
phenylephrine (Sudafed PE® Childrens)	**Nasal congestion** Age 4 to less than 6 years 2.5 mg PO Q4 hr PRN for ≤ 7 days Age 6 to less than 12 years 5 mg PO Q4 hr PRN for ≤ 7 days Age 12 years or greater 10 mg PO Q4 hr PRN for ≤ 7 days	Age 4 to < 6 years: 15 mg/day Age 6 to < 12 years: 30 mg/day Age ≥ 12 years: 60 mg/day
Qvar® (beclomethasone)	**Asthma** Age 5 to 11 years 40 – 80 mcg inhaled BID Age 12 years or greater 40 – 320 mcg inhaled BID	Age 5 to 11 years: 80 mcg BID/day Age ≥ 12 years: 320 mcg BID/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: General Information

- Per the FDA Drug Safety Communication in April 2017, the following labeling changes were required for codeine- and tramadol- containing medications:
  - Contraindications:
    - Codeine should not be used to treat pain or cough in children less than age 12 years
    - Tramadol should not be used to treat pain in children less than age 12 years
    - Tramadol should not be used to treat pain post-tonsillectomy or post-adenoidectomy in children less than age 18 years
  - Warnings:
    - Codeine and tramadol should not be used in adolescents age 12 to 18 years who are obese, or have obstructive sleep apnea or severe lung disease
  - Strengthened warning:
    - Breastfeeding is not recommended when taking codeine or tramadol medicines
- Per the FDA Drug Safety Communication in January 2018, the following labeling changes were required for codeine- and hydrocodone-containing medications:
  - Codeine or hydrocodone prescription cough and cold medications should not be used in children younger than age 18 years
  - Boxed warning: Risks of misuse, abuse, addiction, overdose, death and slowed or difficult breathing

V. Dosage and Administration

There are various codeine-, tramadol-, and hydrocodone-containing medications commercially available. Please refer to the respective package inserts for dosing and administration.

VI. Product Availability

Please refer to the respective package inserts for product availability.

VII. References

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2. Food and Drug Administration. FDA Drug Safety Communication: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeeding women. 2017. https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.13.18	05.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

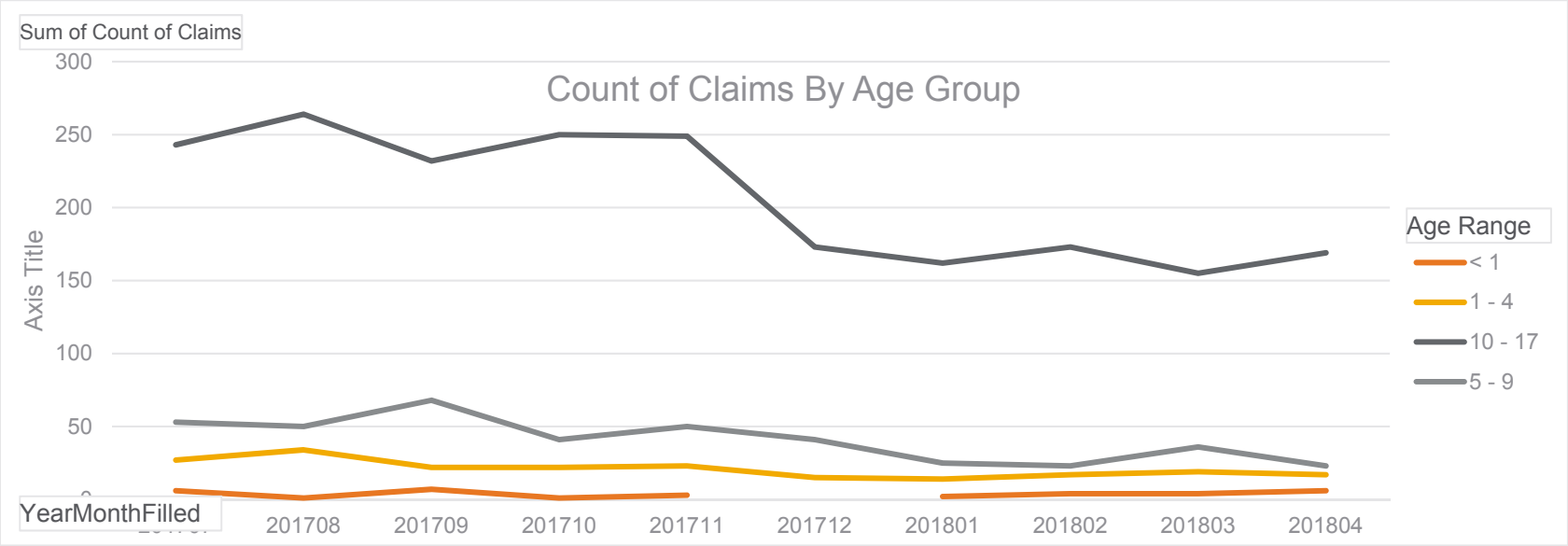
This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

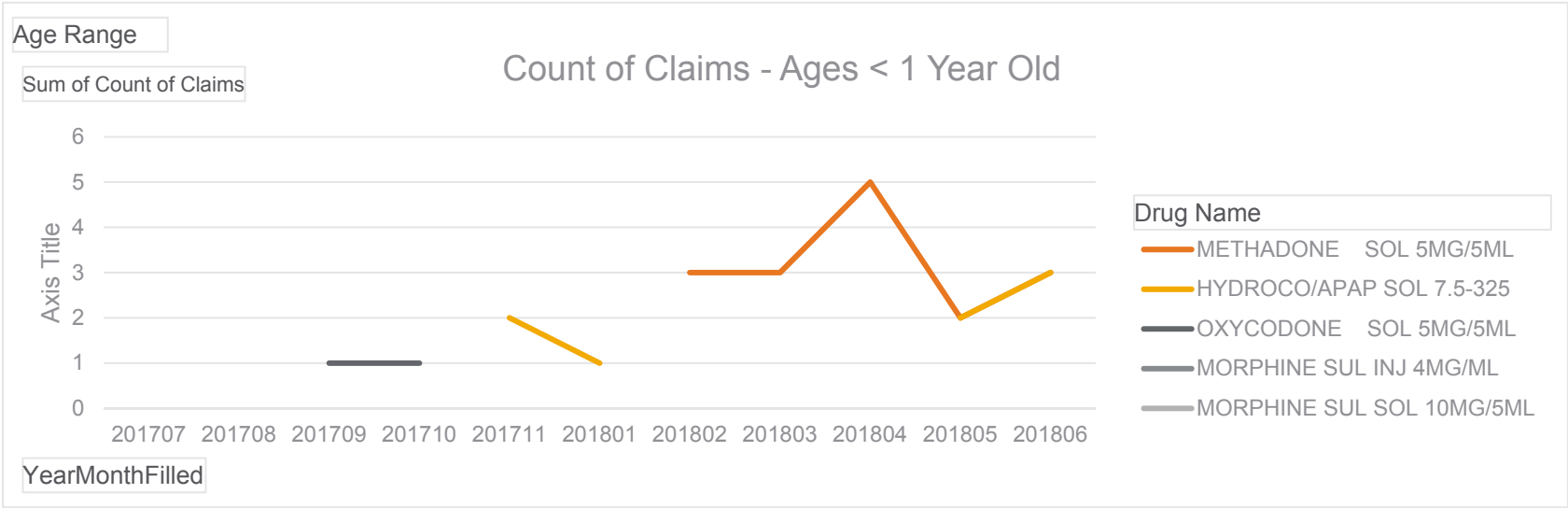
Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

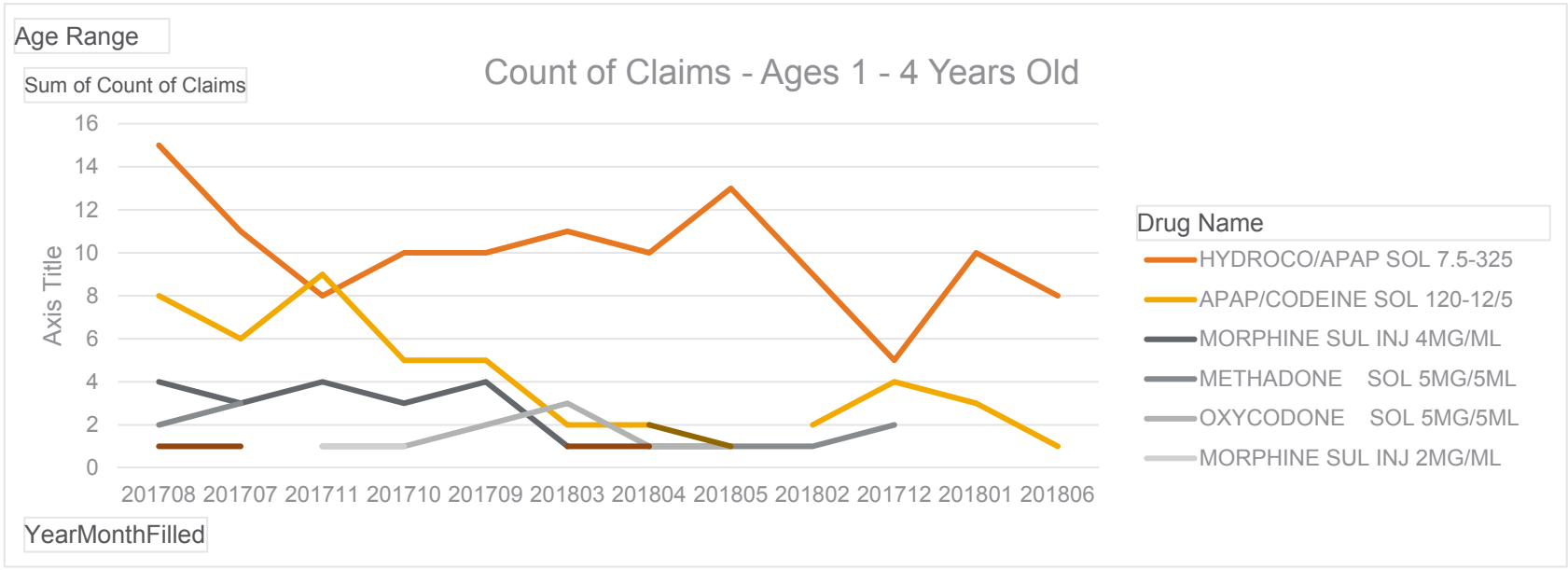
For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

Opioid Utilization in Members Under 18 Years Old

Fee for Service Medicaid
July 1, 2017 - June 30, 2018






Age Range
Sum of Count of Claims
Count of Claims - Ages 1 - 4 Years Old
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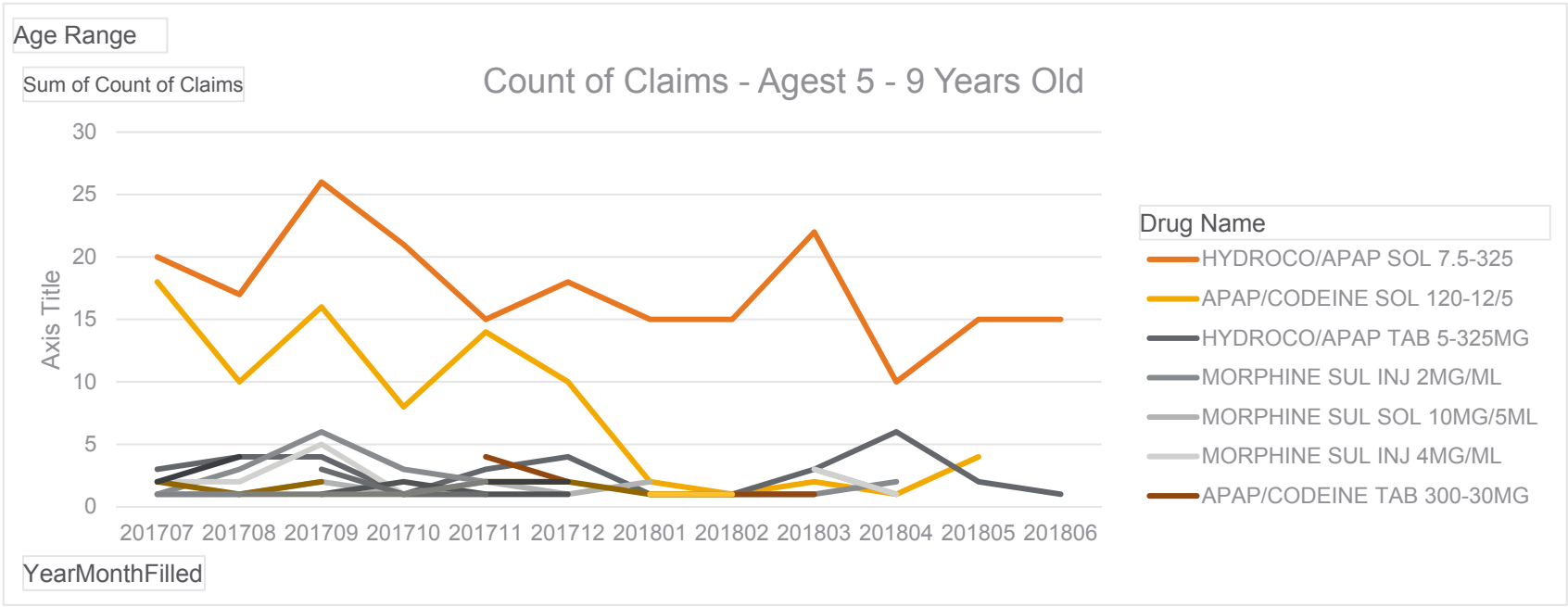
14
12
10
8
6
4
2
0
Axis Title
201708 201707 201711 201710 201709 201803 201804 201805 201802 201712 201801 201806
YearMonthFilled
Drug Name
HYDROCO/APAP SOL 7.5-325
APAP/CODEINE SOL 120-12/5
MORPHINE SUL INJ 4MG/ML
METHADONE SOL 5MG/5ML
OXYCODONE SOL 5MG/5ML
MORPHINE SUL INJ 2MG/ML


Age Range
Sum of Count of Claims
Count of Claims - Agest 5 - 9 Years Old
30
25
20
15
10
5
0
Axis Title
201707 201708 201709 201710 201711 201712 201801 201802 201803 201804 201805 201806
YearMonthFilled
Drug Name
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APAP/CODEINE SOL 120-12/5
HYDROCO/APAP TAB 5-325MG
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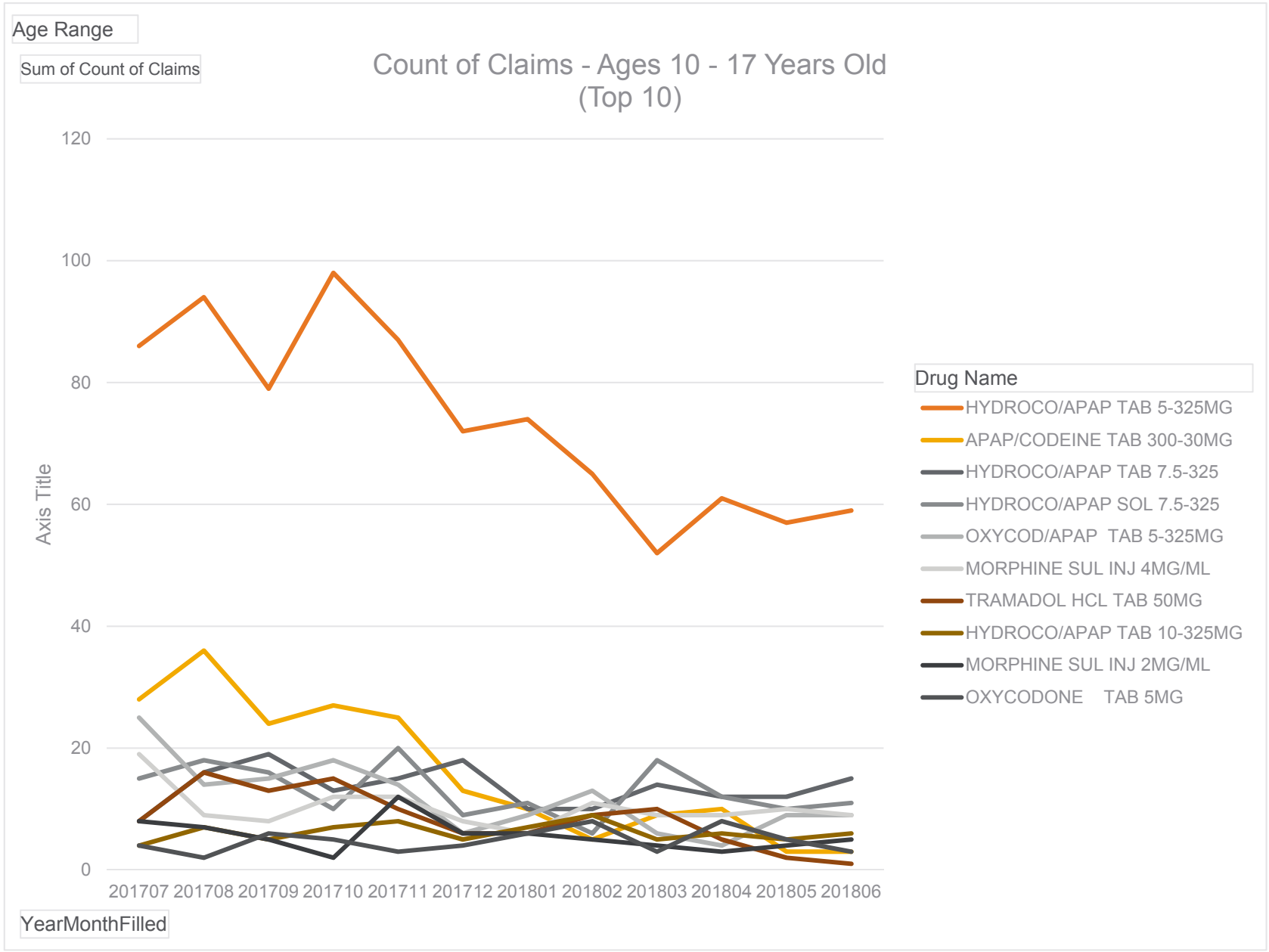
APAP/CODEINE TAB 300-30MG


Age Range
Sum of Count of Claims
Count of Claims - Ages 10 - 17 Years Old (Top 10)
120
100
80
60
40
20
0
Axis Title
201707 201708 201709 201710 201711 201712 201801 201802 201803 201804 201805 201806
YearMonthFilled
Drug Name
HYDROCO/APAP TAB 5-325MG
APAP/CODEINE TAB 300-30MG
HYDROCO/APAP TAB 7.5-325
HYDROCO/APAP SOL 7.5-325
OXYCOD/APAP TAB 5-325MG
MORPHINE SUL INJ 4MG/ML
TRAMADOL HCL TAB 50MG
HYDROCO/APAP TAB 10-325MG
MORPHINE SUL INJ 2MG/ML
OXYCODONE TAB 5MG

Opioid Use in Children Under 18

Fee for Service Medicaid
July 1, 2017 - June 30, 2018
Count of Members

	Age Range				
Drug Name	**< 1**	**1 - 4**	**5 - 9**	**10 - 17**	**Grand Total**
HYDROCO/APAP TAB 5-325MG		1	32	824	857
HYDROCO/APAP SOL 7.5-325	9	109	198	144	460
APAP/CODEINE TAB 300-30MG		1	11	187	199
APAP/CODEINE SOL 120-12/5		47	81	38	166
HYDROCO/APAP TAB 7.5-325			5	157	162
MORPHINE SUL INJ 4MG/ML	2	21	15	112	150
OXYCOD/APAP TAB 5-325MG		1	11	129	141
TRAMADOL HCL TAB 50MG			3	96	99
MORPHINE SUL INJ 2MG/ML	1	7	23	65	96
HYDROCO/APAP TAB 10-325MG	1			74	75
OXYCODONE TAB 5MG			2	52	54
HYDROMORPHON INJ 2MG/ML	1	4	1	41	47
OXYCODONE SOL 5MG/5ML	3	9	10	24	46
MORPHINE SUL INJ 10MG/ML		2	8	23	33
OXYCOD/APAP TAB 10-325MG			1	29	30
HYDROMORPHON INJ 1MG/ML		2		28	30
METHADONE SOL 5MG/5ML	16	9		4	29
MORPHINE SUL SOL 10MG/5ML	2	5	14	2	23
FENTANYL DIS 50MCG/HR				19	19
MORPHINE SUL TAB 15MG			1	15	16
HYDROMORPHON TAB 2MG				15	15
MEPERIDINE INJ 25MG/ML		1	2	11	14
MORPHINE SUL INJ 5MG/ML			3	11	14
LORTAB ELX 10-300MG		1	6	6	13
MEPERIDINE INJ 50MG/ML		1	1	11	13
OXYCOD/APAP TAB 7.5-325				11	11
FENTANYL DIS 100MCG/H				9	9
APAP/CODEINE TAB 300-60MG				8	8
TRAMADL/APAP TAB 37.5-325				7	7
FENTANYL DIS 25MCG/HR				6	6
DEMEROL INJ 25MG/ML		1		5	6
MORPHINE SUL TAB 15MG ER				6	6
MORPHINE SUL TAB 30MG ER				6	6
APAP/CODEINE TAB 300-15MG				5	5
DILAUDID INJ 1MG/ML				5	5
ULTIVA INJ 1MG		1	1	3	5
ALFENTANIL INJ 1000/2ML	1			4	5
OXYCODONE TAB 10MG				4	4
HYDROCO/APAP TAB 5-300MG				4	4
BUT/APAP/CAF CAP CODEINE				3	3
MORPHINE SUL SOL 20MG/5ML			1	2	3
MORPHINE SUL TAB 30MG				3	3
DURAMORPH INJ 1MG/ML	1			2	3

Drug Name	< 1	1 - 4	5 - 9	10 - 17	Grand Total
OXYCODONE CAP 5MG				2	2
MEPERIDINE SOL 50MG/5ML			2		2
METHADONE TAB 5MG				2	2
MORPHINE SUL CAP 30MG ER				2	2
ULTIVA INJ 5MG				1	1
MORPHINE SUL INJ 8MG/ML		1			1
OXYCOD/APAP TAB 2.5-325				1	1
NUCYNTA TAB 50MG				1	1
VICODIN ES TAB 7.5-300				1	1
DEMEROL INJ 100MG/ML				1	1
VICODIN TAB 5-300MG				1	1
METHADONE TAB 10MG				1	1
BUT/ASA/CAF/ CAP COD 30MG				1	1
DEMEROL INJ 25MG/0.5			1		1
ALFENTANIL INJ 500/ML				1	1
Grand Total	**37**	**224**	**433**	**2225**	**2919**

ANTHEM under 18 Opioid	3Q 2017	4Q 2017	1Q 2018	2Q 2018	TOTAL
ACETAMINOP-CODEINE 120-12 MG/5	115	82	26	7	230
ACETAMINOPHEN-COD #2 TABLET	2	1	2	1	6
ACETAMINOPHEN-COD #3 TABLET	77	81	25	20	203
ACETAMINOPHEN-COD #4 TABLET	3				3
BUTALB-CAFF-ACETAMINOPH-CODEIN		1			1
HYDROCODONE-ACETAMIN 10-325 MG	7	10	3	3	23
HYDROCODONE-ACETAMIN 2.5-325		1			1
HYDROCODONE-ACETAMIN 5-300 MG	1				1
HYDROCODONE-ACETAMIN 5-325 MG	227	230	108	74	639
HYDROCODONE-ACETAMIN 7.5-325	49	46	16	25	136
HYDROCODONE-ACETAMN 7.5-325/15	100	83	66	72	321
HYDROMORPHONE 2 MG TABLET	4	1	2	2	9
LORTAB 10 MG-300 MG/15 ML ELXR		1			1
MEPERIDINE 50 MG TABLET	1				1
METHADONE 10 MG/5 ML SOLUTION				1	1
METHADONE 5 MG/5 ML SOLUTION	1				1
METHADONE HCL 5 MG TABLET		1			1
MORPHINE SULF ER 15 MG TABLET				1	1
MORPHINE SULF ER 30 MG TABLET	1				1
MORPHINE SULFATE IR 15 MG TAB	4	1		1	6
OXYCODON-ACETAMINOPHEN 7.5-325	1	5	2	3	11
OXYCODONE HCL 10 MG TABLET		1			1
OXYCODONE HCL 15 MG TABLET			1		1
OXYCODONE HCL 5 MG TABLET	8	9	9	13	39
OXYCODONE HCL 5 MG/5 ML SOLN		2		1	3
OXYCODONE-ACETAMINOPHEN 10-325	7	7	4	3	21
OXYCODONE-ACETAMINOPHEN 5-325	37	26	24	15	102
TRAMADOL HCL 50 MG TABLET	19	15	4	1	39
TRAMADOL-ACETAMINOPHN 37.5-325	7	4	1	1	13
Grand Total	**671**	**608**	**293**	**244**	**1816**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioids Utilization for Members Under 18 Years Old

July 1, 2017 - June 30, 2018

Q3 2017				
Drug Name	Member Count (0-5 years)	Member Count (6-11 years)	Member Count (12-17 years)	Total
HYDROCO/APAP TAB 5-325MG	0	12	235	247
HYDROCO/APAP TAB 7.5-325	55	92	52	199
APAP/CODEINE SOL 120-12/5	45	92	31	168
APAP/CODEINE TAB 300-30MG	0	11	117	128
OXYCOD/APAP TAB 5-325MG	0	2	44	46
HYDROCO/APAP SOL 7.5-325	0	0	38	38
PROMETH/COD SYP 6.25-10	2	5	21	28
VIRTUSSIN AC SOL 100-10/5	0	7	15	22
TRAMADOL HCL TAB 50MG	0	1	15	16
GG/CODEINE SOL 100-10/5	0	4	11	15
HYDROCO/APAP TAB 10-325MG	0	0	11	11
PROMETH VC SOL PLAIN	0	3	7	10
OXYCODONE TAB 5MG	0	2	6	8
OXYCODONE SOL 5MG/5ML	3	3	1	7
CODEINE/GG SOL 10-100/5	0	1	2	3
METHADONE SOL 5MG/5ML	3	0	0	3
APAP/CODEINE TAB 300-15MG	0	2	0	2
BUT/APAP/CAF CAP CODEINE	0	0	2	2
CHERATUSSIN SYP 100-10/5	0	0	2	2
OXYCOD/APAP TAB 10-325MG	0	0	2	2
APAP/CODEINE TAB 300-60MG	0	0	1	1
HYDROMORPHON TAB 2MG	0	0	1	1
LORTAB ELX 10-300MG	0	1	0	1
METHADONE TAB 5MG	0	0	1	1
MORPHINE SUL SOL 10MG/5ML	0	1	0	1
MORPHINE SUL TAB 15MG	0	0	1	1
MORPHINE SUL TAB 15MG ER	0	0	1	1
OXYCOD/APAP TAB 7.5-325	0	0	1	1
ASCOMP/COD CAP 30MG	0	0	0	0
METHADONE TAB 10MG	0	0	0	0
OXYCODONE TAB 10MG	0	0	0	0
OXYCODONE TAB 15MG	0	0	0	0
PROMETH VC/ SYP CODEINE	0	0	0	0
TRAMADL/APAP TAB 37.5-325	0	0	0	0

Q4 2017				
Drug Name	Member Count (0-5 years)	Member Count (6-11 years)	Member Count (12-17 years)	Total
HYDROCO/APAP TAB 5-325MG	3	24	479	506
HYDROCO/APAP SOL 7.5-325	87	169	65	321
APAP/CODEINE SOL 120-12/5	60	147	63	270
APAP/CODEINE TAB 300-30MG	0	16	218	234
HYDROCO/APAP TAB 7.5-325	1	2	129	132
OXYCOD/APAP TAB 5-325MG	0	4	79	83
PROMETH/COD SYP 6.25-10	1	19	39	59
VIRTUSSIN AC SOL 100-10/5	2	16	38	56
TRAMADOL HCL TAB 50MG	0	6	49	55
GG/CODEINE SOL 100-10/5	3	13	25	41
PROMETH VC SOL PLAIN	0	11	19	30
OXYCODONE TAB 5MG	0	3	24	27
HYDROCO/APAP TAB 10-325MG	3	1	21	25
CHERATUSSIN SYP 100-10/5	1	4	8	13
OXYCODONE SOL 5MG/5ML	4	8	1	13
CODEINE/GG SOL 10-100/5	0	1	5	6
METHADONE SOL 5MG/5ML	5	0	0	5
APAP/CODEINE TAB 300-15MG	0	2	2	4
BUT/APAP/CAF CAP CODEINE	0	0	3	3
MORPHINE SUL TAB 15MG	0	0	3	3
OXYCOD/APAP TAB 7.5-325	0	1	2	3
APAP/CODEINE TAB 300-60MG	0	0	2	2
LORTAB ELX 10-300MG	0	2	0	2
OXYCOD/APAP TAB 10-325MG	0	0	2	2
ASCOMP/COD CAP 30MG	0	0	1	1
HYDROMORPHON TAB 2MG	0	0	1	1
METHADONE TAB 10MG	0	0	1	1
METHADONE TAB 5MG	0	0	1	1
MORPHINE SUL SOL 10MG/5ML	0	1	0	1
OXYCODONE TAB 10MG	0	0	1	1
OXYCODONE TAB 15MG	0	1	0	1
TRAMADL/APAP TAB 37.5-325	0	0	1	1
MORPHINE SUL TAB 15MG ER	0	0	0	0
PROMETH VC/ SYP CODEINE	0	0	0	0

Q1 2018				
Drug Name	Member Count (0-5 years)	Member Count (6-11 years)	Member Count (12-17 years)	Total
HYDROCO/APAP TAB 5-325MG	0	7	133	140
HYDROCO/APAP SOL 7.5-325	0	49	22	71
HYDROCO/APAP TAB 7.5-325	32	0	36	68
APAP/CODEINE TAB 300-30MG	0	9	51	60
APAP/CODEINE SOL 120-12/5	15	23	11	49
OXYCOD/APAP TAB 5-325MG	0	3	20	23
OXYCODONE TAB 5MG	0	1	15	16
PROMETH/COD SYP 6.25-10	0	5	8	13
TRAMADOL HCL TAB 50MG	0	0	12	12
VIRTUSSIN AC SOL 100-10/5	1	3	7	11
HYDROCO/APAP TAB 10-325MG	0	0	8	8
GG/CODEINE SOL 100-10/5	0	1	4	5
OXYCODONE SOL 5MG/5ML	2	1	1	4
MORPHINE SUL SOL 10MG/5ML	1	1	1	3
APAP/CODEINE TAB 300-15MG	0	0	2	2
METHADONE SOL 5MG/5ML	1	0	0	1
METHADONE TAB 10MG	0	0	1	1
OXYCOD/APAP TAB 10-325MG	0	0	1	1
OXYCOD/APAP TAB 7.5-325	0	0	1	1
PROMETH VC/ SYP CODEINE	0	0	1	1
APAP/CODEINE TAB 300-60MG	0	0	0	0
ASCOMP/COD CAP 30MG	0	0	0	0
BUT/APAP/CAF CAP CODEINE	0	0	0	0
CHERATUSSIN SYP 100-10/5	0	0	0	0
CODEINE/GG SOL 10-100/5	0	0	0	0
HYDROMORPHON TAB 2MG	0	0	0	0
LORTAB ELX 10-300MG	0	0	0	0
METHADONE TAB 5MG	0	0	0	0
MORPHINE SUL TAB 15MG	0	0	0	0
MORPHINE SUL TAB 15MG ER	0	0	0	0
OXYCODONE TAB 10MG	0	0	0	0
OXYCODONE TAB 15MG	0	0	0	0
PROMETH VC SOL PLAIN	0	0	0	0
TRAMADL/APAP TAB 37.5-325	0	0	0	0

Q2 2018				
Drug Name	Member Count (0-5 years)	Member Count (6-11 years)	Member Count (12-17 years)	Total
HYDROCO/APAP TAB 5-325MG	0	14	115	129
HYDROCO/APAP SOL 7.5-325	40	62	24	126
HYDROCO/APAP TAB 7.5-325	0	0	44	44
APAP/CODEINE TAB 300-30MG	0	3	35	38
OXYCOD/APAP TAB 5-325MG	0	3	28	31
APAP/CODEINE SOL 120-12/5	5	17	7	29
OXYCODONE TAB 5MG	0	0	18	18
TRAMADOL HCL TAB 50MG	0	0	13	13
HYDROCO/APAP TAB 10-325MG	0	0	4	4
OXYCODONE SOL 5MG/5ML	1	2	0	3
MORPHINE SUL TAB 15MG ER	0	0	2	2
VIRTUSSIN AC SOL 100-10/5	0	0	2	2
METHADONE SOL 5MG/5ML	1	0	0	1
MORPHINE SUL TAB 15MG	0	1	0	1
OXYCOD/APAP TAB 7.5-325	0	0	1	1
PROMETH VC/ SYP CODEINE	0	0	1	1
PROMETH/COD SYP 6.25-10	0	0	1	1
APAP/CODEINE TAB 300-15MG	0	0	0	0
APAP/CODEINE TAB 300-60MG	0	0	0	0
ASCOMP/COD CAP 30MG	0	0	0	0
BUT/APAP/CAF CAP CODEINE	0	0	0	0
CHERATUSSIN SYP 100-10/5	0	0	0	0
CODEINE/GG SOL 10-100/5	0	0	0	0
GG/CODEINE SOL 100-10/5	0	0	0	0
HYDROMORPHON TAB 2MG	0	0	0	0
LORTAB ELX 10-300MG	0	0	0	0
METHADONE TAB 10MG	0	0	0	0
METHADONE TAB 5MG	0	0	0	0
MORPHINE SUL SOL 10MG/5ML	0	0	0	0
OXYCOD/APAP TAB 10-325MG	0	0	0	0
OXYCODONE TAB 10MG	0	0	0	0
OXYCODONE TAB 15MG	0	0	0	0
PROMETH VC SOL PLAIN	0	0	0	0
TRAMADL/APAP TAB 37.5-325	0	0	0	0

Opioid Utilization for Members Under 18 Years Old
Q3 2017 - Q2 2018
SilverSummit Healthplan

Drug Name	Member Count (0-5 years)	Member Count (6-11 years)	Member Count (12-17 years)	Total
APAP/CODEINE SOL 120-12/5	11	15	2	28
APAP/CODEINE TAB 300-15MG			1	1
APAP/CODEINE TAB 300-30MG		3	23	26
HYDROCO/APAP SOL 7.5-325	15	7	9	31
HYDROCO/APAP TAB 10-325MG			3	3
HYDROCO/APAP TAB 5-300MG		1		1
HYDROCO/APAP TAB 5-325MG		5	68	73
HYDROCO/APAP TAB 7.5-325			16	16
OXYCOD/APAP TAB 10-325MG			3	3
OXYCOD/APAP TAB 5-325MG			8	8
OXYCOD/APAP TAB 7.5-325			3	3
OXYCODONE SOL 5MG/5ML	4	2		6
OXYCODONE TAB 5MG		1	5	6
TRAMADL/APAP TAB 37.5-325			1	1
TRAMADOL HCL TAB 50MG			3	3

Z. Opioids

Therapeutic Class: Opioids
Last Reviewed by the DUR Board: October 27, 2016

Opioids are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the SSA and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

a. Opioids will be covered without Prior Authorization (PA):

1. For initial prescriptions of seven days or less; and

2. For a total of 13 seven-day prescriptions in any rolling 12 month period; and

3. For prescriptions of 60 mg morphine equivalents or less per day.

b. Recipients currently on chronic opioid medications will not be subject to the seven-day requirement for an opioid(s) they have been receiving in the past 45 days.

c. Prior Authorization Criteria: To exceed the number of seven-day prescriptions, or to exceed the seven-day limit, or to exceed the 60 mg morphine equivalents or less per day:

1. All of the following criteria must be met and documented:

a. The recipient has chronic pain or requires an extended opioid therapy and is under the supervision of a licensed prescriber; and

b. Pain cannot be controlled through the use of non-opioid therapy (acetaminophen, NSAIDs, antidepressants, anti-seizure medications, physical therapy, etc.); and

c. The lowest effective dose is being requested; and

d. A pain contract is on file.

d. Exceptions to this policy:

1. Recipients with cancer/malignancy related pain; or

2. Recipients who are post-surgery with an anticipated prolonged recovery (greater than three months); or

3. Recipients receiving palliative care; or

4. Recipients residing in a long-term care facility; or

5. Recipients receiving treatment for HIV/AIDS; or

6. Prescriptions written by or in consultation with a pain specialist.

2. Prior Authorization Guidelines

a. Prior Authorization approval will be for one year.

b. Prior Authorization forms are available at: http://www.medicaid.nv.gov/providers/rx/rxforms.aspx

3. CDC Guidance:

a. http://www.cdc.gov/drugoverdose/prescribing/guideline.html.

TTT. Codeine and Tramadol for Children

Therapeutic Class: Opioid Analgesic
Last Reviewed by the DUR Board: October 19, 2017

Codeine, codeine with acetaminophen and tramadol, tramadol with acetaminophen are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the SSA and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

A. Codeine, codeine with acetaminophen

1. All of the following criteria must be met:

a. The recipient must be 12 years of age or older; and

b. The lowest effective dose for the shortest period of time is being requested; and

c. The recipient must not be obese (BMI > 30 kg/m²), have obstructive sleep apnea, or severe lung disease; and

d. The recipient is not being prescribed the drug for post-surgical pain following a tonsillectomy and/or adenoidectomy.

B. Tramadol, tramadol with acetaminophen

1. All of the following criteria must be met:

a. The recipient must be 12 years of age or older; and

b. The lowest effective dose for the shortest period of time is being requested; and

c. The recipient must not be obese (BMI > 30 kg/m²), have obstructive sleep apnea, or severe lung disease; and

d. The recipient is not being prescribed the drug for post-surgical pain following a tonsillectomy and/or adenoidectomy; and

e. The prescribed dose does not exceed 200mg/day and does not exceed a five day supply.

2. Tramadol Extended Release (ER) will not be approved for children under

18 years of age and will reject at point of sale.

C. Prior Authorization Guidelines

1. Codeine, codeine with acetaminophen

a. Prior authorization approval will be given for the lowest effective dose for the shortest period of time requested.

1. Prior authorization will be given for a one month time period.

2. Prior authorization forms are available at: http://www.medicaid.nv.gov/providers/rx/rxforms.aspx

2. Tramadol, tramadol with acetaminophen

a. Prior authorization approval will be given for the lowest effective dose for the shortest period of time requested.

b. Prior authorization will be given for a one month time period.

c. Prior authorization forms are available at: http://www.medicaid.nv.gov/providers/rx/rxforms.aspx

Nevada Medicaid
CGRP Inhibitor Products
Pharmacy Coverage Guideline

CRITERIA FOR COVERAGE/NONCOVERAGE

Indications
Migraine Indicated for the preventive treatment of migraine in adults

Approval Length: 6 months

The requested medication must meet the following criteria:

Episodic Migraines

1. Diagnosis of episodic migraines
   AND
2. Patient is 18 years of age or older
   AND
3. Patient has 4 to 14 migraine days per month, but no more than 14 headache days per month
   AND
4. Prescribed by or in consultation with one of the following specialists:
   a. Neurologist
   b. Pain specialist
   AND
5. One of the following:
   a. History of failure (after at least a two month trial) or intolerance to Elavil (amitriptyline) or Effexor (venlafaxine)
   OR
   b. Patient has a contraindication to both Elavil (amitriptyline) and Effexor (venlafaxine)
   AND
6. One of the following:
   a. History of failure (after at least a two month trial) or intolerance to Depakote/Depakote ER (divalproex sodium) or Topamax (topiramate)
   OR
   b. Patient has a contraindication to both Depakote/Depakote ER (divalproex sodium) and Topamax (topiramate)
   AND

7. One of the following:
    a. History of failure (after at least a two month trial) or intolerance to one of the following beta blockers: atenolol, propranolol, nadolol, timolol, or metoprolol

    OR

    b. Patient has a contraindication to all of the following beta blockers: atenolol, propranolol, nadolol, timolol, or metoprolol

    AND
8. Medication will not be used in combination with another CGRP inhibitor

Chronic Migraines

1 Diagnosis of chronic migraines

AND

2 Patient has been evaluated for medication overuse headache (MOH) and if MOH diagnosed, treatment will include a plan to taper off the offending medication

AND

3 Patient is 18 years of age or older

AND

4 Patient has greater than or equal to 15 headache days per month, of which at least 8 must be migraine days for at least 3 months

AND

5 Prescribed by or in consultation with one of the following specialists:

- Neurologist
- Pain specialist

AND

6 One of the following:

a. History of failure (after at least a two month trial) or intolerance to Elavil (amitriptyline) or Effexor (venlafaxine)

OR

b. Patient has a contraindication to both Elavil (amitriptyline) and Effexor (venlafaxine)

AND

7 One of the following:

a. History of failure (after at least a two month trial) or intolerance to Depakote/Depakote ER (divalproex sodium) or Topamax (topiramate)

OR

b. Patient has a contraindication to both Depakote/Depakote ER (divalproex sodium) and Topamax (topiramate)

AND

8. One of the following:

a. History of failure (after at least a two month trial) or intolerance to one of the following beta blockers: atenolol, propranolol, nadolol, timolol, or metoprolol

OR

b. Patient has a contraindication to all of the following beta blockers: atenolol, propranolol, nadolol, timolol, or metoprolol

AND

9. Medication will not be used in combination with another CGRP inhibitor

AND

10 Medication will not be used in combination with Botox (onabotulinumtoxinA)

Reauthorization:

Approval Length: 12 months

Chronic Migraines and Episodic Migraines:

1. Patient has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity

AND

2. Use of acute migraine medications (e.g., NSAIDs, triptans) has decreased since the start of CGRP therapy

AND

3. Prescribed by or in consultation with one of the following specialists:

- Neurologist
- Pain specialist

Anthem Aimovig (erenumab)

Override(s)	Approval Duration
Prior Authorization	Initial request: 3 months Renewal requests: 1 year

Medications	Quantity Limit
Aimovig (erenumab)	May be subject to quantity limit

APPROVAL CRITERIA

Initial requests for Aimovig (erenumab) may be approved when the following criteria are met:

I. Individual has a diagnosis of one of the following:
   A. Episodic migraine defined as at least 4 and fewer than 15 migraine days per month and fewer than 15 headache days per month on average during the previous 3 month period; **OR**
   B. Chronic migraine defined as a headache occurring on 15 or more days per month for more than 3 months, which, on at least 8 days per month, has features of a migraine headache (ICHD-3 beta);

AND

II. Individual is using for prophylaxis of migraine headaches at a frequency of 4 or more migraine days per month;

AND

III. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) of and inadequate response or intolerance to two agents for migraine prophylaxis* (at least one agent in any two of the following classes) or has a contraindication to all of the following medications (AAN/AHA 2012/2015, Level A and B evidence; ICSI 2013, high quality evidence):
   A. The following antidepressants: amitriptyline, venlafaxine; **OR**
   B. One of the following beta blockers: Metoprolol, propranolol, timolol (oral), nadolol, atenolol, nebivolol; **OR**
   C. The following calcium channel blocker: verapamil; **OR**
   D. One of the following antiepileptic agents: valproate sodium, divalproex sodium, topiramate, gabapentin; **OR**
   E. Botox (for chronic migraine).

*Agents for migraine prophylaxis – May require Prior Authorization

Renewal requests for Aimovig (erenumab) may be approved when the following criteria are met:

I. Individual has a reduction in the overall number of migraine days or reduction in number of severe migraine days per month; **AND**
II. Individual has obtained clinical benefit deemed significant by individual or prescriber.

State Specific Mandates		
State name N/A	Date effective N/A	Mandate details (including specific bill if applicable) N/A

Key References:

Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2018. URL: http://www.clinicalpharmacology.com. Updated periodically.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed January 3, 2018.

DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.

UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for CGRP

Program	Prior Authorization
Medication	Aimovig (erenumab), fremanezumab, galcanezumab
Markets in Scope	Arizona, California, Florida- CHIP, Hawaii, Maryland, New Jersey, New Mexico, Nevada, New York, New York EPP, Ohio, Rhode Island
Issue Date	3/2018
Pharmacy and Therapeutics Approval Date	3/2018
Effective Date	5/2018

1. Background:

Pending

2. Coverage Criteria:

A. <u>Episodic Migraine</u>

1. <u>Initial Therapy</u>

a. **CGRP** will be approved based upon **<u>all</u>** of the following criteria:

(1) Diagnosis of episodic migraines with **<u>both</u>** of the following:

(a) Less than 15 headache days per month
(b) Patient has 4 to 14 migraine days per month

-AND-

(2) Prescribed by or in consultation with one of the following specialists:

(a) Neurologist
(b) Pain Specialist

-AND-

(3) History of failure (after a trial of at least two months), contraindication, or intolerance to **<u>two</u>** of the following prophylactic therapies from the list below:

(a) amitriptyline (Elavil)
(b) One of the following beta-blockers: atenolol (Tenormin), metoprolol (Lopressor/Toprol XL), nadolol (Corgard), propranolol (Inderal), or timolol (Blocadren)
(c) divalproex sodium (Depakote/Depakote ER)
(d) topiramate (Topamax)
(e) venlafaxine (Effexor)

Authorization will be issued for 3 months.

2. Reauthorization

a. **CGRP** will be approved based on **both** of the following criteria:

(1) Prescribed by or in consultation with one of the following specialists:

(a) Neurologist
(b) Pain Specialist

-AND-

(2) Patient has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity

Authorization will be issued for 12 months.

B. Chronic Migraine

1. Initial Therapy

a. **CGRP** will be approved based upon **all** of the following criteria:

(1) Diagnosis of chronic migraines with **both** of the following:

(a) Greater than or equal to 15 headache days per month
(b) Greater than or equal to 8 migraine days per month

-AND-

(2) Prescribed by or in consultation with one of the following specialists:

(a) Neurologist
(b) Pain Specialist

-AND-

(3) History of failure (after a trial of at least two months), contraindication, or intolerance to **two** of the following prophylactic therapies from the list below:

(a) amitriptyline (Elavil)
(b) One of the following beta-blockers: atenolol (Tenormin), metoprolol (Lopressor/Toprol XL), nadolol (Corgard), propranolol (Inderal), or timolol (Blocadren)
(c) divalproex sodium (Depakote/Depakote ER)
(d) topiramate (Topamax)
(e) venlafaxine (Effexor)
(f) Botox (Onabotulinumtoxin A)

Authorization will be issued for 3 months.

2. Reauthorization

a. **CGRP** will be approved based on **both** of the following criteria:

(1) Prescribed by or in consultation with one of the following specialists:

(a) Neurologist
(b) Pain Specialist

-AND-

(2) Patient has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity

Authorization will be issued for 12 months.

3. References:

1. International Headache Society (IHS); Headache Classification Committee. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013; 33: 629-808.
2. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012 Apr 24;78(17):1337-45.

3. Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016 May 10;86(19):1818-26.

Program	Prior Authorization
Change Control	
Date	Change
3/2018	New Program

Clinical Policy: Erenumab-aaoe (Aimovig)

Reference Number: CP.PHAR.128
Effective Date: 07.10.18
Last Review Date: 08.18
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Erenumab-aaoe (Aimovig™) is a calcitonin gene-related peptide (CGRP) receptor antagonist.

FDA Approved Indication(s)

Aimovig is indicated for the preventive treatment of migraine in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Aimovig is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Migraine Prophylaxis (must meet all)**:**

1. Diagnosis of episodic or chronic migraine;
2. Member experiences ≥ 4 migraine days per month for at least 3 months;
3. Prescribed by or in consultation with a neurologist, headache, or pain specialist;
4. Age ≥ 18 years;
5. Failure of an 8-week trial of at least 2 of the following oral migraine preventative therapies, each from different therapeutic classes, unless contraindicated or clinically significant adverse effects are experienced: antiepileptic drugs (e.g., divalproex sodium, sodium valproate, topiramate), beta-blockers (e.g., metoprolol, propranolol, timolol), antidepressants (e.g., amitriptyline, venlafaxine);
6. Dose does not exceed one of the following (a or b):
   a. 70 mg (1 injection) once monthly;
   b. 140 mg (2 injections) once monthly if medical justification is provided.

Approval duration: 3 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Migraine Prophylaxis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by a reduction in migraine days per month from baseline;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. 70 mg (1 injection) once monthly;
   b. 140 mg (2 injections) once monthly if medical justification is provided.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
CGRP: calcitonin gene-related peptide

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Anticonvulsants such as: divalproex (Depakote®), topiramate (Topamax®)	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*
Beta-blockers such as: propranolol (Inderal®), metoprolol (Lopressor®)*, timolol	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*
Antidepressants/tricyclic antidepressants* such as: amitriptyline (Elavil®), venlafaxine (Effexor®)	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label use*

Appendix C: Contraindications
Not applicable

Appendix D: General Information
- In clinical trials, a migraine day was defined as any calendar day in which the patient experiences a qualified migraine headache (onset, continuation, or recurrence of the migraine headache). A qualified migraine headache is defined as a migraine with or without aura, lasting for ≥ 30 minutes, and meeting at least one of the following criteria (a and/or b):
  a) ≥ 2 of the following pain features: unilateral, throbbing, moderate to severe, exacerbated with exercise/physical activity;
  b) ≥ 1 of the following associated symptoms: nausea and/or vomiting, photophobia, and phonophobia.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Migraine prophylaxis	70 mg SC once monthly Some patients may benefit from a dosage of 140 mg injected subcutaneously once monthly, which is administered as two consecutive subcutaneous injections of 70 mg each	140 mg/month

VI. Product Availability
Single-dose prefilled SureClick® autoinjector or prefilled syringe: 70 mg/mL

VII. References
1. Aimovig Prescribing Information. Thousand Oaks, CA: Amgen Inc.; May 2018. Available at: www.aimovig.com. Accessed June 6, 2018.
2. Silberstein SD, Holland S, Freitag F, et al. American Academy of Neurology: Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. Neurology 2012; 78: 1337-45.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.10.18	08.18

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Calcitonin Gene-Related Peptide (CGRP) Receptor Antogonists

Fee for Service Medicaid

July 1, 2017 - June 30, 2018

Year Month Filled	Drug Name		Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
201806	AIMOVIG	INJ 70MG/ML	1	1	28	1	$ 585.17

Anthem CGRP Inhibitors (only 1 claim found under Pharmacy Benefit in time period)

Quarter Serviced	DOS	Patient Age	Drug Label	Prescriber Type
2nd Quarter 2018	6/28/2018	31	AIMOVIG 70 MG/ML AUTOINJECTOR	NP

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

CGRP Inhibitors (Aimovig) Utilization

April 1, 2018 - September 30, 2018

Q2 2018				
Drug Name	**Count of Members**	**Count of Claims**	**Sum of Days Supply**	**Sum of Qty**
AIMOVIG INJ 70MG/ML	1	1	1	1

Therapeutic Class Overview
Calcitonin gene related peptide (CGRP) inhibitors

INTRODUCTION

- Migraine is a common, recurrent, incapacitating disorder characterized by moderate to severe headaches and disabling features, including nausea, vomiting, neurologic symptoms, photophobia, and phonophobia (*International Headache Society [IHS] 2013, Starling et al 2015).*
- There are 4 phases of a migraine attack, although not all migraine attacks unfold into all 4 phases. These phases include prodrome, development of aura, the headache phase, and postdrome. Combined, all 4 phases can last anywhere between 3 and 5 days (*Burgos−Vega et al 2015).*
- The pathophysiology of migraines is assumed to involve the activation of trigeminal sensory nerves, which triggers the release of vasoactive neuropeptides including CGRP, neurokinin A, and substance P. CGRP is involved in migraine pathophysiology through nociceptive mechanisms in the trigeminovascular system. CGRP is a vasodilator and is found at higher concentrations during a migraine attack. Vasodilation of dural blood vessels may occur with extravasation of dural plasma, resulting in inflammation *(Goadsby et al 2017, Starling et al 2015, Silberstein et al 2012)*.
- The International Classification of Headache Disorders (ICHD) defines chronic migraine as ≥ 15 headache days per month for > 3 months with the features of migraine headache for at least 8 migraine days per month (MMD). The most common cause of symptoms suggestive of chronic migraine is medication overuse. According to the ICHD, around 50% of patients apparently with chronic migraine revert to an episodic migraine type after drug withdrawal; such patients are in a sense wrongly diagnosed with chronic migraine. In most clinical trials, migraine that is not chronic (ie, with < 15 headache days per month) is considered to be episodic migraine, although the condition is not clearly defined in the ICHD (*IHS 2013, Silberstein et al 2008, Starling et al 2015*).
- Migraines have a global prevalence of 15 to 18% and are a leading cause of disability worldwide. Chronic migraine is estimated to occur in 2 to 8% of patients with migraine, whereas episodic migraine occurs in more than 90% of patients (*Global Burden of Disease Study [GBD] 2016, IHS 2013, Lipton et al 2016, Manack et al 2011*).
- Treatments for migraines are divided into acute and preventive therapies. Evidence and reputable guidelines clearly delineate appropriate therapies for episodic migraine treatment and prophylaxis; options stretch across a wide variety of therapeutic classes and are usually oral therapies. For the prevention of migraines, treatment options include oral prophylactic therapies, injectable prophylactic therapies, and neuromodulator devices. Guidelines discourage the overuse of acute headache therapies, including analgesics, triptans, and ergots, which can precipitate medication overuse headache. Additionally, opioids and barbiturates should not be prescribed as they may contribute to the development of chronic daily headache (*American Migraine Foundation [AMF] 2017, Edvinsson et al 2017, IHS 2013, Silberstein et al 2008, Silberstein et al 2012, Simpson et al 2016, Starling et al 2015)*.
  - Oral prophylactic therapies have modest efficacy (with reduction estimates of 1.5 headaches/month to standard mean differences of −0.57 from baseline [*Jackson et al 2015*]); however, certain oral therapies may not be appropriate for individual patients due to intolerability or eventual lack of efficacy.
  - Onabotulinumtoxin A (Botox), the first injectable drug approved for the prophylaxis of chronic migraine, has been found to be ineffective for the prophylactic treatment of episodic migraines.
  - Other options include devices which leverage electrical, temperature−altering, or magnetic approaches to treatment (ie, Cefaly, SpringTMS, and gammaCore); these devices are considered to have no significant adverse events known or expected.
- Aimovig (erenumab−aooe) is a first−in−class CGRP inhibitor. Other CGRP inhibitors under clinical development include:
  - Fremanezumab (administered subcutaneously [SC] monthly or quarterly) and galcanezumab (administered SC monthly), which are anticipated to be FDA−approved in September 2018 (*BioPharmCatalyst 2018, Eli Lilly press release 2018, House 2018, Teva press release 2018*).
  - Eptinezumab (administered intravenously) and atogepant (the first oral CGRP inhibitor), which are anticipated to pursue the indication for prevention of migraines with potential 2019 FDA−approval dates (*Alder press release 2018, Allergan press release 2018*).
- Medispan class: Migraine products – monoclonal antibodies; Calcitonin gene−related peptide (CGRP) receptor antagonists

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Aimovig (erenumab−aooe)	–

(*Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Aimovig (erenumab−aooe)
Prevention treatment of migraine in adults	✔

(*Aimovig prescribing information 2018)*

- Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

- The approval of erenumab−aooe was based on 4 pivotal trials in approximately 2500 patients with episodic or chronic migraine subtypes and 2 incomplete, open−label extension (OLE) trials with data from interim analyses in published and unpublished formats.
  - The episodic migraine program included 3 trials in 1778 episodic migraine patients. All patients had a history of 4 to 14 MMD:
    - The STRIVE trial was a 6−month, double−blind (DB), placebo−controlled (PC), multi−center (MC), Phase 3 trial in which 955 patients with episodic migraine were randomized to placebo (n = 319), erenumab−aooe 70 mg (n = 317), or erenumab−aooe 140 mg (n = 319) once monthly. A total of 2.5 to 3.1% of patients had current use of add−on preventive therapy during the trial. Patients with medication overuse were not permitted. The primary endpoint was the change in mean MMD from baseline to months 4 to 6, which favored treatment with erenumab−aooe 70 mg (mean change vs placebo, −1.4; 95% confidence interval [CI], −1.9 to −0.9; $p < 0.001$) and erenumab−aooe 140 mg (mean change vs placebo, −1.9; 95% CI, −2.3 to −1.4; $p < 0.001$). Erenumab−aooe significantly increased the proportion of patients achieving ≥ 50% reduction in MMD (difference for 70 mg vs placebo, 16.7%; odds ratio [OR], 2.13; difference for 140 mg vs placebo, 23.4%; OR, 2.81). Erenumab−aooe was also associated with a significant decrease in the mean monthly acute migraine−specific medication treatment days (difference for 70 mg vs placebo, −0.9; difference for 140 mg vs placebo, −1.4) (*Goadsby et al 2017*).
    - The ARISE trial was a 12−week, DB, PC, MC, Phase 3 trial in which 577 patients with episodic migraine were randomized to placebo (n = 291) or erenumab−aooe 70 mg (n = 286) once monthly. A total of 5.5 to 6.6% of patients had current use of add−on preventive therapy during the trial. Patients with medication overuse were not permitted. The primary endpoint was the change in MMD from baseline to weeks 9 to 12, which favored treatment with erenumab−aooe 70 mg (mean change vs placebo, −1.0; 95% CI, −1.6 to −0.5; $p < 0.001$). Compared to placebo, erenumab−aooe significantly increased the proportion of patients achieving ≥ 50% reduction in MMD (difference, 10.2%; OR, 1.59). Erenumab−aooe was also associated with a significant decrease in the mean monthly acute migraine−specific medication treatment days (difference, −0.6) (*Dodick et al 2018*).
    - The LIBERTY trial was a currently unpublished, 12−week, DB, PC, MC, Phase 3b trial in which 246 patients with episodic migraine who failed 2 to 4 prior preventive migraine treatments were randomized to placebo (n = 125) or erenumab−aooe 70 mg (n = 121) once monthly. Erenumab−aooe significantly increased the primary endpoint, the proportion of patients with ≥ 50% reduction in MMD from baseline to the last 4 weeks of DB treatment (weeks 9 to 12) over placebo (difference, 16.6%; OR, 2.73; 95% CI, 1.43 to 5.19; $p = 0.002$). Compared to placebo, a total of 5.9% more patients treated with erenumab−aooe 140 mg reported a 100% reduction in MMD, or migraine cessation. Erenumab 70 mg/month compared with placebo significantly reduced the MMD (difference, −1.61; 95% CI, −2.70 to −0.52; $p = 0.004$). Erenumab−aooe was also associated with a significant decrease in the mean monthly acute migraine−specific medication treatment days (difference, −1.73) (*Reuter et al 2018*).

- The chronic migraine program included 1 trial in 667 chronic migraine patients. All patients had a history of ≥ 15 MMD (baseline average, 17.8 to 18.2):
  - *Tepper et al* was a 12−week, DB, PC, MC, Phase 2 trial in which 667 patients with chronic migraine were randomized to placebo (n = 286), erenumab−aooe 70 mg (n = 191), or erenumab−aooe 140 mg (n = 190) once monthly. No patients were allowed current use of add−on preventive therapy during the trial. Patients with medication overuse were permitted to participate. The primary endpoint was the change in MMD from baseline to weeks 9 to 12, which favored treatment with erenumab−aooe 70 mg and erenumab−aooe 140 mg (mean change for both doses vs placebo, −2.5; 95% CI, −3.5 to −1.4; p < 0.0001). Erenumab−aooe significantly increased the proportion of patients achieving ≥ 50% reduction in MMD (difference for 70 mg vs placebo, 17%; OR, 2.2; difference for 140 mg vs placebo, 18%; OR, 2.3). Of note, these outcomes were not dose−dependent. Both erenumab−aooe 70 mg (difference, −1.9) and erenumab−aooe 140 mg (difference, −2.6) significantly reduced the mean acute migraine−specific medication days; however, the higher 140 mg dose had a greater reduction numerically over placebo and reductions may be dose−dependent (*Tepper et al 2017*).
- Two 5−year OLE trials are currently underway in patients with episodic and chronic migraine:
  - Episodic migraine patients from a 12−week, DB, PC parent study continued within an OLE study and received erenumab−aooe 70 mg monthly up to 5 years, of which an interim analysis of data was published with data at 1 year. Of 472 patients in the parent study, 383 (81.1%) remained in the OLE and 307 (80.2%) completed 1 year of treatment. Patients had 8.8 MMDs at parent study baseline. After 3 months of treatment in the parent study, the number of MMDs was reduced to 6.3 days (mean change, 2.5). After a total of 16 months of treatment, the number of MMDs was reduced to 3.7 days (mean change, 5.1). After 64 weeks, a total of 65% (n = 184) of episodic migraine patients achieved a ≥ 50% reduction in MMD and 26% (n = 73) had achieved a 100% reduction in MMDs or migraine−free status (*Ashina et al 2017*).
  - Caution should be exercised in interpreting results from extension trials. The open−label design may contribute to biased reports. Extension trials may have biased outcomes because those experiencing benefit are included in extension trials; however, results are useful for reporting trends in treatment.

CLINICAL GUIDELINES

- According to the American Academy of Neurology and American Headache Society (AAN/AHS) − Evidence−based guideline update on the pharmacologic treatment for episodic migraine prevention in adults (*Silberstein et al 2012*), the following medications are effective preventive treatment options (see Appendix A for a definition of classifications):
  - Level A (established efficacy and > 2 Class I trials):
    - Antiepileptic drugs: divalproex sodium, sodium valproate, and topiramate
    - Beta blockers: metoprolol, propranolol, and timolol
    - Triptans (for menstrual related migraine [MRM]): for short−term prophylaxis, frovatriptan
  - Level B (probably effective and 1 Class I or 2 Class II trials):
    - Antidepressants: amitriptyline and venlafaxine
    - Beta blockers: atenolol and nadolol
    - Triptans (for MRM): for short−term prophylaxis, naratriptan and zolmitriptan
  - Level C (possibly effective and 1 Class II trial):
    - Angiotensin−converting enzyme (ACE) inhibitors: lisinopril
    - Angiotensin II receptor blockers (ARBs): candesartan
    - Alpha agonists: clonidine and guanfacine
    - Antiepileptic drugs: carbamazepine
    - Beta blockers: nebivolol and pindolol
    - Antihistamines: cyproheptadine
- The AAN recommends onabotulinumtoxin A as an effective treatment option that should be offered for chronic migraine. However, onabotulinumtoxin A is considered ineffective for the treatment of episodic migraines and should not be offered. There is insufficient evidence to compare the effectiveness of botulinum neurotoxin A with that of oral prophylactic topiramate (*Simpson et al 2016*).

SAFETY SUMMARY

- There are no contraindications or warnings and precautions associated with erenumab−aooe.

- The most common adverse reactions (% difference from placebo) observed in erenumab−aooe studies included injection site reactions (erenumab−aooe 70 mg, 3%; erenumab−aooe 140 mg, 2%) and constipation (erenumab−aooe 70 mg, 0%; erenumab−aooe 140 mg, 2%).
  - Across studies, adverse effects were generally mild and/or similar to placebo with 1.3% of patients treated with erenumab−aooe discontinuing treatment due to adverse events during trials.
- CGRP is a vasodilator and is found at higher concentrations during a migraine attack. The long−term implications of prolonged CGRP inhibition are not fully established and safety has not been fully characterized for erenumab−aooe.
  - In the 1−year interim analysis of the OLE study, 2 patients had severe adverse events (an arteriosclerosis event and a myocardial ischemia event), of which 1 was fatal and 1 was confounded by sumatriptan administration (*Ashina et al 2017*).
- There are no adequate data on the risks associated in patients who are pregnant, nursing, or in adolescent or pediatric populations. Caution should be exercised in these populations.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Aimovig (erenumab−aooe)	Injection	SC	Once monthly	May be self−administered by patients in the abdomen, thigh, or upper arm. Latex−sensitive patients may have an allergic reaction to the needle shield within the white cap and the gray needle cap of the syringe. There are no data in pregnant women or breastfed infants. A benefit/risk assessment should be taken into consideration prior to administering.

See the current prescribing information for full details

CONCLUSION

- Migraine is a common, recurrent, incapacitating disorder characterized by moderate to severe headaches and disabling features, including nausea, vomiting, neurologic symptoms, photophobia, and phonophobia. Migraines have a spectrum of frequency and severity that can significantly affect the quality of life of patients (*IHS 2013, Silberstein et al 2008, Starling et al 2015*).
- Guidelines have not been updated to include the CGRP inhibitors. Current evidence−based prophylactic treatment options and guidance are limited for chronic migraine, and oral prophylactic medications prescribed for episodic migraine are often used also for the preventive treatment of chronic migraine. Prophylactic migraine treatment options include oral agents (mainly anti−seizure agents, antidepressants, and beta blockers), injectable agents (onabotulinumtoxin A for chronic subtypes only), or neuromodulation devices for migraine or headache attacks (ie, Cefaly, Spring TMS, gammaCore). There is no optimal prophylactic migraine therapy and head−to−head trials are lacking (*AMF 2017, Silberstein et al 2012, Simpson et al 2016*).
- Erenumab−aooe is a first−in−class CGRP inhibitor with limited long−term data. Compared to placebo, erenumab−aooe has consistently demonstrated modest, but statistically significant, reductions in MMDs ranging from 1 to 2.5 days after 3 to 6 months of treatment. Overall, the odds for a 50% reduction in MMDs were approximately 2 times higher with erenumab−aooe than placebo. There are no head−to−head studies with erenumab−aooe and no prophylactic migraine agent is clearly superior to others (*Ashina et al 2017, Dodick et al 2018, Goadsby et al 2017, Reuter et al 2018, Tepper et al 20117*).

- CGRP is a vasodilator and is found at higher concentrations during a migraine attack. The long−term implications of prolonged CGRP inhibition are not fully established and safety has not been fully characterized for erenumab−aooe *(Ashina et al 2017, Goadsby et al 2017, Starling et al 2015).*
- Lack of information during pregnancy and breastfeeding is a consideration as many migraine patients are women of childbearing potential. The unknown risks of monoclonal antibodies and the effects on certain vascular conditions are not fully characterized. Important co−morbid populations which suffer migraines were excluded from trials (eg, patients with anxiety, depression, hypertension, or fibromyalgia), which also limits the generalizability to broader groups. Based on current data, the safety profile of erenumab−aooe is generally mild with the most common adverse effects observed being constipation and injection site reactions.
- Overall, erenumab−aooe represents another therapy option in the prevention of episodic or chronic migraines. Based on currently available evidence and the mild safety profile of erenumab−aooe, this product may have a role in a subset of patients unable to tolerate established oral prophylactic therapies.

APPENDIX

- **Appendix A. AAN levels of evidence classification** *(Gronseth et al 2011)*

Rating of recommendation	
A	Established as effective, ineffective, or harmful for the given condition in the specified population
B	Probably effective, ineffective, or harmful for the given condition in the specified population
C	Possibly effective, ineffective, or harmful for the given condition in the specified population
U	Data inadequate or conflicting; given current knowledge, treatment is unproven.
Rating of therapeutic article	
Class I	RCT in representative population with masked outcome assessment. The following are required: a) concealed allocation; b) primary outcome(s) is/are clearly defined; c) exclusion/inclusion criteria are clearly defined; d) adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias; e) certain requirements are needed for noninferiority or equivalence trials claiming to prove efficacy for 1 or both drugs.
Class II	Cohort study that meets a–e (Class I) or RCT that lacks 1 criterion from above (b−e).
Class III	Controlled trials (including well−defined natural history controls or patients serving as own controls), a description of major confounding differences between groups, and where outcome assessment is independent of patient treatment.
Class IV	Does not include patients with the disease, different interventions, undefined/unaccepted interventions or outcomes measures, and/or no measures of effectiveness or statistical precision presented or calculable.

REFERENCES

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Publication Date: August 7, 2018

Prior Authorizations Over $10,000

Fee for Service Medicaid

Aug 6, 2018 - Oct 3, 2018

		Final PA Status		
AHFS Description	**Drug Name**	**Approved**	**Rejected**	**Grand Total**
ALPHA- AND BETA-ADRENERGI			1	1
	EPIPEN-JR INJ 2-PAK		1	1
AMINOGLYCOSIDE ANTIBIOTIC		6	3	9
	TOBI PODHALR CAP 28MG	6	3	9
AMMONIA DETOXICANTS		1		1
	BUPHENYL TAB 500MG	1		1
ANTICONVULSANTS, MISCELLA		4	1	5
	SABRIL POW 500MG	1	1	2
	SABRIL TAB 500MG	1		1
	VIGABATRIN PAK 500MG	2		2
ANTINEOPLASTIC AGENTS		39	12	51
	AFINITOR TAB 10MG	1		1
	AFINITOR TAB 2.5MG	2		2
	AFINITOR TAB 5MG		1	1
	AFINITOR TAB 7.5MG	2		2
	BOSULIF TAB 500MG	1		1
	CALQUENCE CAP 100MG	1		1
	IBRANCE CAP 100MG	2		2
	IBRANCE CAP 125MG	6	1	7
	ICLUSIG TAB 45MG	1		1
	IMBRUVICA TAB 420MG	2		2
	JAKAFI TAB 5MG	1		1
	KISQALI TAB 200DOSE		1	1
	LONSURF TAB 20-8.19		1	1
	LYNPARZA TAB 150MG		1	1
	MEKINIST TAB 2MG		1	1
	NERLYNX TAB 40MG	2		2
	NEXAVAR TAB 200MG	1		1
	OPDIVO INJ 240/24	1		1
	PERJETA INJ 420/14ML		1	1
	POMALYST CAP 4MG	1		1
	REVLIMID CAP 10MG	5		5
	REVLIMID CAP 20MG	1		1
	REVLIMID CAP 5MG		1	1
	RITUXAN INJ 100MG		1	1
	RITUXAN INJ 500MG		1	1
	SPRYCEL TAB 100MG	2		2
	TAGRISSO TAB 80MG	1		1
	TASIGNA CAP 150MG	2	1	3
	VERZENIO TAB 150MG	1	1	2
	VOTRIENT TAB 200MG	1		1
	XTANDI CAP 40MG	1		1
	ZEJULA CAP 100MG	1		1
ANTIPRURITICS AND LOCAL A			3	3

AHFS Description	Drug Name	Approved	Rejected	Grand Total
	DERMACINRX PAK ZRM		3	3
ANTITOXINS AND IMMUNE GLO		5	2	7
	GAMMAGARD INJ 20GM/200	1		1
	OCTAGAM INJ 20/200ML	2	1	3
	PRIVIGEN INJ 20GRAMS	2	1	3
CARDIOTONIC AGENTS			1	1
	MILRINONE/D5 INJ 20/100ML		1	1
CENTRAL NERVOUS SYSTEM AG		2	1	3
	RADICAVA INJ 30MG	1	1	2
	XYREM SOL 500MG/ML	1		1
CYCLIC LIPOPEPTIDE ANTIBI			1	1
	DAPTOMYCIN INJ 500MG		1	1
ELECTROLYTIC,CALORIC,WATE		2		2
	CRYSVITA INJ 20MG/ML	1		1
	CRYSVITA INJ 30MG/ML	1		1
GONADOTROPINS			1	1
	TRIPTODUR SUS 22.5MG		1	1
HEAVY METAL ANTAGONISTS		1	2	3
	FERRIPROX TAB 500MG		1	1
	JADENU TAB 360MG	1	1	2
HEMATOPOIETIC AGENTS		1	1	2
	NEULASTA KIT 6MG/0.6M	1		1
	PROMACTA TAB 75MG		1	1
IMMUNOMODULATORY AGENTS		2	5	7
	ACTIMMUNE INJ 2MU/0.5	1		1
	AUBAGIO TAB 14MG	1	3	4
	COPAXONE INJ 40MG/ML		1	1
	GILENYA CAP 0.5MG		1	1
INSULINS			4	4
	HUMALOG KWIK INJ 200/ML		1	1
	HUMULIN R INJ U-500		3	3
INTERFERON ANTIVIRALS			1	1
	PLEGRIDY INJ PEN		1	1
NON-SEL.ALPHA-ADRENERGIC			1	1
	PHENOXYBENZA CAP 10MG		1	1
OTHER MISCELLANEOUS THERA		2	2	4
	KUVAN POW 500MG	1	1	2
	ORFADIN CAP 20MG		1	1
	ORFADIN CAP 5MG	1		1
PITUITARY		2	2	4
	H.P. ACTHAR INJ 80UNIT	2	2	4
POLYENE ANTIFUNGALS			1	1
	NYSTATIN POW 10BU		1	1
PROTON-PUMP INHIBITORS			1	1
	OMEPRA/BICAR POW 20-1680		1	1
RESPIRATORY TRACT AGENTS,		2		2
	GLASSIA INJ	1		1
	ZEMAIRA INJ 1000MG	1		1
SKIN AND MUCOUS MEMBRANE		1		1

AHFS Description	Drug Name	Approved	Rejected	Grand Total
	TREMFYA INJ 100MG/ML	1		1
SOMATOSTATIN AGONISTS			1	1
	SOMATULINE INJ 120/.5ML		1	1
SOMATOTROPIN AGONISTS		3		3
	GENOTROPIN INJ 12MG	3		3
VASODILATING AGENTS (RESP		11	1	12
	ORENITRAM TAB 5MG	1	1	2
	REMODULIN INJ 10MG/ML	2		2
	TRACLEER TAB 62.5MG	1		1
	TYVASO REFIL SOL 0.6MG/ML	3		3
	UPTRAVI TAB 1600MCG	2		2
	UPTRAVI TAB 600MCG	1		1
	UPTRAVI TAB 800MCG	1		1
VASOPRESSIN ANTAGONISTS		1		1
	JYNARQUE PAK 45-15MG	1		1
Grand Total		**85**	**48**	**133**

HEALTH PLAN OF NEVADA
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>$10,000 Claim Prior Authorizations

July 1, 2017 - June 30, 2018

Year/Month Filled/Paid	Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
No data to report					

No rejects exist for claims where the sole reason for the rejection was >$10,000. All >$10,000 rejects were for drugs that already required clinical prior authorization.

All >$10,000 claims that processed were for claims that were reviewed for clinical prior authorization (ie. Hepatitis C, growth hormone, etc)

Prior Authorizations over $10,000- Q3 2017–Q2 2018

SilverSummith Healthplan

Total PA Requests over $10,000	Approvals	Denials
74	27	47

TPA Name	Total Requests	Approvals
Nevada Silver Summit Medicaid	8,066	4,752

Approval Percent	Denials	Denial Percent
58.9%	3,314	41.09%

TPA Type	Total Requests	Approvals	Approval Percent
Medicaid	8,066	4,752	58.9%

Denials	Denial Percent
3,314	41.1%

Opioid Utilization by Member

Top 15 Members by Claim Count
July 1, 2017 - June 30, 2018
Fee for Service Medicaid

Encrypted Member ID	Count of Claims	Sum of Qty
11112116747	**69**	**1,950**
APAP/CODEINE TAB 300-30MG	8	150
APAP/CODEINE TAB 300-60MG	27	810
BUT/APAP/CAF CAP CODEINE	34	990
11114292001	**56**	**4,538**
METHADONE TAB 10MG	23	2,178
OXYCOD/APAP TAB 10-325MG	33	2,360
99995072837	**56**	**3,110**
FENTANYL DIS 12MCG/HR	12	120
FENTANYL DIS 50MCG/HR	11	110
OXYCODONE TAB 15MG	12	1,440
SUBSYS SPR 200MCG	21	1,440
22222264138	**50**	**999**
HYDROMORPHON TAB 4MG	4	105
HYDROMORPHON TAB 8MG	2	140
SUBOXONE MIS 12-3MG	21	141
SUBOXONE MIS 2-0.5MG	2	60
SUBOXONE MIS 8-2MG	21	553
77779814158	**47**	**728**
SUBOXONE MIS 8-2MG	47	728
56292500001	**46**	**7,230**
APAP/CODEINE TAB 300-60MG	21	3,780
BUT/ASA/CAF/ CAP COD 30MG	12	1,170
HYDROCO/APAP TAB 10-325MG	3	480
HYDROCOD/IBU TAB 7.5-200	10	1,800
99991130999	**44**	**2,832**
HYDROCO/APAP TAB 10-325MG	31	1,302
OXYCODONE TAB 30MG	13	1,530
44447412422	**43**	**2,417**
HYDROCO/APAP TAB 10-325MG	22	936
MORPHINE SUL TAB 30MG ER	1	60
OXYCODONE TAB 15MG	19	1,385
TRAMADOL HCL TAB 50MG	1	36
27483344445	**43**	**6,780**
MORPHINE SUL TAB 200MG ER	11	990
MORPHINE SUL TAB 30MG	12	2,130
OXYCOD/APAP TAB 10-325MG	10	1,560
OXYCODONE TAB 15MG	2	360
TRAMADOL HCL TAB 50MG	8	1,740
00000048459	**41**	**724**
OXYCOD/APAP TAB 7.5-325	2	180
SUBOXONE MIS 8-2MG	39	544
88882873004	**40**	**470**

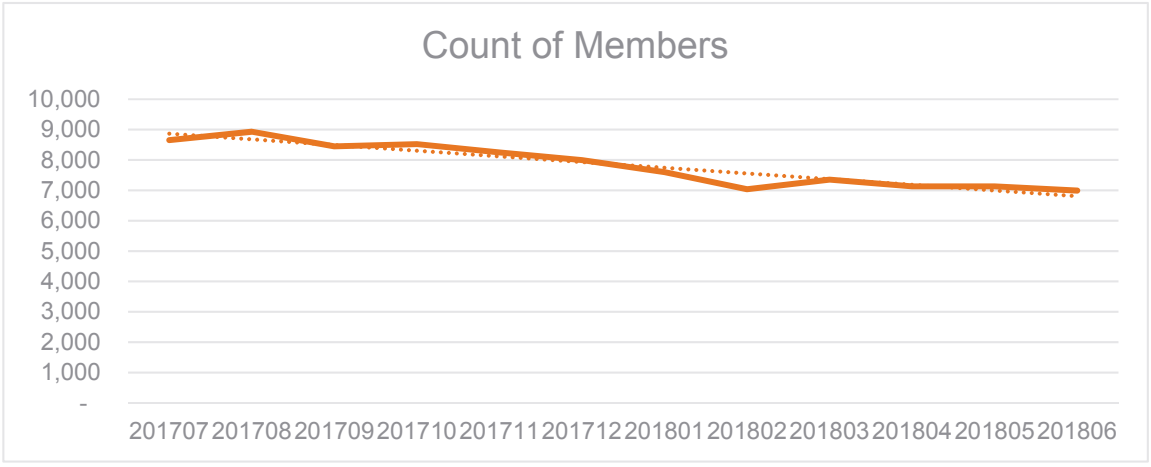
SUBOXONE MIS 8-2MG	40	470
88888849672	**39**	**2,287**
FENTANYL DIS 50MCG/HR	13	125
MORPHINE SUL TAB 15MG ER	13	700
OXYCODONE TAB 10MG	13	1,462
55554574244	**39**	**2,593**
HYDROMORPHON TAB 4MG	13	1,125
MORPHINE SUL TAB 30MG ER	13	718
MORPHINE SUL TAB 60MG ER	13	750
55558574916	**38**	**2,630**
APAP/CODEINE TAB 300-30MG	1	20
MORPHABOND TAB 15MG ER	1	60
MORPHABOND TAB 30MG ER	1	60
MORPHINE SUL TAB 15MG ER	12	720
MORPHINE SUL TAB 30MG ER	10	600
OXYCOD/APAP TAB 10-325MG	12	1,080
PRIMLEV TAB 10-300MG	1	90
00009186655	**38**	**2,420**
FENTANYL DIS 100MCG/H	13	130
FENTANYL DIS 25MCG/HR	13	130
OXYCODONE TAB 20MG	12	2,160
11110100737	**38**	**4,610**
FENTANYL DIS 100MCG/H	12	180
HYDROCO/APAP TAB 10-325MG	1	60
METHADONE TAB 10MG	12	3,200
MORPHINE SUL TAB 100MG ER	13	1,170
00000005744	**38**	**2,653**
OXYCOD/APAP TAB 10-325MG	15	1,734
OXYCOD/APAP TAB 7.5-325	5	235
OXYCODONE TAB 60MG ER	2	120
OXYCODONE TAB 80MG ER	10	402
OXYCONTIN TAB 40MG CR	5	134
TRAMADOL HCL TAB 50MG	1	28
33330458115	**38**	**5,376**
MORPHINE SUL TAB 100MG ER	16	1,446
OXYCODONE TAB 10MG	9	1,620
OXYCODONE TAB 20MG	13	2,310
Grand Total	**803**	**54,347**

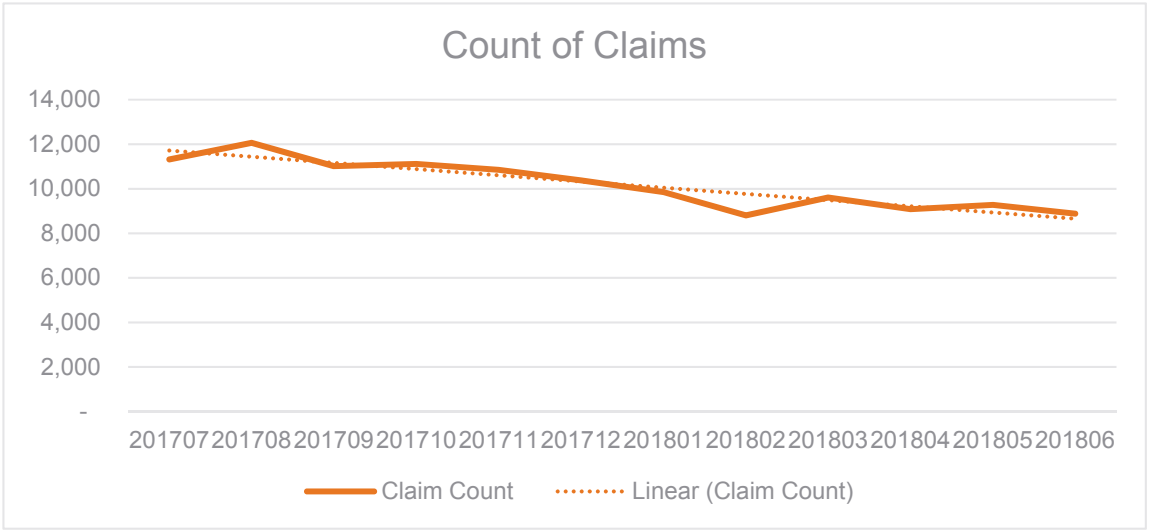
Opioid Utilization

Fee for Service Medicaid

July 1, 2017 - June 30, 2018

Year Month Filled	Member Count	Claim Count	Sum of Days Supply	Sum of Qty	Sum of Pd Amt
201707	8,655	11,317	244,339	881,364	$ 564,725.24
201708	8,931	12,064	258,247	929,117	$ 597,967.30
201709	8,447	11,016	238,254	862,634	$ 531,196.94
201710	8,522	11,118	240,713	872,643	$ 554,505.93
201711	8,249	10,850	235,523	849,815	$ 533,639.90
201712	7,995	10,377	230,882	830,210	$ 517,578.71
201801	7,603	9,855	231,217	804,608	$ 493,763.50
201802	7,038	8,806	210,422	722,200	$ 478,220.23
201803	7,354	9,608	229,041	788,008	$ 499,561.42
201804	7,131	9,085	217,778	741,507	$ 518,396.35
201805	7,134	9,280	218,275	745,255	$ 495,513.76
201806	6,993	8,881	210,508	716,192	$ 480,838.76





Top 10 Prescribers by Count of Claims

Fee for Service Medicaid

	Encrypted ID	Specialty	Degree	City	Member Count	Claim Count	Sum of Days Supply	Sum of Qty	Sum of Pd Amt
October 1, 2017 - Septembe	A	Anesthesiology	DO	Henderson	215	2,309	66,607	266,547	$ 221,399.23
	B	Pain Management	NP	Las Vegas	172	1,473	43,729	136,606	$ 100,454.91
	C	Pain Management	MD	Carson City	151	1,434	35,203	91,976	$ 516,346.76
	D		NP	Fallon	216	1,400	25,944	128,855	$ 41,826.65
	E	Maxillofacial Surgery	PA	Henderson	276	1,265	37,388	114,700	$ 63,834.77
	F		PA	Las Vegas	95	1,182	34,710	130,467	$ 45,186.20
	G		PA	Las Vegas	193	1,152	34,791	102,590	$ 94,869.67
	H			Las Vegas	320	1,119	32,817	98,790	$ 65,561.41
	I		PA	Las Vegas	139	903	25,556	90,010	$ 42,052.58
	J		MD	Las Vegas	361	851	23,364	71,412	$ 46,093.97
July 1, 2017 - June 30, 201	A	Anesthesiology	DO	Henderson	194	1,875	54,512	218,486	$ 181,679.56
	B	Pain Management	NP	Las Vegas	175	1,739	51,500	162,349	$ 121,582.36
	D		NP	Fallon	227	1,694	29,590	153,364	$ 51,492.40
	F		PA	Las Vegas	102	1,383	40,774	154,529	$ 57,075.23
	C	Pain Management	MD	Carson City	140	1,367	34,663	93,943	$ 464,673.50
	G		PA	Las Vegas	188	1,218	36,377	108,195	$ 101,216.53
	H			Las Vegas	311	1,129	33,076	98,196	$ 73,725.49
	K		PB	Las Vegas	148	1,019	28,488	95,163	$ 67,075.63
	E	Maxillofacial Surgery	PA	Henderson	262	994	29,440	89,448	$ 47,210.92
	I		PA	Las Vegas	130	889	25,180	87,764	$ 45,036.41
April 1, 2017 - March 31, 20	B	Pain Management	NP	Las Vegas	188	1,954	57,840	182,956	$ 144,870.24
	D		NP	Fallon	242	1,757	29,589	158,382	$ 52,436.24
	A	Anesthesiology	DO	Henderson	192	1,533	44,362	179,610	$ 140,313.70
	F		PA	Las Vegas	114	1,439	42,549	163,079	$ 69,479.80
	G		PA	Las Vegas	172	1,312	38,637	117,085	$ 111,393.76
	C	Pain Management	MD	Carson City	135	1,306	34,277	98,128	$ 430,613.14
	H			Las Vegas	261	1,183	34,829	103,241	$ 80,918.60
	K		PB	Las Vegas	155	1,177	32,794	111,536	$ 83,786.71
	L	Oncology	PA	Las Vegas	165	1,084	30,342	103,253	$ 58,354.66
	I		PA	Las Vegas	135	964	27,222	94,231	$ 52,491.49

Anthem Top Opioid Utilization 7/1/17-6/30/18

View by Prescriber

Prescriber	Claim Count	Sum Days of Therapy	Sum of Quantity
15MD	**208**	**5939**	**4656**
17MD	**135**	**3722**	**3454**
13MD	**118**	**3194**	**3453**
11DO	**102**	**2818**	**2553**
15MD	**94**	**2685**	**3195**
12MD	**91**	**2477**	**5320**
12MD	**84**	**2505**	**2505**
12MD	**68**	**2001**	**2388**
13MD	**67**	**1845**	**1845**

View by Member

Member rank	Claim Count	Sum Days of Therapy	Sum of Total Quantity
1	26	752	528
2	27	746	264
3	24	694	203
4	22	648	988
5	22	621	1214
6	21	616	448
7	20	560	484
8	19	540	540
9	17	450	450
10	15	436	227

HEALTH PLAN OF NEVADA
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Top 10 Prescribers of Opioids

July 1, 2017 - June 30, 2018

By Member Count Q3 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
A	492	516	50	10589
B	483	864	191	82068
C	475	987	168	100050
D	443	652	108	62506
E	436	762	110	77004
F	349	457	129	43233
G	331	605	206	57762
H	316	646	152	65566
I	296	581	211	56609
J	268	348	131	32769

By Member Count Q4 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	527	1143	178	115469
A	462	483	54	10387
G	454	932	161	86652
E	357	614	71	61361
K	327	491	65	48600
D	327	469	44	44477
L	294	304	37	6767
H	289	623	176	62312
F	262	539	122	51491
I	252	519	146	50625

By Member Count Q1 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	530	1118	244	100721
M	493	1113	241	87560
G	480	1020	111	87736
E	344	618	85	60682
K	337	541	37	51799
D	309	457	60	42734
L	273	282	32	5372
N	258	400	264	34497
I	257	553	149	53530

By Member Count Q2 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
G	465	933	170	80864
C	460	1024	183	90096
E	375	682	134	66813
K	320	491	60	46309
M	280	650	205	61076
N	252	327	301	24534
H	250	579	96	56370
F	250	386	94	38493
I	236	500	177	47747
AJ	235	339	169	30771

By Count of Claims Q3 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	475	987	168	100050
B	483	864	191	82068
E	436	762	110	77004
D	443	652	108	62506
H	316	646	152	65566
G	331	605	206	57762
I	296	581	211	56609
A	492	516	50	10589
O	235	513	296	47880
P	151	491	109	46974

By Count of Claims Q4 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	527	1143	178	115469
G	454	932	161	86652
H	289	623	176	62312
E	357	614	71	61361
Q	181	558	204	69606
F	262	539	122	51491
I	252	519	146	50625
P	147	504	129	48534
K	327	491	65	48600
A	462	483	54	10387

By Count of Claims Q1 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	530	1118	244	100721
M	493	1113	241	87560
G	480	1020	111	87736
H	257	634	132	62181
E	344	618	85	60682
Q	199	592	173	70538
I	257	553	149	53530
K	337	541	37	51799
D	309	457	60	42734
P	135	444	86	42270

By Count of Claims Q2 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	460	1024	183	90096
G	465	933	170	80864
E	375	682	134	66813
M	280	650	205	61076
Q	196	647	162	75848
H	250	579	96	56370
I	236	500	177	47747
K	320	491	60	46309
P	128	437	107	42328
F	250	386	94	38493

By Days Supply Q3 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
O	235	513	296	47880
R	82	126	291	8705
S	79	126	279	9247
T	178	374	273	30111
U	169	322	254	35293
V	102	186	253	17365
W	84	199	244	18298
X	93	200	243	16966
Y	211	397	240	37703
Z	85	147	227	11816

By Days Supply Q4 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
AA	78	126	305	13366
T	164	304	295	24012
AB	216	417	284	39546
AC	135	288	271	28730
X	76	184	266	15249
R	82	135	262	9589
V	97	194	258	18126
AD	74	187	248	24168
N	150	342	246	31985
AE	73	124	245	9629

By Days Supply Q1 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
T	168	336	310	26125
N	258	400	264	34497
C	530	1118	244	100721
S	72	128	241	9678
M	493	1113	241	87560
AA	71	114	231	10158
R	71	103	224	6339
X	69	164	216	13875
AF	76	155	198	12352
AE	51	84	193	6738

By Days Supply Q2 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
N	252	327	301	24534
S	75	141	222	10627
R	74	115	216	6628
M	280	650	205	61076
AF	81	142	205	10583
X	62	161	188	14253
C	460	1024	183	90096
I	236	500	177	47747
T	117	230	176	16011
AG	42	65	176	2579

By Sum of QTY Q3 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	475	987	168	100050
B	483	864	191	82068
E	436	762	110	77004
H	316	646	152	65566
D	443	652	108	62506
G	331	605	206	57762
I	296	581	211	56609
Q	158	401	219	48120
O	235	513	296	47880
P	151	491	109	46974

By Sum of QTY Q4 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	527	1143	178	115469
G	454	932	161	86652
Q	181	558	204	69606
H	289	623	176	62312
E	357	614	71	61361
F	262	539	122	51491
I	252	519	146	50625
K	327	491	65	48600
P	147	504	129	48534
D	327	469	44	44477

By Sum of QTY Q1 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	530	1118	244	100721
G	480	1020	111	87736
M	493	1113	241	87560
Q	199	592	173	70538
H	257	634	132	62181
E	344	618	85	60682
I	257	553	149	53530
K	337	541	37	51799
D	309	457	60	42734
P	135	444	86	42270

By Sum of QTY Q2 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
C	460	1024	183	90096
G	465	933	170	80864
Q	196	647	162	75848
E	375	682	134	66813
M	280	650	205	61076
H	250	579	96	56370
I	236	500	177	47747
K	320	491	60	46309
P	128	437	107	42328
F	250	386	94	38493

By Pharmacy Paid Amt Q3 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
AH	50	90	184	8295
T	178	374	273	30111
H	316	646	152	65566
E	436	762	110	77004
D	443	652	108	62506
I	296	581	211	56609
C	475	987	168	100050
B	483	864	191	82068
Q	158	401	219	48120
AI	180	392	77	37082

By Pharmacy Paid Amt Q4 2017

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
AH	46	87	177	7925
T	164	304	295	24012
H	289	623	176	62312
C	527	1143	178	115469
Q	181	558	204	69606
D	327	469	44	44477
G	454	932	161	86652
E	357	614	71	61361
I	252	519	146	50625
AJ	216	350	143	33039

By Pharmacy Paid Amt Q1 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
AH	13	24	118	2270
T	168	336	310	26125
M	493	1113	241	87560
H	257	634	132	62181
Q	199	592	173	70538
C	530	1118	244	100721
G	480	1020	111	87736
I	257	553	149	53530
E	344	618	85	60682
D	309	457	60	42734

By Pharmacy Paid Amt Q2 2018

Prescriber ID	Member Count	Claim Count	Sum of Days	Sum of Qty
T	117	230	176	16011
Q	196	647	162	75848
M	280	650	205	61076
H	250	579	96	56370
AK	57	166	156	5896
G	465	933	170	80864
I	236	500	177	47747
C	460	1024	183	90096
E	375	682	134	66813
AL	75	133	87	3231

Report Summary: Utilized Medispan GPI number 65** - Analgesic Opioid to generate report.

Top 10 Opioid Prescriber Reports for Nevada SSHP

Top 10 Opioid Prescribers by Unique Utilizer

7/1/2017 - 6/30/18

Rank	Physician NPI	Unique Utilizers	Claim Count	Sum Metric Quantity	Sum Days' Supply
1	********941	208	681	59166	20012
2	********014	185	319	26558	9154
3	********730	169	637	57670	18703
4	********870	120	590	54143	17152
5	********756	80	499	51031	14695
6	********552	79	89	1798	476
7	********686	79	347	30117	9537
8	********005	77	84	1700	422
9	********195	72	499	27283	12396
10	********583	65	139	10935	3528

Top 10 Opioid Prescribers by Claim Count

7/1/2017 - 6/30/18

Rank	Physician NPI	Unique Utilizers	Claim Count	Sum Metric Quantity	Sum Days' Supply
1	********941	208	681	59166	20012
2	********730	169	637	57670	18703
3	********870	120	590	54143	17152
4	********709	38	500	13312	7549
5	********195	72	499	27283	12396
6	********756	80	499	51031	14695
7	********686	79	347	30117	9537
8	********634	36	338	30474	9688
9	********504	47	327	29342	9753
10	********014	185	319	26558	9154

Antibiotic Utilization

Fee for Service Medicaid

July 1, 2017 - June 30, 2018

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
AMOXICILLIN	18,406	24,328	219,611	2,083,266	$ 258,854.07
AZITHROMYCIN	14,131	19,207	95,063	177,827	$ 246,623.75
AMOXICILLIN/CLAVULANATE P	9,871	12,311	112,997	527,719	$ 221,477.09
CEPHALEXIN	7,431	9,670	82,060	459,706	$ 115,703.48
CEFTRIAXONE SODIUM	4,455	6,503	7,183	241,242	$ 134,401.87
CIPROFLOXACIN HCL	4,746	6,268	48,342	93,397	$ 53,303.50
CEFDINIR	4,607	5,553	52,860	297,575	$ 128,532.44
DOXYCYCLINE HYCLATE	3,027	4,315	62,425	110,398	$ 90,102.55
LEVOFLOXACIN	2,984	3,897	29,528	34,811	$ 35,669.22
PENICILLIN V POTASSIUM	1,631	2,094	21,786	135,640	$ 27,179.66
DOXYCYCLINE MONOHYDRATE	1,444	2,059	32,457	58,154	$ 36,763.81
CEFAZOLIN SODIUM	1,411	1,704	1,878	12,985	$ 10,822.79
MINOCYCLINE HCL	321	841	25,293	38,934	$ 30,040.99
CLARITHROMYCIN	554	628	7,894	18,530	$ 15,306.51
CEFTRIAXONE IN ISO-OSMOTI	456	559	696	37,300	$ 14,292.37
CEFUROXIME AXETIL	484	550	4,954	9,733	$ 12,613.05
CEFEPIME	196	435	1,310	56,385	$ 43,205.41
CEFAZOLIN SODIUM/DEXTROSE	363	407	424	7,493	$ 17,731.16
TOBRAMYCIN	99	379	10,256	94,505	$ 697,558.95
ERYTHROMYCIN ETHYLSUCCINA	70	361	6,457	64,294	$ 197,226.05
CEFTRIAXONE/DEXTROSE	222	338	394	641	$ 6,675.73
AMPICILLIN-SULBACTAM	243	329	336	522	$ 3,197.51
LEVOFLOXACIN IN D5W	237	307	343	44,500	$ 3,581.68
GENTAMICIN SULFATE	160	289	537	1,444	$ 1,705.84
PIPERACILLIN/TAZOBACTAM	178	275	375	797	$ 9,149.98
CIPROFLOXACIN I.V.-IN D5W	189	255	276	70,400	$ 1,312.36
ZOSYN	163	248	450	56,299	$ 30,646.70
BICILLIN L-A	204	224	533	8,609	$ 42,903.93
ZITHROMAX	164	182	190	342	$ 2,781.97
CEFPODOXIME PROXETIL	112	158	1,165	3,089	$ 12,314.56
AMPICILLIN	107	131	1,065	3,550	$ 1,541.14
ERYTHROMYCIN BASE	75	111	1,812	4,515	$ 50,247.97
E.E.S. GRANULES	22	110	1,630	17,780	$ 63,732.62
CEFOXITIN SODIUM	73	95	95	798	$ 5,331.73
NEOMYCIN SULFATE	63	93	803	2,156	$ 1,869.38
CEFAZOLIN	43	70	113	24,400	$ 2,419.72
DICLOXACILLIN SODIUM	61	69	719	2,713	$ 1,939.41
MOXIFLOXACIN HCL	53	66	267	519	$ 799.22
PIPERACILLIN SODIUM/TAZOB	60	64	64	94	$ 970.96
CIPRO	35	62	741	7,084	$ 9,093.70
DOXYCYCLINE HYCLATE DR	42	62	1,450	2,120	$ 19,567.00
AVELOX	34	48	378	8,098	$ 11,990.33
ZITHROMAX Z-PAK	43	47	47	75	$ 7.04
UNASYN	35	44	44	49	$ 649.17
TOBRAMYCIN SULFATE	27	42	122	1,305	$ 1,363.23
TETRACYCLINE HYDROCHLORID	23	41	836	2,179	$ 8,967.43
DEMECLOCYCLINE HCL	5	36	977	1,986	$ 11,520.53

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
CEFEPIME/DEXTROSE	14	34	100	918	$ 3,442.38
CEFTAZIDIME	9	30	83	172	$ 1,561.63
CEFPROZIL	24	29	286	3,010	$ 1,288.94
DOXY 100	23	29	29	51	$ 1,095.41
ERYPED 200	7	28	848	7,300	$ 25,981.64
TOBI PODHALER	10	27	854	6,048	$ 266,096.43
TETRACYCLINE HCL	23	26	322	1,069	$ 4,100.51
LEVOFLOXACIN IN 5% DEXTRO	19	25	25	3,750	$ 171.75
AMPICILLIN SODIUM	18	23	29	67	$ 477.60
ZERBAXA	2	22	54	284	$ 22,270.76
ERYTHROCIN STEARATE	9	20	485	1,080	$ 11,056.10
PFIZERPEN	4	19	19	21	$ 898.23
AUGMENTIN	16	16	140	1,975	$ 10,741.75
BICILLIN C-R	13	15	15	98	$ 5,019.48
CEFOTETAN/DEXTROSE	13	15	15	802	$ 4,019.99
BETHKIS	3	14	454	3,136	$ 45,525.67
CEFOTETAN	10	14	14	15	$ 538.57
TAZICEF	6	14	14	27	$ 136.60
MAXIPIME	12	13	13	601	$ 497.16
TEFLARO	9	13	16	29	$ 4,778.70
CEFACLOR	7	11	200	540	$ 517.77
CIPROFLOXACIN	4	11	11	11	$ 2.24
DOXYCYCLINE	8	11	151	4,100	$ 949.85
ISOTONIC GENTAMICIN	8	11	20	4,700	$ 194.30
LEVAQUIN	6	11	74	79	$ 960.88
SOLODYN	2	11	330	330	$ 12,097.31
SULFADIAZINE	1	11	360	2,340	$ 8,611.09
CIPROFLOXACIN HYDROCHLORI	7	10	10	10	$ 1.37
CEFTIN	9	9	88	1,400	$ 3,150.93
AMIKACIN SULFATE	7	8	23	66	$ 281.80
CLARITHROMYCIN ER	6	8	62	124	$ 236.40
CIPROFLOXACIN ER	7	7	90	139	$ 875.69
ERYTHROMYCIN	5	7	107	301	$ 995.04
MINOCYCLINE HCL ER	2	7	208	208	$ 2,185.86
PENICILLIN G POTASSIUM	3	6	17	14	$ 1,563.68
CEFADROXIL	5	5	37	94	$ 155.86
CEFIXIME	4	5	40	233	$ 802.45
KITABIS PAK	2	5	140	1,400	$ 22,550.85
BIAXIN	2	4	4	4	$ 1.96
CEFTAZIDIME/DEXTROSE	4	4	10	802	$ 301.22
ERY-TAB	3	4	47	121	$ 352.30
GENTAMICIN SULFATE/0.9% S	4	4	6	1,050	$ 59.94
MOXIFLOXACIN HYDROCHLORI	2	4	4	1,000	$ 176.28
DIFICID	3	3	30	60	$ 7,096.01
XIMINO	1	3	90	90	$ 2,127.51
AVYCAZ	1	2	2	2	$ 655.36
BACTOCILL IN DEXTROSE	1	2	2	100	$ 41.58
BAXDELA	1	2	28	56	$ -
ERYPED 400	1	2	40	200	$ 1,272.86
GENTAMICIN SULFATE PEDIAT	2	2	2	4	$ 3.20
OXACILLIN SODIUM	1	2	2	8	$ 118.40

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
SUPRAX	2	2	56	6	$ 186.89
TOBI	1	2	112	560	$ 12,641.41
VIBRAMYCIN	2	2	31	962	$ 1,031.78
CEFOTAXIME SODIUM	1	1	1	1	$ 2.20
CEFUROXIME SODIUM	1	1	1	1	$ 2.25
FORTAZ	1	1	1	1	$ 23.71
MINOCIN	1	1	1	2	$ 308.83
MINOCYCLINE HYDROCHLORIDE	1	1	10	20	$ 19.09
PAROMOMYCIN SULFATE	1	1	7	42	$ 180.27
ZINACEF	1	1	1	1	$ 5.64
Total					**$ 3,186,130.92**

ANTHEM Antibiotic Utilization	3Q 2017	4Q 2017	1Q 2018	2Q 2018	TOTAL
ALINIA 500 MG TABLET			1		1
AMOX-CLAV 200-28.5 MG TAB CHEW	1	1	1	1	4
AMOX-CLAV 200-28.5 MG/5 ML SUS	18	15	17	19	69
AMOX-CLAV 250-125 MG TABLET	2	3	6	4	15
AMOX-CLAV 250-62.5 MG/5 ML SUS	199	266	304	222	991
AMOX-CLAV 400-57 MG TAB CHEW	6	4	1	3	14
AMOX-CLAV 400-57 MG/5 ML SUSP	335	609	704	457	2105
AMOX-CLAV 500-125 MG TABLET	232	277	325	258	1092
AMOX-CLAV 600-42.9 MG/5 ML SUS	326	517	650	425	1918
AMOX-CLAV 875-125 MG TABLET	1865	2053	2284	1835	8037
AMOX-CLAV ER 1,000-62.5 MG TAB	9	9	8	8	34
AMOXICILLIN 125 MG TAB CHEW	1	1	1	1	4
AMOXICILLIN 125 MG/5 ML SUSP	157	217	207	188	769
AMOXICILLIN 200 MG/5 ML SUSP	99	208	164	107	578
AMOXICILLIN 250 MG CAPSULE	70	62	52	46	230
AMOXICILLIN 250 MG TAB CHEW	21	26	28	23	98
AMOXICILLIN 250 MG/5 ML SUSP	1231	1631	1834	1186	5882
AMOXICILLIN 400 MG/5 ML SUSP	2542	4550	5445	3209	15746
AMOXICILLIN 500 MG CAPSULE	3295	3745	3968	3250	14258
AMOXICILLIN 500 MG TABLET	143	134	142	125	544
AMOXICILLIN 875 MG TABLET	387	491	708	556	2142
AMPICILLIN 250 MG CAPSULE	2	5	2	1	10
AMPICILLIN 500 MG CAPSULE	25	35	40	27	127
ATOVAQUONE 750 MG/5 ML SUSP	9	3	3	2	17
AUGMENTIN 125-31.25 MG/5 ML		1	1	1	3
AZITHROMYCIN 1 GM PWD PACKET	88	72	46	31	237
AZITHROMYCIN 100 MG/5 ML SUSP	159	342	371	197	1069
AZITHROMYCIN 200 MG/5 ML SUSP	706	1293	1534	861	4394
AZITHROMYCIN 250 MG TABLET	2445	3809	4151	2365	12770
AZITHROMYCIN 500 MG TABLET	459	511	595	500	2065
AZITHROMYCIN 600 MG TABLET	37	23	37	28	125
BAXDELA 450 MG TABLET				1	1
BICILLIN L-A 1,200,000 UNITS	1				1
BICILLIN L-A 2,400,000 UNITS			1		1
BICILLIN L-A 600,000 UNIT/ML	1				1
CAYSTON 75 MG INHAL SOLUTION	1	3	4	2	10
CEFACLOR 125 MG/5 ML SUSP	1				1
CEFACLOR 250 MG/5 ML SUSP	1		1		2
CEFACLOR 500 MG CAPSULE	1	1	2		4
CEFADROXIL 250 MG/5 ML SUSP			1		1
CEFADROXIL 500 MG CAPSULE	5	2	4	4	15

ANTHEM Antibiotic Utilization	3Q 2017	4Q 2017	1Q 2018	2Q 2018	TOTAL
CEFAZOLIN 1 GM VIAL		2			2
CEFAZOLIN 10 GM VIAL	5	1	3		9
CEFAZOLIN 2 G/100 ML-DEXTROSE			1		1
CEFDINIR 125 MG/5 ML SUSP	250	435	573	303	1561
CEFDINIR 250 MG/5 ML SUSP	603	1066	1356	811	3836
CEFDINIR 300 MG CAPSULE	348	397	496	413	1654
CEFEPIME HCL 2 GRAM VIAL	36	30	16		82
CEFIXIME 100 MG/5 ML SUSP	1			1	2
CEFIXIME 200 MG/5 ML SUSP				1	1
CEFPODOXIME 100 MG TABLET	9	7	9	4	29
CEFPODOXIME 200 MG TABLET	7	14	10	9	40
CEFPROZIL 125 MG/5 ML SUSP			1	1	2
CEFPROZIL 250 MG TABLET	1	3	2	2	8
CEFPROZIL 250 MG/5 ML SUSP	2	1	5	1	9
CEFPROZIL 500 MG TABLET	1	1	3	1	6
CEFTIN 250 MG/5 ML ORAL SUSP		5	4	3	12
CEFTRIAXONE 1 GM VIAL	8		4		12
CEFTRIAXONE 2 GM VIAL	21	13	2		36
CEFTRIAXONE 250 MG VIAL	8	13	9	9	39
CEFTRIAXONE 500 MG VIAL		1			1
CEFUROXIME AXETIL 250 MG TAB	22	22	21	13	78
CEFUROXIME AXETIL 500 MG TAB	85	62	63	45	255
CEPHALEXIN 125 MG/5 ML SUSP	82	83	67	93	325
CEPHALEXIN 250 MG CAPSULE	106	133	124	111	474
CEPHALEXIN 250 MG TABLET	1		2		3
CEPHALEXIN 250 MG/5 ML SUSP	710	673	583	596	2562
CEPHALEXIN 500 MG CAPSULE	2100	1873	1806	1941	7720
CEPHALEXIN 500 MG TABLET	3	5	1	8	17
CEPHALEXIN 750 MG CAPSULE	1	5	4	4	14
CIPRO 10% SUSPENSION				1	1
CIPRO 5% SUSPENSION		1		1	2
CIPROFLOXACIN ER 500 MG TABLET	1	7	1		9
CIPROFLOXACIN HCL 250 MG TAB	144	122	110	114	490
CIPROFLOXACIN HCL 500 MG TAB	1177	1051	989	971	4188
CIPROFLOXACIN HCL 750 MG TAB	12	7	19	20	58
CLARITHROMYCIN 125 MG/5 ML SUS	1	7	5	3	16
CLARITHROMYCIN 250 MG TABLET	5	14	6	8	33
CLARITHROMYCIN 250 MG/5 ML SUS	9	13	14	9	45
CLARITHROMYCIN 500 MG TABLET	154	172	164	188	678
CLARITHROMYCIN ER 500 MG TAB	2	2	2	1	7
CLINDAMYCIN 75 MG/5 ML SOLN	43	32	29	5	109

ANTHEM Antibiotic Utilization	3Q 2017	4Q 2017	1Q 2018	2Q 2018	TOTAL
CLINDAMYCIN HCL 150 MG CAPSULE	339	289	281	340	1249
CLINDAMYCIN HCL 300 MG CAPSULE	866	908	831	875	3480
CLINDAMYCIN PEDIATR 75 MG/5 ML	59	80	101	107	347
CLINDAMYCIN PH 900 MG/6 ML VL	4				4
DALVANCE 500 MG VIAL	2				2
DAPSONE 100 MG TABLET	5	6	8	9	28
DAPSONE 25 MG TABLET			1		1
DAPTOMYCIN 500 MG VIAL	54	32	16		102
DICLOXACILLIN 250 MG CAPSULE	8	4	7	5	24
DICLOXACILLIN 500 MG CAPSULE	25	23	18	15	81
DIFICID 200 MG TABLET	1	1			2
DOXYCYCLINE 25 MG/5 ML SUSP	1		1		2
DOXYCYCLINE HYC DR 100 MG TAB			3	1	4
DOXYCYCLINE HYC DR 150 MG TAB			1	1	2
DOXYCYCLINE HYC DR 200 MG TAB				1	1
DOXYCYCLINE HYC DR 50 MG TAB	2				2
DOXYCYCLINE HYCLATE 100 MG CAP	24	25	35	27	111
DOXYCYCLINE HYCLATE 100 MG TAB	17	6	10	17	50
DOXYCYCLINE HYCLATE 150 MG TAB	1				1
DOXYCYCLINE HYCLATE 20 MG TAB			1	1	2
DOXYCYCLINE HYCLATE 50 MG CAP	9	10	1		20
DOXYCYCLINE MONO 100 MG CAP	679	807	921	905	3312
DOXYCYCLINE MONO 100 MG TABLET	14	8	9	7	38
DOXYCYCLINE MONO 150 MG CAP	6	5	3	1	15
DOXYCYCLINE MONO 50 MG CAP	51	57	51	54	213
DOXYCYCLINE MONO 75 MG CAPSULE			2	1	3
E.E.S. 400 FILMTAB	1		2		3
ERYPED 400 MG/5 ML SUSPENSION			1		1
ERY-TAB DR 250 MG TABLET		1			1
ERY-TAB DR 333 MG TABLET	2		1	1	4
ERYTHROCIN 250 MG FILMTAB	2		3	1	6
ERYTHROMYCIN 200 MG/5 ML GRAN	3	5	1	2	11
ERYTHROMYCIN 250 MG FILMTAB	8	8	9	8	33
ERYTHROMYCIN 500 MG FILMTAB	20	14	11	9	54
ERYTHROMYCIN DR 250 MG CAP	3	3		1	7
ERYTHROMYCIN ES 400 MG TAB	3		1	3	7
INVANZ 1 GM VIAL	31	12	8		51
LEVOFLOXACIN 25 MG/ML SOLUTION			2		2
LEVOFLOXACIN 250 MG TABLET	16	12	13	10	51

ANTHEM Antibiotic Utilization	3Q 2017	4Q 2017	1Q 2018	2Q 2018	TOTAL
LEVOFLOXACIN 500 MG TABLET	261	275	388	227	1151
LEVOFLOXACIN 500 MG/100 ML-D5W	7				7
LEVOFLOXACIN 750 MG TABLET	210	242	271	195	918
LEVOFLOXACIN 750 MG/150 ML-D5W	1	2			3
LINEZOLID 100 MG/5 ML SUSP	2		2	1	5
LINEZOLID 600 MG TABLET	23	25	16	19	83
LINEZOLID 600 MG/300 ML-D5W	16	3			19
MEROPENEM IV 1 GM VIAL	4	3	3	1	11
MEROPENEM IV 500 MG VIAL		1	1		2
MEROPENEM-0.9% NACL 500 MG/50		1			1
METRONIDAZOLE 250 MG TABLET	142	119	113	102	476
METRONIDAZOLE 375 MG CAPSULE		2	3	1	6
METRONIDAZOLE 500 MG TABLET	2035	1841	1953	1872	7701
METRONIDAZOLE 500 MG/100 ML			8		8
MINOCYCLINE 100 MG CAPSULE	152	162	151	143	608
MINOCYCLINE 50 MG CAPSULE	47	59	74	38	218
MINOCYCLINE 75 MG CAPSULE	6	6	4	3	19
MINOCYCLINE ER 90 MG TABLET	1				1
MINOCYCLINE HCL 100 MG TABLET	55	50	48	54	207
MINOCYCLINE HCL 50 MG TABLET	17	16	18	22	73
MINOCYCLINE HCL 75 MG TABLET	3	1	5	3	12
MOXIFLOXACIN HCL 400 MG TABLET	3	1	5	2	11
OFLOXACIN 400 MG TABLET		1			1
PENICILLIN VK 125 MG/5 ML SOLN	25	19	21	28	93
PENICILLIN VK 250 MG TABLET	24	17	18	16	75
PENICILLIN VK 250 MG/5 ML SOLN	95	108	121	105	429
PENICILLIN VK 500 MG TABLET	445	452	426	429	1752
PFIZERPEN 5 MILLION UNIT VIAL			1		1
PIPERACIL-TAZOBACT 4.5 GM VIAL	2	1			3
PIPERACIL-TAZOBACT 40.5 GRAM		3			3
SULFAMETHOXAZOLE-TMP DS TABLET	1659	1522	1330	1328	5839
SULFAMETHOXAZOLE-TMP SS TABLET	49	45	55	51	200
SULFAMETHOXAZOLE-TMP SUSP	288	288	254	243	1073
SULFATRIM PEDIATRIC SUSPENSION	3	5	2	3	13
SUPRAX 400 MG CAPSULE	1	1		2	4
TEFLARO 400 MG VIAL	2				2
TEFLARO 600 MG VIAL	6	1			7
TETRACYCLINE 250 MG CAPSULE	5	7	6	2	20

ANTHEM Antibiotic Utilization	3Q 2017	4Q 2017	1Q 2018	2Q 2018	TOTAL
TETRACYCLINE 500 MG CAPSULE	30	28	15	18	91
TINIDAZOLE 500 MG TABLET	21	21	16	22	80
TRIMETHOPRIM 100 MG TABLET	1	1	1		3
VANCOMYCIN 1 G/200ML-0.9% NACL			2		2
VANCOMYCIN 1 GM VIAL		1	4		5
VANCOMYCIN 750 MG/150 ML BAG	2	1			3
VANCOMYCIN HCL 10 GM VIAL	42	9	18		69
VANCOMYCIN HCL 125 MG CAPSULE	1	4	3	2	10
VANCOMYCIN HCL 1G/200 ML BAG	2	2			4
VANCOMYCIN HCL 250 MG CAPSULE	5	6	5	1	17
VANCOMYCIN HCL 5 GM VIAL	3	2	2		7
XIFAXAN 550 MG TABLET	33	41	28	24	126
ZOSYN 3.375 GM/50 ML GALAXY	4				4
Grand Total	**28827**	**34903**	**37891**	**28993**	**130615**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Antibiotic Utilization

July 1, 2017 - June 30, 2018

Q3 2017

Drug Name	Count of Members	Count of Claims	Sum Of Days Supply	Sum of Qty
Amoxicillin	13,065	13,709	1,992	1,082,999
Amox/clav	3,963	4,070	1,094	202,404
Cephalexin	4,411	4,555	772	292,755
Fluroquinolones	2,873	3,010	808	42,300
Macrolide	5,956	6,349	1,424	72,290
2nd gen cephalosporins	19	20	74	1,960
3rd gen cephalosporins	1,964	2,027	870	115,703
3rd gen quinolone	6	6	1424	32
4th gen cephalosporins	0	0	0	0
5th gen cephalosporins	54	55	121	1781

Q4 2017

Drug Name	Count of Members	Count of Claims	Sum Of Days Supply	Sum of Qty
Amoxicillin	16,934	17,797	2,003	1,656,047
Amox/clav	5,316	5,477	1,004	300,015
Cephalexin	4,167	4,308	809	299,659
Fluroquinolones	2,826	2,934	704	39,195
Macrolide	8,887	9,480	1,484	110,327
2nd gen cephalosporins	38	39	146	2,753
3rd gen cephalosporins	2,899	3,004	907	182,094
3rd gen quinolone	3	3	26	26
4th gen cephalosporins	5	8	8	431
5th gen cephalosporins	37	41	114	1234

Q1 2018

Drug Name	Count of Members	Count of Claims	Sum Of Days Supply	Sum of Qty
Amoxicillin	18,726	19,643	2,039	1,943,558
Amox/clav	5,925	6,104	1,247	361,441
Cephalexin	3,948	4,076	768	271,490
Fluroquinolones	2,867	2,971	673	38,095
Macrolide	10,299	10,954	1,466	125,144
2nd gen cephalosporins	30	30	117	3,038
3rd gen cephalosporins	3,600	3,730	960	227,054
3rd gen quinolone	11	11	45	90
4th gen cephalosporins	3	6	9	1226
5th gen cephalosporins	34	36	104	1343

Antibiotic Utilization (Cont)

Q2 2018				
Drug Name	Count of Members	Count of Claims	Sum Of Days Supply	Sum of Qty
Amoxicillin	13,364	13,956	1,741	1,251,886
Amox/clav	4,352	4,487	1,100	236,406
Cephalexin	3,960	4,087	683	274,002
Fluroquinolones	2,570	2,666	730	35,951
Macrolide	6,160	6,527	1,469	75,979
2nd gen cephalosporins	18	18	68	1,490
3rd gen cephalosporins	2,510	2,593	965	149,980
3rd gen quinolone	10	11	41	80
4th gen cephalosporins	0	0	0	0
5th gen cephalosporins	31	31	69	1047

Antibiotic Utilization - Q3 2017–Q2 2018

SilverSummith Healthplan

Antibiotic Class	Total Claims	Unique Members	Number of units	Days Supply
Aminoglycosides	13	13	374	123
Carbapenems	3	1	20	10
Cephalosporins	2,827	2,472	151,581	24,230
Fluroquinolones	1,440	1,226	18,121	10,900
Macrolides	4,958	3,999	81,232.50	28,500
Penicillins	8,370	6,579	569,412	74,809
Tetracyclines	978	735	28,794	16,297

Oncology Utilization

Fee for Service Medicaid
July 1, 2017 - June 30, 2018
Physician Administered Drug Claims

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
AVASTIN	426	1,323	1,323	9,722	$ 1,755,880.38
CARBOPLATIN	137	631	631	101,510	$ 27,428.41
PACLITAXEL	102	546	546	17,116	$ 31,270.95
LEUCOVORIN CALCIUM	70	484	484	5,619	$ 31,637.85
OPDIVO	51	420	420	19,932	$ 1,844,929.41
VINCRISTINE SULFATE	54	351	351	604	$ 3,284.09
OXALIPLATIN	64	342	342	8,902	$ 48,192.15
ADRUCIL	53	286	286	20,760	$ 7,037.35
RITUXAN	77	280	280	16,120	$ 1,129,993.97
HERCEPTIN	44	279	279	63,512	$ 1,026,631.21
FLUOROURACIL	38	241	241	15,512	$ 8,957.08
VELCADE	24	233	233	220	$ 299,401.57
CYCLOPHOSPHAMIDE	70	222	222	374	$ 234,403.31
ETOPOSIDE	27	208	208	27,823	$ 4,354.34
IRINOTECAN	40	205	205	2,991	$ 41,848.54
CISPLATIN	45	198	198	94,510	$ 5,842.35
DOCETAXEL	51	198	198	4,188	$ 164,330.25
GEMCITABINE HCL	47	190	190	1,289	$ 27,760.63
KEYTRUDA	39	180	180	1,412	$ 1,603,669.91
AZACITIDINE	9	160	160	226	$ 87,839.27
GEMCITABINE	31	160	160	8,821	$ 14,967.40
KYPROLIS	10	160	160	1,090	$ 329,085.93
DOXORUBICIN HCL	51	155	155	5,682	$ 7,532.27
METHOTREXATE SODIUM	33	129	129	344	$ 620.61
LUPRON DEPOT (3-MONTH)	64	124	124	125	$ 352,921.55
ERBITUX	14	116	116	25,351	$ 298,458.31
ABRAXANE	22	110	110	227	$ 285,089.88
LUPRON DEPOT (1-MONTH)	41	108	108	109	$ 126,381.89
FASLODEX	17	106	106	1,115	$ 184,451.33
ALIMTA	20	96	96	181	$ 432,992.10
CYTARABINE	9	90	90	541	$ 639.37
DARZALEX	7	84	84	3,330	$ 291,670.18
PERJETA	18	81	81	1,246	$ 412,066.61
CYRAMZA	7	73	73	2,830	$ 300,850.55
VECTIBIX	12	61	61	972	$ 202,869.76
DECITABINE	5	54	54	52	$ 69,290.65
VINBLASTINE SULFATE	5	53	53	575	$ 2,069.93
MEGESTROL ACETATE	25	46	46	780	$ 129.28
TOPOTECAN HCL	5	46	46	111	$ 4,109.15
TOPOSAR	9	45	45	460	$ 576.98
INTRON A	17	42	42	728	$ 76,052.45
BENDEKA	10	38	38	587	$ 120,078.46
HYDROXYUREA	22	38	38	62	$ 18.81
HALAVEN	5	35	35	186	$ 96,440.00
BLEOMYCIN SULFATE	7	34	34	44	$ 2,003.23
LUPRON DEPOT (6-MONTH)	27	34	34	55	$ 177,463.35
MESNA	9	33	33	632	$ 2,742.06
JEVTANA	11	32	32	216	$ 781,439.78

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
XOFIGO	6	29	29	3,258	$ 928,530.00
IRINOTECAN HYDROCHLORIDE	8	25	25	94	$ 747.30
EMPLICITI	1	23	23	69	$ 129,148.14
NAVELBINE	3	23	23	91	$ 1,717.96
VINCASAR PFS	12	23	23	39	$ 349.45
LUPRON DEPOT (4-MONTH)	13	20	20	20	$ 46,057.36
CLADRIBINE	1	18	18	180	$ 7,830.00
GEMZAR	14	18	18	18	$ 2,667.42
FIRMAGON	11	17	17	24	$ 15,238.14
GAZYVA	3	17	17	40,720	$ 104,305.92
KADCYLA	6	17	17	23	$ 67,236.80
DACOGEN	3	16	16	4	$ 2,299.12
ELIGARD	14	16	16	18	$ 22,167.84
IRINOTECAN HCL	9	15	15	160	$ 967.17
CLOFARABINE	1	14	14	560	$ 82,172.72
TAMOXIFEN CITRATE	8	14	14	37	$ 11.70
DACARBAZINE	2	13	13	61	$ 384.50
ONCASPAR	4	12	12	66	$ 56,070.92
TICE BCG	3	12	12	12	$ 1,836.46
DEPO-PROVERA	8	11	11	39	$ 4,540.60
MITOMYCIN	8	11	11	16	$ 6,963.57
ONIVYDE	4	10	10	4,310	$ 79,832.40
ARZERRA	1	8	8	715	$ 79,291.46
DOXORUBICIN HCL LIPOSOME	3	8	8	240	$ 23,256.20
FLUDARABINE PHOSPHATE	1	8	8	16	$ 2,175.04
IMFINZI	3	8	8	67	$ 23,462.18
METHOTREXATE	6	8	8	30	$ 27.30
THERACYS	1	8	8	8	$ 1,365.28
YERVOY	4	6	6	250	$ 174,918.39
ZOLADEX	2	6	6	6	$ 3,630.00
ANASTROZOLE	4	5	5	5	$ 0.74
LEVOLEUCOVORIN	2	5	5	350,875	$ 1,302.00
RITUXAN HYCELA	2	4	4	47	$ 25,294.52
ZALTRAP	1	4	4	32	$ 12,800.00
BICALUTAMIDE	2	3	3	3	$ 0.55
DOXIL	2	3	3	130	$ 14,492.36
ELITEK	3	3	3	7	$ 8,723.66
IFOSFAMIDE	1	3	3	360	$ 645.24
IXEMPRA KIT	2	3	3	7	$ 5,731.62
TECENTRIQ	2	3	3	260	$ 45,229.30
TREANDA	2	3	3	13	$ 8,719.21
VIDAZA	1	3	3	5	$ 3,019.83
COSMEGEN	1	2	2	10	$ 16,894.60
DACTINOMYCIN	1	2	2	4	$ 9.50
DOCETAXEL (NON-ALCOHOL FO	2	2	2	7	$ 1,397.50
FEMARA	1	2	2	2	$ 2.00
LETROZOLE	2	2	2	2	$ 0.28
PROVENGE	1	2	2	251	$ 47,200.63
CAPECITABINE	1	1	1	4	$ 18.95
DAUNORUBICIN HCL	1	1	1	8	$ 268.28
FUSILEV	1	1	1	2	$ 40.00
TORISEL	1	1	1	1	$ 1,718.05

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
TRELSTAR MIXJECT	1	1	1	1	$ 2,439.72
VANTAS	1	1	1	1	$ 3,668.28
Total					**$ 15,026,523.05**

Oncology Utilization

Fee for Service Medicaid

July 1, 2017 - June 30, 2018

Pharmacy Point of Sale

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
METHOTREXATE	411	1,891	63,830	59,031	$ 55,225.95
MEGESTROL ACETATE	436	1,333	37,941	377,634	$ 25,060.07
ANASTROZOLE	206	1,001	44,573	41,014	$ 11,956.10
TAMOXIFEN CITRATE	136	650	27,600	28,620	$ 17,711.29
LETROZOLE	122	645	25,320	25,530	$ 7,951.60
HYDROXYUREA	99	434	14,977	30,476	$ 11,417.73
MERCAPTOPURINE	43	241	7,964	12,597	$ 16,402.80
EXEMESTANE	41	176	7,146	7,146	$ 21,965.45
CAPECITABINE	41	150	3,280	11,654	$ 73,116.52
BICALUTAMIDE	35	128	5,710	5,710	$ 1,031.59
AFINITOR	12	106	2,960	3,324	$ 1,619,473.28
IBRANCE	16	102	2,772	2,086	$ 1,041,081.04
METHOTREXATE SODIUM	38	96	3,235	548	$ 1,975.47
LEUCOVORIN CALCIUM	23	83	3,044	3,058	$ 9,801.76
IMATINIB MESYLATE	11	62	2,250	2,340	$ 207,152.08
SPRYCEL	8	55	1,710	1,710	$ 645,640.99
TEMOZOLOMIDE	6	50	981	401	$ 24,740.93
HERCEPTIN	5	36	567	96	$ 145,000.02
OPDIVO	4	32	686	664	$ 171,273.86
PACLITAXEL	10	31	553	2,176	$ 4,852.39
ZYTIGA	8	28	840	2,670	$ 199,627.24
TASIGNA	4	27	756	2,800	$ 281,674.16
RITUXAN	6	23	656	2,170	$ 192,354.02
XTANDI	2	22	660	2,640	$ 233,454.76
LUPRON DEPOT (3-MONTH)	13	20	1,788	20	$ 59,856.59
POMALYST	4	20	504	364	$ 240,135.21
VOTRIENT	4	17	510	2,040	$ 183,013.56
CYCLOPHOSPHAMIDE	6	16	289	212	$ 12,065.62
TREXALL	5	16	510	108	$ 2,603.57
ACTIMMUNE	2	14	392	84	$ 694,941.66
AVASTIN	2	14	288	308	$ 59,336.11
LUPRON DEPOT (1-MONTH)	6	13	388	13	$ 15,281.85
TYKERB	5	13	363	1,584	$ 74,059.33
IMBRUVICA	3	12	350	770	$ 136,835.99
TAGRISSO	1	12	360	360	$ 172,965.36
CARBOPLATIN	3	11	232	1,095	$ 1,711.25
FASLODEX	1	11	266	110	$ 20,918.72
TARCEVA	4	11	330	345	$ 52,877.87
AFINITOR DISPERZ	1	10	300	795	$ 361,117.15
BOSULIF	2	10	300	300	$ 138,875.20
NEXAVAR	5	10	225	840	$ 102,123.51
TRETINOIN	3	9	241	1,008	$ 24,555.64
HYCAMTIN	1	8	168	80	$ 26,209.16
ICLUSIG	1	8	240	300	$ 165,691.36
PURIXAN	4	8	254	1,465	$ 16,380.02
DOCETAXEL	2	7	127	104	$ 5,375.82
GEMCITABINE HCL	3	6	78	12	$ 1,362.71

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
GLEEVEC	2	6	180	180	$ 58,950.50
PERJETA	1	6	126	140	$ 48,726.62
DOXORUBICIN HCL	3	5	77	325	$ 443.14
TAFINLAR	1	5	150	192	$ 11,617.80
CALQUENCE	1	4	120	240	$ 56,296.68
NERLYNX	1	4	120	720	$ 45,820.68
TABLOID	3	4	42	86	$ 1,380.68
ALECENSA	1	3	114	720	$ 39,971.34
ALIMTA	2	3	24	5	$ 16,683.34
BENDEKA	1	3	84	48	$ 29,328.11
CISPLATIN	2	3	49	102	$ 61.11
DEPO-PROVERA	2	3	204	6	$ 1,241.67
ETOPOSIDE	2	3	15	15	$ 225.96
VENCLEXTA	1	3	90	180	$ 16,756.32
VERZENIO	2	3	84	168	$ 33,874.11
GLEOSTINE	1	2	84	8	$ 2,167.20
IRINOTECAN HYDROCHLORIDE	2	2	2	6	$ 47.70
JAKAFI	2	2	60	90	$ 7.40
KISQALI	1	2	56	126	$ 27,900.78
LYNPARZA	1	2	30	120	$ 3,390.84
COTELLIC	1	1	28	63	$ 7,015.14
ELIGARD	1	1	84	1	$ 1,365.24
ERBITUX	1	1	1	300	$ 3,566.34
FLUOROURACIL	1	1	1	12	$ 11.28
GILOTRIF	1	1	30	30	$ 8,164.94
MELPHALAN	1	1	10	50	$ 122.75
MESNEX	1	1	4	8	$ 638.90
RYDAPT	1	1	31	56	$ 7,505.17
STIVARGA	1	1	28	84	$ 14,891.66
SUTENT	1	1	42	28	$ 17,029.37
TICE BCG	1	1	7	1	$ 158.22
VENCLEXTA STARTING PACK	1	1	28	42	$ 2,416.83
XATMEP	1	1	56	120	$ 1,906.17
ZELBORAF	1	1	28	224	$ 10,137.59
Total					**$ 8,058,055.94**

Anthem Oncology (Claims from Pharmacy Benefit only for timeframe)

	3Q 2017	4Q 2017	1Q 2018	2Q 2018	TOTAL
AFINITOR 10 MG TABLET	3	4	3	2	12
AFINITOR 2.5 MG TABLET		1	2		3
AFINITOR 5 MG TABLET		5	3	3	11
ALECENSA 150 MG CAPSULE	2	2	1	1	6
ANASTROZOLE 1 MG TABLET	141	128	138	136	543
AVASTIN 400 MG/16 ML VIAL	3				3
BICALUTAMIDE 50 MG TABLET	2	10	5	12	29
CAPECITABINE 150 MG TABLET	3		2	1	6
CAPECITABINE 500 MG TABLET	7	7	16	13	43
CYCLOPHOSPHAMIDE 50 MG CAPSULE	2	2	1	1	6
EXEMESTANE 25 MG TABLET	30	29	27	29	115
FIRMAGON 2 X 120 MG KIT			1	2	3
FLUTAMIDE 125 MG CAPSULE	1				1
HYDROXYPROGESTERONE 1.25 G/5ML	1			1	2
HYDROXYUREA 500 MG CAPSULE	31	19	24	23	97
IBRANCE 100 MG CAPSULE	3		2	4	9
IBRANCE 125 MG CAPSULE	8	6	7	6	27
IMATINIB MESYLATE 100 MG TAB		2	2	2	6
IMATINIB MESYLATE 400 MG TAB	16	13	15	17	61
IMBRUVICA 140 MG CAPSULE	3	2	4	3	12
IMBRUVICA 420 MG TABLET				1	1
LENVIMA 18 MG DAILY DOSE		4	3	3	10
LETROZOLE 2.5 MG TABLET	79	74	63	78	294
LEUCOVORIN CALCIUM 10 MG TAB				1	1
LEUCOVORIN CALCIUM 25 MG TAB	2	3	4	6	15
LEUCOVORIN CALCIUM 5 MG TAB	8	14	15	14	51
LONSURF 15 MG-6.14 MG TABLET		1	3		4
LONSURF 20 MG-8.19 MG TABLET		1	3		4
LUPRON DEPOT 11.25 MG 3MO KIT	6	4	6	6	22
LUPRON DEPOT 22.5 MG 3MO KIT		1		1	2
LUPRON DEPOT 3.75 MG KIT	7	9	12	17	45
LUPRON DEPOT 45 MG 6MO KIT		3		1	4
LUPRON DEPOT 7.5 MG KIT	1				1
MEGESTROL 20 MG TABLET	10	10	9	8	37
MEGESTROL 40 MG TABLET	23	15	20	22	80
MEGESTROL ACET 40 MG/ML SUSP	77	72	76	75	300
MERCAPTOPURINE 50 MG TABLET	32	31	26	22	111
METHOTREXATE 2.5 MG TABLET	311	270	214	236	1031
METHOTREXATE 250 MG/10 ML VIAL		1	1	1	3

Anthem Oncology					
	3Q 2017	**4Q 2017**	**1Q 2018**	**2Q 2018**	**TOTAL**
METHOTREXATE 50 MG/2 ML VIAL	16	11	15	17	59
NERLYNX 40 MG TABLET		4	1	4	9
NEXAVAR 200 MG TABLET			4	4	8
ODOMZO 200 MG CAPSULE				1	1
OPDIVO 100 MG/10 ML VIAL	1				1
OPDIVO 40 MG/4 ML VIAL	1				1
POMALYST 2 MG CAPSULE	3	3	1		7
POMALYST 4 MG CAPSULE	1				1
RYDAPT 25 MG CAPSULE			1		1
SPRYCEL 100 MG TABLET	2	2	6	4	14
SUTENT 50 MG CAPSULE	3	1			4
TABLOID 40 MG TABLET	2		2	2	6
TAMOXIFEN 10 MG TABLET	4	4	7	9	24
TAMOXIFEN 20 MG TABLET	89	90	82	76	337
TARCEVA 150 MG TABLET	2	3	3	3	11
TASIGNA 150 MG CAPSULE	6	7	5	3	21
TEMOZOLOMIDE 100 MG CAPSULE	3	2	2		7
TEMOZOLOMIDE 140 MG CAPSULE	1			2	3
TEMOZOLOMIDE 180 MG CAPSULE	3	1			4
TEMOZOLOMIDE 250 MG CAPSULE	6	2	3		11
TEMOZOLOMIDE 5 MG CAPSULE	6			2	8
TRETINOIN 10 MG CAPSULE	1			1	2
TREXALL 5 MG TABLET	3	2	1	1	7
TREXALL 7.5 MG TABLET				1	1
VOTRIENT 200 MG TABLET			2	7	9
XALKORI 250 MG CAPSULE			1	1	2
ZEJULA 100 MG CAPSULE	3				3
ZYDELIG 150 MG TABLET		1			1
ZYTIGA 250 MG TABLET	5				5
Grand Total	**973**	**876**	**844**	**886**	**3580**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Oncology Utilization

July 1, 2017 - June 30, 2018

Q3 2017 - POS - 1 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
AFINITOR TAB 10MG	1	2	28	56
AFINITOR TAB 5MG	1	3	28	84
ALECENSA CAP 150MG	1	3	30	720
ANASTROZOLE TAB 1MG	106	219	106	5,485
BICALUTAMIDE TAB 50MG	9	21	58	622
BOSULIF TAB 500MG	1	1	30	30
CAPECITABINE TAB 150MG	2	5	49	392
CAPECITABINE TAB 500MG	13	26	63	2,198
CYCLOPHOSPH CAP 50MG	4	7	30	450
ERIVEDGE CAP 150MG	1	3	30	90
EXEMESTANE TAB 25MG	12	28	30	789
GILOTRIF TAB 30MG	1	4	30	120
HYDROXYUREA CAP 500MG	21	40	89	2,285
IBRANCE CAP 100MG	1	1	28	21
IBRANCE CAP 125MG	5	8	28	168
IMATINIB MES TAB 100MG	1	1	30	30
IMATINIB MES TAB 400MG	4	12	30	360
IMBRUVICA CAP 140MG	2	3	30	300
INTRON A INJ 10MU	1	1	14	1
JAKAFI TAB 10MG	1	1	30	60
JAKAFI TAB 5MG	1	1	30	60
LETROZOLE TAB 2.5MG	56	124	104	3,606
LEUCOVOR CA TAB 5MG	15	29	58	283
MEGESTROL AC SUS 40MG/ML	64	111	180	37,360
MEGESTROL AC TAB 20MG	16	26	81	975
MEGESTROL AC TAB 40MG	15	21	54	1,428
MEKINIST TAB 2MG	2	4	30	120
MERCAPTOPUR TAB 50MG	18	31	58	1,822
METHOTREXATE INJ 25MG/ML	12	18	117	82
METHOTREXATE INJ 50MG/2ML	4	5	58	22
METHOTREXATE TAB 2.5MG	303	566	261	13,972
MYLERAN TAB 2MG	1	3	30	180
NEXAVAR TAB 200MG	4	11	30	780
POMALYST CAP 4MG	2	2	28	42
SPRYCEL TAB 100MG	3	6	30	180

Q3 2017 - POS - 2 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
SPRYCEL TAB 140MG	2	4	30	120
SPRYCEL TAB 20MG	1	3	30	270
SPRYCEL TAB 50MG	1	1	30	30
SPRYCEL TAB 70MG	2	4	30	120
SUTENT CAP 50MG	1	1	28	28
TAFINLAR CAP 75MG	2	4	30	480
TAGRISSO TAB 40MG	1	1	30	30
TAGRISSO TAB 80MG	1	2	30	60
TAMOXIFEN TAB 10MG	6	9	30	450
TAMOXIFEN TAB 20MG	56	130	30	3,990
TARCEVA TAB 100MG	1	4	30	120
TARCEVA TAB 150MG	1	4	30	120
TASIGNA CAP 150MG	4	11	28	1,148
TEMOZOLOMIDE CAP 100MG	1	3	5	15
TEMOZOLOMIDE CAP 140MG	1	3	5	30
VENCLEXTA TAB START PK	1	1	28	42
XALKORI CAP 250MG	1	1	30	60
ZEJULA CAP 100MG	1	1	30	90

Q3 2017 - PAD - 1 of 2			
Drug Name	Count of Members	Count of Claims	Sum of Qty
DOXORUBICIN HCL, 10 MG	43	43	55
INJECTION, BENDAMUSTINE HCL BENDEKA., 1 MG	15	15	25
INJECTION, BEVACIZUMAB, 10 MG	120	120	219
INJECTION, BLINATUMOMAB, 1 MICROGRAM (BLINCYTO)	2	2	4
BLEOMYCIN SULFATE, 15 UNITS	16	16	24
BORTEZOMIB INJECTION	6	6	14
CARBOPLATIN, 50 MG	52	52	75
INJECTION, CARFILZOMIB, 1 MG	9	9	23
CISPLATIN, POWDEROR S0LUTION, PER 10 MG	38	38	75
CYCLOPHOSPHAMIDE, 100 MG	48	48	64
DACTINOMYCIN, 0.5 MG	6	6	7
DACARBAZINE, 100 MG	7	7	11
INJECTION, DARATUMUMAB, 10 MG	2	2	7
DOCETAXEL INJECTION	44	44	60
ETOPOSIDE, 10 MG	13	13	35
FLUDARABINE PHOSPHATE, 50 MG	1	1	2
FLUOROURACIL, 500 MG	38	38	75

Q3 2017 - PAD - 2 of 2			
Drug Name	**Count of Members**	**Count of Claims**	**Sum of Qty**
GEMCITABINE HC1, 200 MG	19	19	36
GOSERELIN ACETATE IMPLANT, PER 3.6 MG	5	5	5
IRINOTECAN, 20 MG	18	18	29
IFOSFAMIDE, 1 GM	4	4	8
MESNA, 200 MG	6	6	10
LEUPROLIDE ACETATE (FOR DEPOT SUSPENSION), 7.5 MG	16	16	18
SUPPRELIN LA IMPLANT	1	1	1
INJECTION, IPILIMUMAB, 1MG	4	4	4
METHOTREXATE SODIUM, 50 MG	11	11	17
INJECTION, OXALIPLATIN, 0.5 MG	25	25	45
PACLITAXEL INJECTION	4	4	6
INJECTION, PACLITAXEL, 1 MG	47	47	75
INJECTION, NIVOLUMAB, 1 MG (OPDIVO)	9	9	15
PEMETREXED INJECTION	12	12	12
INJECTION, PERTUZUMAB, 1 MG	14	14	18
INJECTION, RAMUCIRUMAB, 5 MG (CYRAMZA)	3	3	4
RITUXIMAB, 100 MG	43	43	58
TRASTUZUMAB, 10 MG	44	44	57
VINBLASTINE SULFATE, 1 MG	7	7	11
VINCRISTINE SULFATE, 1 MG	33	33	67
VINORELBINE TARTRATE, PER 10 MG	3	3	6
INJECTION, FULVESTRANT, 25 MG	1	1	1
INJECTION, ZIV-AFLIBERCEPT, 1 MG	4	4	5
NOT OTHERWISE CLASSIFIED, ANTINEOPLASTIC	3	3	8

J-CODES PROCESSED INCLUDE: J9000 TO J9999

Q4 2017 - POS - 1 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
AFINITOR TAB 10MG	3	3	14	42
AFINITOR TAB 7.5MG	2	2	28	56
ANASTROZOLE TAB 1MG	229	229	135	5529
BICALUTAMIDE TAB 50MG	16	16	58	474
BOSULIF TAB 100MG	1	1	15	60
BOSULIF TAB 500MG	3	3	30	90
CAPECITABINE TAB 150MG	9	9	35	504
CAPECITABINE TAB 500MG	26	26	93	2390
CYCLOPHOSPH CAP 50MG	3	3	58	190
ERIVEDGE CAP 150MG	3	3	30	90
EXEMESTANE TAB 25MG	21	21	30	613
GILOTRIF TAB 30MG	3	3	30	90
HYDROXYUREA CAP 500MG	45	45	83	2589
IBRANCE CAP 100MG	3	3	28	63
IBRANCE CAP 125MG	12	12	28	252
IBRANCE CAP 75MG	2	2	28	42
IMATINIB MES TAB 400MG	14	14	30	420
IMBRUVICA CAP 140MG	6	6	30	600
INTRON A INJ 10MU	5	5	42	16
LETROZOLE TAB 2.5MG	156	156	88	4515
LEUCOVOR CA TAB 10MG	1	1	3	30
LEUCOVOR CA TAB 25MG	4	4	58	42
LEUCOVOR CA TAB 5MG	27	27	58	279
LUPRON DEPOT INJ 11.25MG	1	1	90	1
LUPRON DEPOT INJ 3.75MG	2	2	30	2
MEGESTROL AC SUS 40MG/ML	88	88	214	28850
MEGESTROL AC TAB 20MG	18	18	35	725
MEGESTROL AC TAB 40MG	23	23	55	1380
MEKINIST TAB 2MG	3	3	30	90
MERCAPTOPUR TAB 50MG	47	47	101	2440
METHOTREXATE INJ 25MG/ML	19	19	145	154
METHOTREXATE INJ 50MG/2ML	9	9	58	52
METHOTREXATE TAB 2.5MG	567	567	238	14439
NEXAVAR TAB 200MG	7	7	45	375
SPRYCEL TAB 100MG	6	6	30	180
SPRYCEL TAB 140MG	8	8	45	210
SPRYCEL TAB 20MG	3	3	30	270
SPRYCEL TAB 70MG	3	3	30	90
STIVARGA TAB 40MG	3	3	28	252
SUTENT CAP 50MG	2	2	28	56
TAFINLAR CAP 75MG	3	3	30	360
TAGRISSO TAB 40MG	3	3	30	90
TAMOXIFEN TAB 10MG	6	6	30	210
TAMOXIFEN TAB 20MG	116	116	30	3480

Q4 2017 - POS - 2 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
TARCEVA TAB 100MG	3	3	30	90
TARCEVA TAB 150MG	5	5	30	150
TASIGNA CAP 150MG	17	17	42	1624
TEMOZOLOMIDE CAP 100MG	4	4	33	20
TEMOZOLOMIDE CAP 140MG	1	1	5	10
TEMOZOLOMIDE CAP 180MG	3	3	28	30
TRETINOIN CAP 10MG	2	2	44	410
VENCLEXTA TAB 100MG	2	2	30	240
VOTRIENT TAB 200MG	3	3	15	180
XTANDI CAP 40MG	6	6	30	720
ZEJULA CAP 100MG	1	1	30	90
ZYTIGA TAB 250MG	3	3	30	360

Q4 2017 - PAD 1 of 2			
Drug Name	Count of Members	Count of Claims	Sum of Qty
DOXORUBICIN HCL, 10 MG	23	23	26
INJECTION, BENDAMUSTINE HCL BENDEKA., 1 MG	13	13	23
INJECTION, BEVACIZUMAB, 10 MG	130	130	242
INJECTION, BLINATUMOMAB, 1 MICROGRAM (BLINCYTO)	5	5	14
BLEOMYCIN SULFATE, 15 UNITS	4	4	6
BORTEZOMIB INJECTION	9	9	24
CARBOPLATIN, 50 MG	50	50	73
INJECTION, CARFILZOMIB, 1 MG	7	7	18
CETUXIMAB INJECTION, 10 MG	6	6	14
CISPLATIN, POWDEROR S0LUTION, PER 10 MG	33	33	64
CYCLOPHOSPHAMIDE, 100 MG	33	33	42
CYTARABINE 100 MG	10	10	24
DACTINOMYCIN, 0.5 MG	4	4	4
DACARBAZINE, 100 MG	1	1	2
DAUNORUBICIN HYDROCHLORIDE, 10 MG	1	1	2
DOCETAXEL INJECTION	34	34	46
INJECTION, ELOTUZUMAB, 1 MG	2	2	5
INJECTION, ERIBULIN MESYLATE, 0.1 MG	3	3	6
ETOPOSIDE, 10 MG	17	17	35
FLUDARABINE PHOSPHATE, 50 MG	4	4	6
FLUOROURACIL, 500 MG	58	58	89
GEMCITABINE HC1, 200 MG	28	28	49

Q4 2017 - PAD 2 of 2			
Drug Name	Count of Members	Count of Claims	Sum of Qty
GOSERELIN ACETATE IMPLANT, PER 3.6 MG	6	6	8
IRINOTECAN, 20 MG	23	23	41
IXABEPILONE INJECTION	1	1	1
IFOSFAMIDE, 1 GM	4	4	7
MESNA, 200 MG	6	6	8
LEUPROLIDE ACETATE (FOR DEPOT SUSPENSION), 7.5 MG	13	13	14
SUPPRELIN LA IMPLANT	2	2	2
INJECTION, IPILIMUMAB, 1MG	1	1	1
METHOTREXATE SODIUM, 50 MG	12	12	17
INJECTION, OXALIPLATIN, 0.5 MG	30	30	37
PACLITAXEL INJECTION	2	2	3
PEGASPARGASE, PER SINGLE DOSE VIAL	4	4	5
INJECTION, PACLITAXEL, 1 MG	62	62	101
INJECTION, PEMBROLIZUMAB, 1 MG (KEYTRUDA)	4	4	5
MITOMYCIN, 5 MG	1	1	2
INJECTION, NIVOLUMAB, 1 MG (OPDIVO)	14	14	18
PEMETREXED INJECTION	11	11	13
INJECTION, PERTUZUMAB, 1 MG	10	10	13
INJECTION, RAMUCIRUMAB, 5 MG (CYRAMZA)	2	2	2
RITUXIMAB, 100 MG	35	35	43
INJECTION, ADO-TRASTUZUMBA EMTANSINE, 1 MG	1	1	1
TRASTUZUMAB, 10 MG	33	33	43
VINBLASTINE SULFATE, 1 MG	4	4	7
VINCRISTINE SULFATE, 1 MG	23	23	45
VINORELBINE TARTRATE, PER 10 MG	2	2	4
INJECTION, FULVESTRANT, 25 MG	7	7	8
INJECTION, ZIV-AFLIBERCEPT, 1 MG	1	1	1
NOT OTHERWISE CLASSIFIED, ANTINEOPLASTIC DRUGS	5	5	5

J-CODES PROCESSED INCLUDE: J9000 TO J9999

Q1 2018 - POS - 1 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
AFINITOR TAB 10MG	3	9	14	42
AFINITOR TAB 7.5MG	1	2	28	56
ANASTROZOLE TAB 1MG	106	232	230	5529
BICALUTAMIDE TAB 50MG	11	24	58	474
BOSULIF TAB 100MG	1	1	15	60
CAPECITABINE TAB 150MG	7	14	63	90
CAPECITABINE TAB 500MG	17	32	63	504
CYCLOPHOSPH CAP 50MG	3	5	83	2390
EXEMESTANE TAB 25MG	10	25	30	190
GILOTRIF TAB 30MG	1	3	30	90
HYDROXYUREA CAP 500MG	28	55	90	613
IBRANCE CAP 100MG	2	4	28	90
IBRANCE CAP 125MG	5	10	28	2589
ICLUSIG TAB 45MG	1	2	30	63
IMATINIB MES TAB 400MG	7	17	30	252
IMBRUVICA CAP 140MG	4	9	30	42
JAKAFI TAB 10MG	1	3	30	420
LENVIMA CAP 14 MG	1	3	30	600
LETROZOLE TAB 2.5MG	58	124	89	16
LEUCOVOR CA TAB 25MG	2	5	28	4515
LEUCOVOR CA TAB 5MG	10	21	58	30
LONSURF TAB 20-8.19	1	2	28	42
LUPRON DEPOT INJ 3.75MG	2	2	30	279
MEGESTROL AC SUS 40MG/ML	43	66	153	1
MEGESTROL AC TAB 20MG	7	14	55	2
MEGESTROL AC TAB 40MG	17	26	54	28850
MEKINIST TAB 2MG	2	4	30	725
MERCAPTOPUR TAB 50MG	26	50	117	1380
METHOTREXATE INJ 25MG/ML	9	14	174	90
METHOTREXATE INJ 50MG/2ML	7	13	104	2440
METHOTREXATE TAB 2.5MG	273	522	193	154
NEXAVAR TAB 200MG	2	2	45	52
POMALYST CAP 4MG	1	1	28	14439
SPRYCEL TAB 100MG	1	1	30	375
SPRYCEL TAB 140MG	2	5	30	180
SPRYCEL TAB 20MG	1	4	30	210
SPRYCEL TAB 50MG	1	1	15	270
SUTENT CAP 50MG	1	1	28	90
TABLOID TAB 40MG	1	1	14	252
TAFINLAR CAP 75MG	2	4	30	56
TAMOXIFEN TAB 10MG	2	2	30	360
TAMOXIFEN TAB 20MG	54	130	30	90
TARCEVA TAB 100MG	1	3	30	210
TARCEVA TAB 150MG	1	3	30	3480

Q1 2018 - POS - 2 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
TASIGNA CAP 150MG	9	20	42	90
TASIGNA CAP 200MG	1	2	28	150
TRETINOIN CAP 10MG	1	1	28	1624
VOTRIENT TAB 200MG	2	5	15	20
XTANDI CAP 40MG	2	4	30	10

Q1 2018 - PAD - 1 of 2			
Drug Name	Count of Members	Count of Claims	Sum of Qty
DOXORUBICIN HCL, 10 MG	27	27	41
ARSENIC TRIOXIDE, 1 MG (TRISENOX)	5	5	21
INJECTION, ATEZOLIZUMAB, 10 MG	3	3	5
INJECTION, BENDAMUSTINE HCL BENDEKA., 1 MG	12	12	23
INJECTION, BEVACIZUMAB, 10 MG	148	148	281
BLEOMYCIN SULFATE, 15 UNITS	5	5	7
BORTEZOMIB INJECTION	10	10	29
CARBOPLATIN, 50 MG	34	34	46
INJECTION, CARFILZOMIB, 1 MG	3	3	8
CETUXIMAB INJECTION, 10 MG	10	10	18
CISPLATIN, POWDEROR S0LUTION, PER 10 MG	29	29	45
CYCLOPHOSPHAMIDE, 100 MG	33	33	50
CYTARABINE 100 MG	6	6	37
DACARBAZINE, 100 MG	1	1	1
DOCETAXEL INJECTION	21	21	29
INJECTION, ERIBULIN MESYLATE, 0.1 MG	1	1	2
ETOPOSIDE, 10 MG	19	19	66
FLUOROURACIL, 500 MG	77	77	130
GEMCITABINE HC1, 200 MG	19	19	34
IRINOTECAN, 20 MG	34	34	53
IFOSFAMIDE, 1 GM	2	2	7
MESNA, 200 MG	4	4	10
LEUPROLIDE ACETATE (FOR DEPOT SUSPENSION), 7.5 MG	18	18	20
INJECTION, IPILIMUMAB, 1MG	2	2	2
METHOTREXATE SODIUM, 50 MG	13	13	21
INJECTION, OXALIPLATIN, 0.5 MG	38	38	56
PACLITAXEL INJECTION	4	4	6
PEGASPARGASE, PER SINGLE DOSE VIAL	3	3	3
INJECTION, PACLITAXEL, 1 MG	32	32	49

Q1 2018 - PAD - 2 of 2			
Drug Name	**Count of Members**	**Count of Claims**	**Sum of Qty**
INJECTION, PEMBROLIZUMAB, 1 MG (KEYTRUDA)	8	8	9
MITOMYCIN, 5 MG	1	1	1
INJECTION, NIVOLUMAB, 1 MG (OPDIVO)	17	17	24
PANITUMUMAB INJECTION	1	1	1
PEMETREXED INJECTION	16	16	18
INJECTION, PERTUZUMAB, 1 MG	10	10	13
INJECTION, RAMUCIRUMAB, 5 MG (CYRAMZA)	3	3	3
RITUXIMAB, 100 MG	33	33	42
INJECTION, ADO-TRASTUZUMBA EMTANSINE, 1 MG	5	5	5
TRASTUZUMAB, 10 MG	28	28	36
VINBLASTINE SULFATE, 1 MG	2	2	3
VINCRISTINE SULFATE, 1 MG	27	27	43
INJECTION, FULVESTRANT, 25 MG	6	6	6

J-CODES PROCESSED INCLUDE: J9000 TO J9999

Q2 2018 - POS - 1 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
AFINITOR TAB 10MG	2	6	42	112
AFINITOR TAB 7.5MG	1	3	28	84
AFINITOR DIS TAB 3MG	1	3	14	84
ANASTROZOLE TAB 1MG	110	250	191	6150
BICALUTAMIDE TAB 50MG	12	24	58	718
CABOMETYX TAB 60MG	1	2	15	30
CAPECITABINE TAB 150MG	4	7	35	394
CAPECITABINE TAB 500MG	12	28	49	2836
COTELLIC TAB 20MG	1	1	28	63
CYCLOPHOSPH CAP 50MG	2	3	30	150
EXEMESTANE TAB 25MG	12	28	30	840
HYDROXYUREA CAP 500MG	23	43	97	2380
IBRANCE CAP 100MG	2	6	28	126
IBRANCE CAP 125MG	3	7	28	147
ICLUSIG TAB 45MG	1	2	30	60
IMATINIB MES TAB 100MG	1	1	30	60
IMATINIB MES TAB 400MG	6	17	30	555
IMBRUVICA CAP 140MG	1	1	30	90
IMBRUVICA TAB 140MG	1	1	28	112
IMBRUVICA TAB 420MG	1	2	28	56
IMBRUVICA TAB 560MG	1	2	28	56
JAKAFI TAB 10MG	1	3	30	180
LENVIMA CAP 14 MG	1	2	30	120
LETROZOLE TAB 2.5MG	52	132	35	3854
LEUCOVOR CA TAB 25MG	3	5	33	21
LEUCOVOR CA TAB 5MG	9	17	101	206
LONSURF TAB 20-8.19	1	1	28	60
LUPRON DEPOT INJ 11.25MG	3	3	120	3
LUPRON DEPOT INJ 3.75MG	2	3	30	3
MEGESTROL AC SUS 40MG/ML	50	79	148	25670
MEGESTROL AC TAB 20MG	7	11	30	480
MEGESTROL AC TAB 40MG	18	29	94	1663
MEKINIST TAB 2MG	2	4	30	120
MERCAPTOPUR TAB 50MG	23	48	123	2541
METHOTREXATE INJ 25MG/ML	14	18	175	72
METHOTREXATE INJ 50MG/2ML	8	11	79	60
METHOTREXATE TAB 2.5MG	279	551	240	13487
NERLYNX TAB 40MG	1	1	30	180
NEXAVAR TAB 200MG	1	1	15	60
POMALYST CAP 4MG	1	3	21	63
SPRYCEL TAB 140MG	1	2	30	60
SPRYCEL TAB 20MG	1	3	30	270
SPRYCEL TAB 50MG	1	2	15	30
TABLOID TAB 40MG	3	4	73	89

Q2 2018 - POS - 2 of 2				
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
TAFINLAR CAP 75MG	2	4	30	420
TAGRISSO TAB 80MG	1	2	30	60
TAMOXIFEN TAB 10MG	2	2	30	60
TAMOXIFEN TAB 20MG	53	132	51	4032
TARCEVA TAB 100MG	2	5	45	120
TARCEVA TAB 150MG	2	6	45	120
TASIGNA CAP 150MG	8	20	35	1904
TASIGNA CAP 200MG	1	2	28	224
TEMOZOLOMIDE CAP 100MG	1	2	21	42
TEMOZOLOMIDE CAP 140MG	1	1	42	42
TEMOZOLOMIDE CAP 20MG	1	2	21	42
TEMOZOLOMIDE CAP 5MG	1	1	42	84
TRETINOIN CAP 10MG	1	1	30	300
VENCLEXTA TAB 100MG	1	1	30	120
VOTRIENT TAB 200MG	1	4	15	240
XTANDI CAP 40MG	2	5	45	480
ZELBORAF TAB 240MG	1	1	28	224
ZYTIGA TAB 250MG	1	1	30	120
ZYTIGA TAB 500MG	1	3	30	180

Q2 2018 - PAD - 1 of 2			
Drug Name	Count of Members	Count of Claims	Sum of Qty
DOXORUBICIN HCL, 10 MG	22	22	32
INJECTION, ATEZOLIZUMAB, 10 MG	3	3	3
BCG (INTRAVESICAL) PER INSTALLATION	1	1	2
INJECTION, BENDAMUSTINE HCL BENDEKA., 1 MG	9	9	14
INJECTION, BEVACIZUMAB, 10 MG	103	103	208
BLEOMYCIN SULFATE, 15 UNITS	8	8	15
BORTEZOMIB INJECTION	12	12	36
CARBOPLATIN, 50 MG	41	41	64
INJECTION, CARFILZOMIB, 1 MG	3	3	13
CETUXIMAB INJECTION, 10 MG	5	5	10
CISPLATIN, POWDEROR S0LUTION, PER 10 MG	23	23	37
CYCLOPHOSPHAMIDE, 100 MG	22	22	27
CYTARABINE 100 MG	5	5	14
DACARBAZINE, 100 MG	2	2	5
INJECTION, DARATUMUMAB, 10 MG	2	2	10
DAUNORUBICIN HYDROCHLORIDE, 10 MG	1	1	2
DOCETAXEL INJECTION	14	14	17

Q2 2018 - PAD - 2 of 2			
Drug Name	Count of Members	Count of Claims	Sum of Qty
INJECTION, ERIBULIN MESYLATE, 0.1 MG	1	1	1
ETOPOSIDE, 10 MG	23	23	58
FLUOROURACIL, 500 MG	59	59	98
GEMCITABINE HC1, 200 MG	21	21	29
IRINOTECAN, 20 MG	23	23	37
IFOSFAMIDE, 1 GM	2	2	6
MESNA, 200 MG	2	2	6
LEUPROLIDE ACETATE (FOR DEPOT SUSPENSION), 7.5 MG	17	17	21
SUPPRELIN LA IMPLANT	1	1	1
INJECTION, IPILIMUMAB, 1MG	4	4	5
METHOTREXATE SODIUM, 50 MG	12	12	25
INJECTION, OXALIPLATIN, 0.5 MG	32	32	54
PACLITAXEL INJECTION	6	6	11
PEGASPARGASE, PER SINGLE DOSE VIAL	6	6	7
INJECTION, PACLITAXEL, 1 MG	35	35	67
INJECTION, PEMBROLIZUMAB, 1 MG (KEYTRUDA)	8	8	11
MITOMYCIN, 5 MG	1	1	1
INJECTION, NIVOLUMAB, 1 MG (OPDIVO)	18	18	25
PANITUMUMAB INJECTION	2	2	3
PEMETREXED INJECTION	7	7	8
INJECTION, PERTUZUMAB, 1 MG	12	12	14
INJECTION, RAMUCIRUMAB, 5 MG (CYRAMZA)	2	2	2
RITUXIMAB, 100 MG	29	29	45
INJECTION, ADO-TRASTUZUMBA EMTANSINE, 1 MG	3	3	4
TRASTUZUMAB, 10 MG	21	21	28
VINBLASTINE SULFATE, 1 MG	2	2	5
VINCRISTINE SULFATE, 1 MG	30	30	54
INJECTION, FULVESTRANT, 25 MG	2	2	2
INJECTION, ZIV-AFLIBERCEPT, 1 MG	1	1	2

J-CODES PROCESSED INCLUDE: J9000 TO J9999

Top 10 Products by Number of Claims - Q3 2017–Q2 2018

SilverSummit Healthplan

Report Type	Report Date Range	Rank Number	Rank Name	Number of claims	Number of Units	Number of Members	Days Supply
Top 10 Products by claims	04/01/2017 - 06/30/2018	1	METHOTREXATE TAB 2.5MG	142	3231	51	4052
Top 10 Products by claims	04/01/2017 - 06/30/2018	2	ANASTROZOLE TAB 1MG	83	1777	28	2444
Top 10 Products by claims	04/01/2017 - 06/30/2018	3	TAMOXIFEN TAB 20MG	64	1950	13	1950
Top 10 Products by claims	04/01/2017 - 06/30/2018	4	MEGESTROL AC SUS 40MG/ML	57	21480	20	1551
Top 10 Products by claims	04/01/2017 - 06/30/2018	5	EXEMESTANE TAB 25MG	16	480	2	480
Top 10 Products by claims	04/01/2017 - 06/30/2018	6	HYDROXYUREA CAP 500MG	13	850	10	374
Top 10 Products by claims	04/01/2017 - 06/30/2018	7	BICALUTAMIDE TAB 50MG	12	360	2	360
Top 10 Products by claims	04/01/2017 - 06/30/2018	8	MERCAPTOPUR TAB 50MG	8	355	3	181
Top 10 Products by claims	04/01/2017 - 06/30/2018	9	TAGRISSO TAB 80MG	8	240	1	240
Top 10 Products by claims	04/01/2017 - 06/30/2018	10	ZYTIGA TAB 250MG	8	960	2	240

Top 10 Drug Group by Paid Amt

Fee for Service Medicaid

Q4 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
85	HEMATOLOGICAL AGENTS - MISC.*	2,904	$ 10,758,751.62
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,056	$ 5,871,009.27
12	ANTIVIRALS*	4,436	$ 5,553,514.06
27	ANTIDIABETICS*	17,269	$ 5,284,226.72
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	39,715	$ 4,715,098.00
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	3,604	$ 4,179,899.65
72	ANTICONVULSANTS*	42,649	$ 3,908,909.37
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	3,278	$ 3,094,916.09
74	NEUROMUSCULAR AGENTS*	356	$ 3,017,053.42
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	4,721	$ 2,199,798.18

Q1 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
85	HEMATOLOGICAL AGENTS - MISC.*	3,188	$ 10,478,484.39
12	ANTIVIRALS*	6,577	$ 7,762,477.83
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	4,377	$ 5,944,037.60
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	32,817	$ 5,909,563.28
27	ANTIDIABETICS*	20,841	$ 5,636,301.14
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	44,101	$ 5,082,129.59
72	ANTICONVULSANTS*	45,878	$ 4,267,432.38
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	4,292	$ 3,900,938.60
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	5,292	$ 2,612,714.21
19	PASSIVE IMMUNIZING AND TREATMENT AGENTS*	768	$ 2,459,251.17

Q2 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
85	HEMATOLOGICAL AGENTS - MISC.*	2,986	$ 12,638,527.40
12	ANTIVIRALS*	3,911	$ 6,204,744.24
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	32,386	$ 6,152,271.30
27	ANTIDIABETICS*	20,452	$ 5,653,348.21
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	4,253	$ 5,649,235.10
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	40,271	$ 4,988,356.81
72	ANTICONVULSANTS*	45,309	$ 4,374,287.85
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	5,366	$ 3,498,445.36
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	5,156	$ 2,858,447.77
74	NEUROMUSCULAR AGENTS*	450	$ 2,238,853.38

Top 10 Drug Group by Claim Count

Fee for Service Medicaid

Q4 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	50,563	$ 1,733,043.38
72	ANTICONVULSANTS*	42,649	$ 3,908,909.37
58	ANTIDEPRESSANTS*	40,379	$ 845,943.59
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	39,715	$ 4,715,098.00
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,056	$ 5,871,009.27
57	ANTIANXIETY AGENTS*	23,658	$ 277,872.17
66	ANALGESICS - ANTI-INFLAMMATORY*	23,370	$ 2,037,887.69
36	ANTIHYPERTENSIVES*	22,242	$ 371,772.47
49	ULCER DRUGS*	21,223	$ 1,071,391.16
39	ANTIHYPERLIPIDEMICS*	20,483	$ 681,151.03

Q1 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	46,549	$ 1,590,769.72
72	ANTICONVULSANTS*	45,878	$ 4,267,432.38
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	44,101	$ 5,082,129.59
58	ANTIDEPRESSANTS*	43,674	$ 868,863.95
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	32,817	$ 5,909,563.28
66	ANALGESICS - ANTI-INFLAMMATORY*	25,409	$ 2,163,691.39
36	ANTIHYPERTENSIVES*	25,402	$ 404,905.80
57	ANTIANXIETY AGENTS*	23,952	$ 268,796.39
49	ULCER DRUGS*	22,985	$ 1,077,154.68
39	ANTIHYPERLIPIDEMICS*	22,121	$ 695,237.95

Q2 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
72	ANTICONVULSANTS*	45,309	$4,374,287.85
65	ANALGESICS - OPIOID*	45,288	$1,610,665.99
58	ANTIDEPRESSANTS*	43,850	$880,469.71
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	40,271	$4,988,356.81
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	32,386	$6,152,271.30
36	ANTIHYPERTENSIVES*	24,945	$409,941.34
66	ANALGESICS - ANTI-INFLAMMATORY*	24,316	$2,075,729.75
57	ANTIANXIETY AGENTS*	23,841	$267,008.29
49	ULCER DRUGS/ANTISPASMODICS/ANTICHOLINERG	22,443	$1,157,415.22
39	ANTIHYPERLIPIDEMICS*	21,601	$678,016.69

Top 10 Drug Classes by Paid Amt

Fee for Service Medicaid

Q4 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	106	$ 10,231,948.35
2710	INSULIN**	5,671	$ 3,257,227.12
4420	SYMPATHOMIMETICS**	27,699	$ 3,154,566.99
1210	ANTIRETROVIRALS**	2,083	$ 3,013,382.63
7260	ANTICONVULSANTS - MISC.**	31,581	$ 2,689,322.15
7470	SPINAL MUSCULAR ATROPHY AGENTS (SMA)**	16	$ 2,375,162.72
1235	HEPATITIS AGENTS**	166	$ 2,357,004.30
5907	BENZISOXAZOLES**	7,044	$ 2,200,274.40
5940	ANTIPSYCHOTICS - MISC.**	2,746	$ 1,573,118.02
6240	MULTIPLE SCLEROSIS AGENTS**	325	$ 1,539,570.79

Q1 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	100	$ 9,623,686.67
1235	HEPATITIS AGENTS**	318	$ 3,934,799.29
4420	SYMPATHOMIMETICS**	31,307	$ 3,450,086.12
2710	INSULIN**	6,925	$ 3,404,808.09
1210	ANTIRETROVIRALS**	2,445	$ 3,399,138.63
7260	ANTICONVULSANTS - MISC.**	34,017	$ 2,956,120.07
5907	BENZISOXAZOLES**	7,492	$ 2,290,111.69
2135	ANTINEOPLASTIC - ANTIBODIES**	394	$ 2,059,367.58
6240	MULTIPLE SCLEROSIS AGENTS**	307	$ 1,910,973.30
5940	ANTIPSYCHOTICS - MISC.**	3,099	$ 1,837,738.18

Q2 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	112	$ 11,760,115.11
1210	ANTIRETROVIRALS**	2,147	$ 3,411,687.72
4420	SYMPATHOMIMETICS**	27,680	$ 3,359,203.65
2710	INSULIN**	6,747	$ 3,322,064.26
7260	ANTICONVULSANTS - MISC.**	33,994	$ 2,986,109.64
1235	HEPATITIS AGENTS**	179	$ 2,711,336.56
5907	BENZISOXAZOLES**	7,173	$ 2,300,277.79
6240	MULTIPLE SCLEROSIS AGENTS**	266	$ 2,155,015.01
3090	METABOLIC MODIFIERS**	2,609	$ 2,117,050.78
2135	ANTINEOPLASTIC - ANTIBODIES**	423	$ 2,113,140.38

Top 10 Drug Classes by Claim Count

Fee for Service Medicaid

Q4 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
7260	ANTICONVULSANTS - MISC.**	31,581	$ 2,689,322.15
4420	SYMPATHOMIMETICS**	27,699	$ 3,154,566.99
6599	OPIOID COMBINATIONS**	27,697	$ 586,127.34
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	22,851	$ 298,000.41
6510	OPIOID AGONISTS**	21,948	$ 912,093.39
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	19,141	$ 254,226.75
3940	HMG COA REDUCTASE INHIBITORS**	17,062	$ 374,381.72
5710	BENZODIAZEPINES**	16,330	$ 173,109.24
7510	CENTRAL MUSCLE RELAXANTS**	14,971	$ 259,985.27
2210	GLUCOCORTICOSTEROIDS**	13,819	$ 449,969.11

Q1 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
7260	ANTICONVULSANTS - MISC.**	34,017	$ 2,956,120.07
4420	SYMPATHOMIMETICS**	31,307	$ 3,450,086.12
6599	OPIOID COMBINATIONS**	25,082	$ 479,509.26
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	24,850	$ 309,860.44
6510	OPIOID AGONISTS**	20,482	$ 878,117.97
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	20,326	$ 247,248.78
3940	HMG COA REDUCTASE INHIBITORS**	18,558	$ 373,057.66
2210	GLUCOCORTICOSTEROIDS**	15,973	$ 515,912.21
7510	CENTRAL MUSCLE RELAXANTS**	15,907	$ 261,402.72
5710	BENZODIAZEPINES**	15,836	$ 157,418.95

Q2 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
7260	ANTICONVULSANTS - MISC.**	33,994	$ 2,986,109.64
4420	SYMPATHOMIMETICS**	27,680	$ 3,359,203.65
6599	OPIOID COMBINATIONS**	24,303	$ 484,060.92
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	23,818	$ 310,320.48
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	20,417	$ 250,420.04
6510	OPIOID AGONISTS**	19,958	$ 880,770.90
3940	HMG COA REDUCTASE INHIBITORS**	18,240	$ 359,836.83
7510	CENTRAL MUSCLE RELAXANTS**	15,812	$ 260,073.50
5710	BENZODIAZEPINES**	15,306	$ 149,728.88
2210	GLUCOCORTICOSTEROIDS**	13,572	$ 279,175.87

Anthem Top Therapeutic Class 12 months

Therapy Class Description	6/2018 Rx Count	5/2018 Rx Count	4/2018 Rx Count	3/2018 Rx Count	2/2018 Rx Count	1/2018 Rx Count	12/2017 Rx Count	11/2017 Rx Count	10/2017 Rx Count	9/2017 Rx Count	8/2017 Rx Count	7/2017 Rx Count
ANTIDEPRESSANT AGENTS	8,017	8,476	8,015	8,175	7,479	8,255	7,655	8,107	8,622	8,213	8,998	8,563
NSAIDS/COX II INHIBITORS	7,035	7,723	7,494	7,878	7,505	8,472	7,723	7,586	8,035	7,515	7,943	7,354
ANTICONVULSANTS	5,708	6,063	5,718	5,845	5,459	5,953	5,645	5,993	6,292	5,983	6,494	6,309
VITAMINS & HEMATINICS	4,912	5,171	4,876	4,963	4,564	4,997	4,707	4,856	5,232	4,880	5,236	4,906
ANTIHISTAMINES	4,715	5,780	6,237	5,516	5,129	5,211	4,942	5,027	5,548	5,159	5,127	4,406
LIPID/CHOLESTEROL LOWERING AGENTS	4,637	4,858	4,656	4,818	4,403	4,821	4,652	4,672	5,022	4,678	5,119	4,912
NON-INSULIN HYPOGLYCEMIC AGENTS	4,464	4,657	4,563	4,593	4,236	4,724	4,512	4,630	4,976	4,644	5,080	4,959
COMBINATION NARCOTIC /ANALGESICS	3,801	3,988	3,778	4,160	3,897	4,384	4,946	5,328	5,856	5,843	6,526	5,923
BETA AGONISTS INHALERS	3,671	4,723	5,006	5,787	5,881	6,208	5,556	5,188	5,184	4,711	4,604	3,718
PENICILLINS	3,394	4,640	4,591	5,547	5,893	6,266	5,712	4,960	4,990	4,407	4,044	3,250

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top 10 Drugs by Group by Paid Amount

Q3 2017		
Class	**Drug Class Name**	**Claim Count**
12	ANTIVIRALS	6,036
27	ANTIDIABETICS	33,875
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	38,393
66	ANALGESICS - ANTI-INFLAMMATORY	37,640
65	ANALGESICS - OPIOID	50,629
90	DERMATOLOGICALS	22,314
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENTS - MISC.	1,769
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS	11,946
94	DIAGNOSTIC PRODUCTS	10,190
72	ANTICONVULSANTS	31,012

Q4 2017		
Class	**Drug Class Name**	**Claim Count**
12	ANTIVIRALS	8,563
27	ANTIDIABETICS	33,321
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	44,842
66	ANALGESICS - ANTI-INFLAMMATORY	38,928
65	ANALGESICS - OPIOID	45,640
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS	11,553
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENTS - MISC.	1,701
90	DERMATOLOGICALS	21,588
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	1,581
94	DIAGNOSTIC PRODUCTS	9,819

Q1 2018		
Class	**Drug Class Name**	**Claim Count**
12	ANTIVIRALS	11,112
27	ANTIDIABETICS	32,589
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	48,221
66	ANALGESICS - ANTI-INFLAMMATORY	39,480
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS	11,754
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENTS - MISC.	1,752
90	DERMATOLOGICALS	22,254
65	ANALGESICS - OPIOID	35,908
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	1,503
72	ANTICONVULSANTS	29,903

Top 10 Drugs by Group by Paid Amount (Cont)

Q2 2018		
Class	Drug Class Name	Claim Count
12	ANTIVIRALS	6,379
27	ANTIDIABETICS	33,122
66	ANALGESICS - ANTI-INFLAMMATORY	36,349
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	41,229
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS	11,580
90	DERMATOLOGICALS	23,952
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENTS - MISC.	1,812
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	1,565
72	ANTICONVULSANTS	29,287
65	ANALGESICS - OPIOID	32,945

Top 10 Drugs by Group by Claim Count

Q3 2017		
Class	**Drug Class Name**	**Claim Count**
65	ANALGESICS - OPIOID	50,629
58	ANTIDEPRESSANTS	42,898
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	38,393
66	ANALGESICS - ANTI-INFLAMMATORY	37,640
36	ANTIHYPERTENSIVES	35,467
27	ANTIDIABETICS	33,875
72	ANTICONVULSANTS	31,012
49	ULCER DRUGS	24,778
39	ANTIHYPERLIPIDEMICS	24,127
90	DERMATOLOGICALS	22,314

Q4 2017		
Class	**Drug Class Name**	**Claim Count**
65	ANALGESICS - OPIOID	45,640
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	44,842
58	ANTIDEPRESSANTS	41,758
66	ANALGESICS - ANTI-INFLAMMATORY	38,928
36	ANTIHYPERTENSIVES	34,948
27	ANTIDIABETICS	33,321
72	ANTICONVULSANTS	30,398
49	ULCER DRUGS	24,107
39	ANTIHYPERLIPIDEMICS	23,934
01	PENICILLINS	23,315

Q1 2018		
Class	**Drug Class Name**	**Claim Count**
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	48,221
58	ANTIDEPRESSANTS	41,304
66	ANALGESICS - ANTI-INFLAMMATORY	39,480
65	ANALGESICS - OPIOID	35,908
36	ANTIHYPERTENSIVES	34,161
27	ANTIDIABETICS	32,589
72	ANTICONVULSANTS	29,903
01	PENICILLINS	25,785
49	ULCER DRUGS	23,882
39	ANTIHYPERLIPIDEMICS	23,422

Top 10 Drugs by Group by Claim Count (Cont)

Q2 2018		
Class	Drug Class Name	Claim Count
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	41,229
58	ANTIDEPRESSANTS	40,983
66	ANALGESICS - ANTI-INFLAMMATORY	36,349
36	ANTIHYPERTENSIVES	33,807
27	ANTIDIABETICS	33,122
65	ANALGESICS - OPIOID	32,945
72	ANTICONVULSANTS	29,287
90	DERMATOLOGICALS	23,952
49	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	23,899
39	DIAGNOSTIC PRODUCTS	23,793

Top 10 Drug Class By Claim Volume- Q3 2017–Q2 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBE	RANK NAME	CLAIM COUNT	UTILIZER COUNT
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	1	Nonsteroidal Anti-inflammatory Agents (NSAIDs)	15,046	8,119
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	2	Anticonvulsants - Misc.	11,397	2,894
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	3	Sympathomimetics	10,512	4,438
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	4	Selective Serotonin Reuptake Inhibitors (SSRIs)	10,108	2,854
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	5	Opioid Combinations	9,925	4,419
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	6	HMG CoA Reductase Inhibitors	8,030	2,135
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	7	Central Muscle Relaxants	7,290	2,861
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	8	ACE Inhibitors	5,717	1,774
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	9	Aminopenicillins	5,619	4,653
Top Drug Class By Claim Volume	04/01/2017 - 06/30/2018	10	Benzodiazepines	5,249	1,662

Top 10 Drug Class By Spend- Q3 2017–Q2 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBER	RANK NAME	CLAIM COUNT	UTILIZER COUNT
Top Drug Class By Spend	07/01/2017 - 06/30/2018	1	Antiretrovirals	2,012	305
Top Drug Class By Spend	07/01/2017 - 06/30/2018	2	Insulin	2,881	653
Top Drug Class By Spend	07/01/2017 - 06/30/2018	3	Hepatitis Agents	71	33
Top Drug Class By Spend	07/01/2017 - 06/30/2018	4	Sympathomimetics	10,512	4,438
Top Drug Class By Spend	07/01/2017 - 06/30/2018	5	Multiple Sclerosis Agents	85	18
Top Drug Class By Spend	07/01/2017 - 06/30/2018	6	Anticonvulsants - Misc.	11,397	2,894
Top Drug Class By Spend	07/01/2017 - 06/30/2018	7	Opioid Partial Agonists	1,606	228
Top Drug Class By Spend	07/01/2017 - 06/30/2018	8	Antipsychotics - Misc.	652	216
Top Drug Class By Spend	07/01/2017 - 06/30/2018	9	Antineoplastic Enzyme Inhibitors	33	10
Top Drug Class By Spend	07/01/2017 - 06/30/2018	10	Incretin Mimetic Agents (GLP-1 Receptor Agonists)	554	142

Top 50 Drugs by Amount - Q4 2017
Fee for Service Medicaid

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	15	$ 3,861,081.75	72,574	9
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	6	$ 2,721,661.02	210,000	30
7470005000	NUSINERSEN	16	$ 2,375,162.72	3	16
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	13	$ 2,213,038.81	95,073	20
5907005010	PALIPERIDONE PALMITATE	747	$ 1,701,137.98	1	24
5940002310	LURASIDONE HCL	1082	$ 1,270,883.76	18	15
1950206000	PALIVIZUMAB	415	$ 1,266,412.21	1	26
4420101010	ALBUTEROL SULFATE	18418	$ 1,122,535.78	36	15
6627001500	ADALIMUMAB	191	$ 1,068,310.03	1	10
2710400300	INSULIN GLARGINE	2047	$ 1,049,529.08	14	33
1235990240	LEDIPASVIR-SOFOSBUVIR	54	$ 1,027,262.86	8	8
1235990265	SOFOSBUVIR-VELPATASVIR	58	$ 994,146.30	11	11
9410003000	GLUCOSE BLOOD	6557	$ 960,063.54	75	24
7260005700	PREGABALIN	2398	$ 925,052.06	44	19
4420990270	FLUTICASONE-SALMETEROL	2461	$ 880,044.40	41	22
3030001000	CORTICOTROPIN	10	$ 764,123.70	2	4
3010002000	SOMATROPIN	204	$ 757,204.88	2	9
4927002510	ESOMEPRAZOLE MAGNESIUM	2684	$ 750,765.50	23	23
5925001500	ARIPIPRAZOLE	4592	$ 745,330.20	17	16
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	346	$ 664,130.13	16	16
4530402000	DORNASE ALFA	186	$ 660,085.40	49	16
2710400500	INSULIN LISPRO	933	$ 659,405.85	13	26
4530990230	LUMACAFTOR-IVACAFTOR	31	$ 586,078.20	39	10
8240157000	PEGFILGRASTIM	100	$ 548,897.82	1	2
7260003600	LACOSAMIDE	956	$ 548,146.29	56	14
7210000700	CLOBAZAM	395	$ 542,066.20	62	14
5915307010	QUETIAPINE FUMARATE	7964	$ 542,007.05	30	21
2710400200	INSULIN ASPART	912	$ 534,069.09	14	27
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2223	$ 527,676.73	8	23
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	1705	$ 520,907.74	22	24
6240552500	DIMETHYL FUMARATE	68	$ 491,731.56	17	9
6135303010	GUANFACINE HCL (ADHD)	1877	$ 486,639.20	18	18
1910002010	IMMUNE GLOBULIN (HUMAN) IV	105	$ 484,572.17	362	5
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	21	$ 465,235.74	11,932	12
3090685000	IDURSULFASE	35	$ 444,859.08	6	3
8580005000	ECULIZUMAB	20	$ 443,564.00	68	1
6110002510	LISDEXAMFETAMINE DIMESYLATE	1720	$ 441,076.56	21	21
2153253000	EVEROLIMUS	28	$ 438,115.47	9	8
6140002010	METHYLPHENIDATE HCL	2300	$ 423,075.05	32	18
9085006000	LIDOCAINE	2304	$ 415,329.84	75	15
6629003000	ETANERCEPT	95	$ 412,422.12	2	11
2710400600	INSULIN DETEMIR	812	$ 377,934.28	13	28
7460003500	ETEPLIRSEN	6	$ 377,661.02	26	9
4016000700	AMBRISENTAN	40	$ 370,591.20	18	18
9037403530	DICLOFENAC SODIUM (ACTINIC KERATOSES)	690	$ 369,511.59	168	19
2160005500	RADIUM RA 223 DICHLORIDE	12	$ 368,220.00	108	1
2755007010	SITAGLIPTIN PHOSPHATE	749	$ 358,272.62	35	35
9310002500	DEFERASIROX	53	$ 356,233.90	19	9
1210301510	DOLUTEGRAVIR SODIUM	243	$ 348,735.50	21	20
6510007510	OXYCODONE HCL	7735	$ 318,857.91	68	17

Top 50 Drugs by Amount - Q1 2018
Fee for Service Medicaid

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	14	$ 4,281,032.48	104,486	12
1235990265	SOFOSBUVIR-VELPATASVIR	95	$ 2,021,558.12	12	12
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	11	$ 1,961,568.27	72,000	18
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	4	$ 1,814,440.68	210,000	30
5907005010	PALIPERIDONE PALMITATE	893	$ 1,782,514.40	1	24
5940002310	LURASIDONE HCL	1,281	$ 1,430,387.78	19	16
1950206000	PALIVIZUMAB	473	$ 1,365,369.98	1	23
4420101010	ALBUTEROL SULFATE	20,684	$ 1,230,782.52	36	15
6627001500	ADALIMUMAB	203	$ 1,142,057.13	1	9
2710400300	INSULIN GLARGINE	2,617	$ 1,075,648.42	14	32
1235990240	LEDIPASVIR-SOFOSBUVIR	49	$ 1,044,772.94	10	10
3030001000	CORTICOTROPIN	14	$ 1,008,824.38	3	6
7260005700	PREGABALIN	2,695	$ 987,946.28	42	18
4420990270	FLUTICASONE-SALMETEROL	2,692	$ 977,238.94	41	22
9410003000	GLUCOSE BLOOD	6,237	$ 836,657.49	76	25
5925001500	ARIPIPRAZOLE	4,841	$ 762,545.22	18	17
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	381	$ 761,836.47	16	16
4530402000	DORNASE ALFA	199	$ 748,583.39	37	12
4927002510	ESOMEPRAZOLE MAGNESIUM	2,676	$ 746,286.65	24	23
8580005000	ECULIZUMAB	32	$ 730,576.00	105	1
8240157000	PEGFILGRASTIM	131	$ 726,236.02	0	1
3010002000	SOMATROPIN	171	$ 712,687.56	2	8
1910002010	IMMUNE GLOBULIN (HUMAN) IV	148	$ 705,699.06	452	4
2710400500	INSULIN LISPRO	1,097	$ 677,326.34	13	25
7210000700	CLOBAZAM	436	$ 636,858.61	66	14
7470005000	NUSINERSEN	5	$ 625,050.85	1	8
2710400200	INSULIN ASPART	1,118	$ 596,207.84	13	27
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2,573	$ 581,795.82	8	23
7260003600	LACOSAMIDE	1,016	$ 573,241.20	54	14
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	1,875	$ 568,857.18	23	26
3090522510	CINACALCET HCL	865	$ 545,944.90	30	5
2133502000	BEVACIZUMAB	338	$ 522,184.81	7	1
6240552500	DIMETHYL FUMARATE	68	$ 512,993.82	14	7
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	13	$ 510,385.76	24,446	10
2135304100	NIVOLUMAB	104	$ 509,189.66	99	2
1235990235	GLECAPREVIR-PIBRENTASVIR	40	$ 503,719.56	41	14
4530990230	LUMACAFTOR-IVACAFTOR	29	$ 502,545.60	36	9
2153253000	EVEROLIMUS	26	$ 478,220.98	10	8
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,721	$ 474,857.44	21	20
3090404500	NITISINONE	6	$ 449,633.19	50	10
1210301510	DOLUTEGRAVIR SODIUM	302	$ 427,225.69	18	18
2135305300	PEMBROLIZUMAB	46	$ 417,472.66	8	1
6629003000	ETANERCEPT	89	$ 407,899.05	1	10
7460003500	ETEPLIRSEN	6	$ 403,261.02	14	5
3090685000	IDURSULFASE	28	$ 400,479.12	12	6
2710400600	INSULIN DETEMIR	996	$ 383,636.27	13	28
2755007010	SITAGLIPTIN PHOSPHATE	849	$ 383,133.21	33	33
6140002010	METHYLPHENIDATE HCL	2,264	$ 380,455.71	26	18
2135306000	RITUXIMAB	74	$ 377,622.73	44	1
1250406020	OSELTAMIVIR PHOSPHATE	2,224	$ 366,676.32	23	3

Top 50 Drugs by Amount - Q2 2018
Fee for Service Medicaid

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	18.00	$ 4,858,864.76	102,504	13
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	8.00	$ 3,628,881.36	210,000	30
5907005010	PALIPERIDONE PALMITATE	772.00	$ 1,808,834.55	1	25
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	11.00	$ 1,690,412.67	56,577	17
7470005000	NUSINERSEN	10.00	$ 1,500,101.70	3	16
5940002310	LURASIDONE HCL	1,328.00	$ 1,451,626.56	18	16
1235990265	SOFOSBUVIR-VELPATASVIR	62.00	$ 1,424,786.06	15	15
6627001500	ADALIMUMAB	193.00	$ 1,137,433.06	1	9
4420101010	ALBUTEROL SULFATE	17,711.00	$ 1,123,195.22	29	14
2710400300	INSULIN GLARGINE	2,478.00	$ 1,032,349.27	13	31
7260005700	PREGABALIN	2,674.00	$ 1,017,205.66	44	18
4420990270	FLUTICASONE-SALMETEROL	2,515.00	$ 954,711.42	43	23
9410003000	GLUCOSE BLOOD	6,612.00	$ 882,953.02	78	25
3090522510	CINACALCET HCL	1,980.00	$ 867,300.76	79	3
1910002010	IMMUNE GLOBULIN (HUMAN) IV	163.00	$ 842,454.21	373	4
5925001500	ARIPIPRAZOLE	4,872.00	$ 801,124.87	18	18
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	355.00	$ 780,531.69	17	17
4927002510	ESOMEPRAZOLE MAGNESIUM	2,523.00	$ 756,908.32	24	23
8580005000	ECULIZUMAB	33.00	$ 717,530.00	94	1
7210000700	CLOBAZAM	440.00	$ 699,014.29	89	18
4530402000	DORNASE ALFA	189.00	$ 680,450.51	37	12
3010002000	SOMATROPIN	152.00	$ 677,560.69	2	8
1235990240	LEDIPASVIR-SOFOSBUVIR	28.00	$ 677,210.88	10	10
2710400500	INSULIN LISPRO	1,057.00	$ 664,586.83	12	24
7260003600	LACOSAMIDE	1,076.00	$ 595,970.15	54	14
2135304100	NIVOLUMAB	99.00	$ 593,788.36	22	2
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2,473.00	$ 572,915.37	8	24
8240157000	PEGFILGRASTIM	95.00	$ 561,749.38	1	1
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	1,758.00	$ 558,608.12	22	25
2710400200	INSULIN ASPART	1,071.00	$ 549,997.48	13	27
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	14.00	$ 541,877.12	17,838	12
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,683.00	$ 469,420.78	22	21
2153253000	EVEROLIMUS	25.00	$ 458,098.68	15	11
3090404500	NITISINONE	6.00	$ 449,633.19	50	10
6240552500	DIMETHYL FUMARATE	61.00	$ 449,182.37	17	8
2135305300	PEMBROLIZUMAB	50.00	$ 442,755.85	7	1
2755007010	SITAGLIPTIN PHOSPHATE	875.00	$ 419,332.38	38	37
4016000700	AMBRISENTAN	45.00	$ 415,761.71	23	24
1210301510	DOLUTEGRAVIR SODIUM	262.00	$ 409,133.62	18	18
1235990235	GLECAPREVIR-PIBRENTASVIR	33.00	$ 408,202.67	39	13
4530990230	LUMACAFTOR-IVACAFTOR	23.00	$ 397,739.42	30	7
7460003500	ETEPLIRSEN	8.00	$ 396,881.36	15	5
6629003000	ETANERCEPT	74.00	$ 391,775.78	2	12
5940001810	CARIPRAZINE HCL	367.00	$ 387,700.69	13	12
2710400600	INSULIN DETEMIR	988.00	$ 378,549.44	11	25
1210990315	ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	136.00	$ 375,969.81	22	22
6140002010	METHYLPHENIDATE HCL	2,210.00	$ 374,433.42	27	18
5925002000	BREXPIPRAZOLE	413.00	$ 363,599.16	14	13
8665501000	AFLIBERCEPT	91.00	$ 360,020.00	1	1
6240506000	OCRELIZUMAB	16.00	$ 358,694.34	12	10

Top 50 Drugs by Claim Count - Q4 2017
Fee for Service Medicaid

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
4420101010	ALBUTEROL SULFATE	18418	$ 1,122,535.78	36	15
6599170210	HYDROCODONE-ACETAMINOPHEN	17475	$ 274,972.07	52	14
7260003000	GABAPENTIN	12790	$ 182,980.11	74	23
6610002000	IBUPROFEN	10590	$ 96,790.93	46	11
3940001010	ATORVASTATIN CALCIUM	9909	$ 112,903.78	30	30
5710001000	ALPRAZOLAM	9092	$ 100,721.08	48	21
6599000220	OXYCODONE W/ ACETAMINOPHEN	8582	$ 269,514.23	50	13
2810001010	LEVOTHYROXINE SODIUM	8140	$ 141,063.27	31	31
3610003000	LISINOPRIL	8069	$ 66,038.04	45	41
5915307010	QUETIAPINE FUMARATE	7964	$ 542,007.05	30	21
6510007510	OXYCODONE HCL	7735	$ 318,857.91	68	17
5812008010	TRAZODONE HCL	7414	$ 85,626.74	30	23
5025006505	ONDANSETRON HCL	7216	$ 33,929.28	4	1
9410003000	GLUCOSE BLOOD	6557	$ 960,063.54	75	24
3400000310	AMLODIPINE BESYLATE	6520	$ 46,402.68	39	38
0120001010	AMOXICILLIN	6464	$ 69,245.86	59	6
5816007010	SERTRALINE HCL	6399	$ 72,993.00	29	24
4220003230	FLUTICASONE PROPIONATE (NASAL)	6313	$ 74,805.08	13	26
7720203200	CHOLECALCIFEROL	6249	$ 48,678.67	26	24
6510005510	MORPHINE SULFATE	6220	$ 138,638.26	21	9
4450505010	MONTELUKAST SODIUM	6208	$ 91,868.91	25	25
6410001000	ASPIRIN	6058	$ 33,821.83	22	22
2725005000	METFORMIN HCL	6039	$ 251,679.37	80	40
5907007000	RISPERIDONE	5690	$ 93,012.22	35	21
7975001000	SODIUM CHLORIDE	5451	$ 13,359.89	460	1
0340001000	AZITHROMYCIN	5317	$ 69,434.58	6	3
2210004500	PREDNISONE	5046	$ 43,208.41	14	8
5025006500	ONDANSETRON	4968	$ 50,715.43	6	3
4155003000	LORATADINE	4895	$ 54,439.01	34	22
4927007010	PANTOPRAZOLE SODIUM	4892	$ 51,323.27	23	22
7510005010	CYCLOBENZAPRINE HCL	4796	$ 51,985.97	43	19
5816004000	FLUOXETINE HCL	4702	$ 87,473.59	32	25
4920002010	RANITIDINE HCL	4626	$ 61,795.57	49	25
7250001010	DIVALPROEX SODIUM	4597	$ 158,284.40	52	19
5925001500	ARIPIPRAZOLE	4592	$ 745,330.20	17	16
6510009510	TRAMADOL HCL	4418	$ 41,233.45	55	16
7210001000	CLONAZEPAM	4370	$ 46,204.59	39	19
7260004000	LAMOTRIGINE	4166	$ 206,097.02	44	22
4155002010	CETIRIZINE HCL	4116	$ 45,824.57	42	22
3320003010	METOPROLOL TARTRATE	4081	$ 33,708.72	64	35
7510009010	TIZANIDINE HCL	4048	$ 90,323.17	48	20
6610005200	MELOXICAM	4042	$ 36,483.87	27	24
5710006000	LORAZEPAM	3889	$ 40,713.00	19	9
4920003000	FAMOTIDINE	3888	$ 30,930.95	23	14
7260004300	LEVETIRACETAM	3838	$ 178,959.13	131	21
7720203000	ERGOCALCIFEROL	3731	$ 39,885.89	5	28
3940007500	SIMVASTATIN	3630	$ 29,028.61	31	31
5830004010	BUPROPION HCL	3541	$ 79,397.11	32	23
5816002010	CITALOPRAM HYDROBROMIDE	3528	$ 34,659.83	27	25
4650001030	DOCUSATE SODIUM	3486	$ 25,513.68	37	19

Top 50 Drugs by Claim Count - Q1 2018
Fee for Service Medicaid

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
4420101010	ALBUTEROL SULFATE	20684	$ 1,230,782.52	36	15
6599170210	HYDROCODONE-ACETAMINOPHEN	15593	$ 236,136.11	53	15
7260003000	GABAPENTIN	14223	$ 195,262.36	70	22
6610002000	IBUPROFEN	11456	$ 101,008.94	39	11
3940001010	ATORVASTATIN CALCIUM	11024	$ 116,909.28	28	28
3610003000	LISINOPRIL	9058	$ 70,819.65	44	40
5710001000	ALPRAZOLAM	8716	$ 93,467.85	47	20
2810001010	LEVOTHYROXINE SODIUM	8713	$ 148,823.57	32	32
5915307010	QUETIAPINE FUMARATE	8545	$ 167,250.14	30	21
5812008010	TRAZODONE HCL	8324	$ 90,861.20	29	22
6599000220	OXYCODONE W/ ACETAMINOPHEN	8252	$ 212,572.55	51	14
3400000310	AMLODIPINE BESYLATE	7642	$ 51,555.98	38	37
6510007510	OXYCODONE HCL	7604	$ 293,997.80	63	17
0120001010	AMOXICILLIN	7375	$ 79,438.13	61	6
5025006505	ONDANSETRON HCL	7347	$ 34,220.72	4	2
4220003230	FLUTICASONE PROPIONATE (NASAL)	7113	$ 81,487.19	13	26
5816007010	SERTRALINE HCL	6946	$ 77,501.60	30	25
2725005000	METFORMIN HCL	6943	$ 219,457.68	81	40
4450505010	MONTELUKAST SODIUM	6617	$ 98,286.00	25	24
0340001000	AZITHROMYCIN	6613	$ 83,476.74	6	3
7720203200	CHOLECALCIFEROL	6475	$ 51,225.47	26	25
9410003000	GLUCOSE BLOOD	6237	$ 836,657.49	76	25
6410001000	ASPIRIN	6068	$ 34,409.97	20	20
5907007000	RISPERIDONE	5892	$ 95,517.55	35	20
2210004500	PREDNISONE	5832	$ 46,937.73	14	8
6510005510	MORPHINE SULFATE	5822	$ 154,335.03	22	9
7975001000	SODIUM CHLORIDE	5444	$ 13,134.75	455	1
5025006500	ONDANSETRON	5415	$ 53,335.85	6	3
4927007010	PANTOPRAZOLE SODIUM	5216	$ 52,010.24	23	22
7250001010	DIVALPROEX SODIUM	5189	$ 150,563.53	49	18
7510005010	CYCLOBENZAPRINE HCL	5041	$ 48,613.22	42	19
4920002010	RANITIDINE HCL	4923	$ 64,749.99	52	26
5816004000	FLUOXETINE HCL	4920	$ 73,955.55	30	23
4155003000	LORATADINE	4850	$ 54,202.47	31	20
5925001500	ARIPIPRAZOLE	4841	$ 762,545.22	18	17
3320003010	METOPROLOL TARTRATE	4803	$ 37,811.22	61	33
7210001000	CLONAZEPAM	4448	$ 45,616.05	36	18
7510009010	TIZANIDINE HCL	4409	$ 90,971.66	43	18
7260004000	LAMOTRIGINE	4391	$ 228,997.58	40	20
6610005200	MELOXICAM	4347	$ 38,887.26	27	24
4920003000	FAMOTIDINE	4246	$ 31,389.76	22	14
5710006000	LORAZEPAM	4149	$ 36,429.28	17	8
4155002010	CETIRIZINE HCL	4089	$ 46,089.67	43	22
7260004300	LEVETIRACETAM	3948	$ 180,794.76	120	20
3720003000	FUROSEMIDE	3910	$ 27,467.86	40	31
3615004020	LOSARTAN POTASSIUM	3904	$ 32,528.02	38	36
5830004010	BUPROPION HCL	3865	$ 81,094.67	33	23
0199000220	AMOXICILLIN & POT CLAVULANATE	3822	$ 72,194.47	30	6
3940007500	SIMVASTATIN	3759	$ 28,872.23	32	32
6610003710	KETOROLAC TROMETHAMINE	3707	$ 17,369.19	2	1

Top 50 Drugs by Claim Count - Q2 2018
Fee for Service Medicaid

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
4420101010	ALBUTEROL SULFATE	17711	$ 1,123,195.22	29	14
6599170210	HYDROCODONE-ACETAMINOPHEN	15294	$ 230,412.48	52	15
7260003000	GABAPENTIN	14005	$ 192,635.12	69	22
3940001010	ATORVASTATIN CALCIUM	11104	$ 116,355.34	31	30
6610002000	IBUPROFEN	10527	$ 96,677.47	41	12
3610003000	LISINOPRIL	8867	$ 70,817.71	45	41
2810001010	LEVOTHYROXINE SODIUM	8599	$ 144,366.34	32	32
5915307010	QUETIAPINE FUMARATE	8480	$ 159,960.63	30	21
5812008010	TRAZODONE HCL	8379	$ 93,010.11	30	23
5710001000	ALPRAZOLAM	8252	$ 86,712.85	45	20
6599000220	OXYCODONE W/ ACETAMINOPHEN	7916	$ 224,656.28	55	15
3400000310	AMLODIPINE BESYLATE	7656	$ 51,866.01	41	40
6510007510	OXYCODONE HCL	7434	$ 282,606.74	63	17
5025006505	ONDANSETRON HCL	7304	$ 33,128.16	4	2
4220003230	FLUTICASONE PROPIONATE (NASAL)	7027	$ 81,300.37	12	24
5816007010	SERTRALINE HCL	6979	$ 78,467.69	28	23
4450505010	MONTELUKAST SODIUM	6932	$ 102,581.09	25	24
7720203200	CHOLECALCIFEROL	6824	$ 54,289.58	25	24
2725005000	METFORMIN HCL	6810	$ 181,121.69	82	41
9410003000	GLUCOSE BLOOD	6612	$ 882,953.02	78	25
6410001000	ASPIRIN	6151	$ 34,610.94	22	21
6510005510	MORPHINE SULFATE	6124	$ 144,198.57	20	9
7975001000	SODIUM CHLORIDE	6006	$ 14,137.78	445	1
5907007000	RISPERIDONE	5772	$ 89,057.38	37	21
0120001010	AMOXICILLIN	5606	$ 59,445.37	54	6
4927007010	PANTOPRAZOLE SODIUM	5245	$ 52,308.68	24	23
5025006500	ONDANSETRON	5227	$ 51,905.43	6	3
4155003000	LORATADINE	5071	$ 57,279.11	31	21
7510005010	CYCLOBENZAPRINE HCL	5029	$ 49,085.17	42	19
7250001010	DIVALPROEX SODIUM	4922	$ 140,073.02	51	19
5925001500	ARIPIPRAZOLE	4872	$ 801,124.87	18	18
5816004000	FLUOXETINE HCL	4856	$ 78,285.84	29	23
3320003010	METOPROLOL TARTRATE	4768	$ 38,372.54	64	35
4155002010	CETIRIZINE HCL	4738	$ 54,771.44	41	21
4920002010	RANITIDINE HCL	4711	$ 62,709.56	55	28
2210004500	PREDNISONE	4697	$ 38,980.56	15	8
7260004000	LAMOTRIGINE	4365	$ 234,596.88	40	20
7510009010	TIZANIDINE HCL	4348	$ 89,110.85	42	17
6610005200	MELOXICAM	4284	$ 38,284.84	29	25
7210001000	CLONAZEPAM	4229	$ 43,822.09	35	17
5710006000	LORAZEPAM	4198	$ 36,430.72	16	8
0340001000	AZITHROMYCIN	4116	$ 53,091.99	6	3
7260004300	LEVETIRACETAM	4109	$ 172,038.51	118	20
4920003000	FAMOTIDINE	4033	$ 31,631.29	24	15
3720003000	FUROSEMIDE	3894	$ 28,663.17	38	30
5830004010	BUPROPION HCL	3892	$ 80,385.99	30	21
3615004020	LOSARTAN POTASSIUM	3878	$ 31,226.28	42	40
6610003710	KETOROLAC TROMETHAMINE	3813	$ 17,965.51	2	1
3940007500	SIMVASTATIN	3622	$ 27,623.39	34	34
7720203000	ERGOCALCIFEROL	3610	$ 38,649.32	5	28

Anthem Nevada Medicaid

Current Period: 06/2018 - 08/2018

Previous Period: 07/2017 - 12/2017

		Current Period		Previous Period		% Change
Drug NDC	Drug Name	Rx Count Rank	Rx Count	Rx Count Rank	Rx Count	Rx Count
001730682	VENTOLIN HFA	1	8,869	1	19,876	-55.4%
551110684	IBU	2	5,179	2	11,367	-54.4%
561511460	TRUE METRIX GLUCOSE TEST STRIP	3	3,851	4	7,513	-48.7%
458020650	LORATADINE	4	3,579	89	1,474	142.8%
643800737	VITAMIN D2	5	2,775	5	6,378	-56.5%
000027715	BASAGLAR KWIKPEN U-100	6	2,326	11	4,418	-47.4%
658620199	GABAPENTIN	7	2,325	19	3,875	-40.0%
293000220	MONTELUKAST SODIUM	8	2,142	14	4,170	-48.6%
651620190	NAPROXEN	9	2,108	16	4,058	-48.1%
605052579	ATORVASTATIN CALCIUM	10	1,928	22	3,780	-49.0%
658620017	AMOXICILLIN	11	1,882	13	4,181	-55.0%
658620008	METFORMIN HCL	12	1,823	10	4,432	-58.9%
001439887	AMOXICILLIN	13	1,806	8	4,934	-63.4%
501110433	TRAZODONE HCL	14	1,805	35	2,951	-38.8%
003787732	ONDANSETRON ODT	15	1,782	12	4,400	-59.5%
458020888	OMEPRAZOLE	16	1,773	24	3,429	-48.3%
293000243	AMLODIPINE BESYLATE	17	1,770	1,024	149	1,087.9%
658620010	METFORMIN HCL	18	1,768	23	3,772	-53.1%
681800122	CEPHALEXIN	19	1,736	26	3,270	-46.9%
690970846	CYCLOBENZAPRINE HCL	20	1,620	29	3,151	-48.6%
501110434	TRAZODONE HCL	21	1,577	30	3,109	-49.3%
501110787	AZITHROMYCIN	22	1,498	6	5,078	-70.5%
435470354	LISINOPRIL	23	1,481	28	3,184	-53.5%
167290183	HYDROCHLOROTHIAZIDE	24	1,450	31	3,105	-53.3%
605052580	ATORVASTATIN CALCIUM	25	1,447	27	3,207	-54.9%
516722131	CHILDREN'S LORATADINE	26	1,443	NA	NA	NA
681800353	SERTRALINE HCL	27	1,435	37	2,866	-49.9%
003788270	ALBUTEROL SULFATE	28	1,434	9	4,849	-70.4%
576640176	HYDROCODONE-ACETAMINOPHEN	29	1,386	33	3,070	-54.9%
686450563	IBUPROFEN	30	1,365	NA	NA	NA
004060125	HYDROCODONE-ACETAMINOPHEN	31	1,338	20	3,844	-65.2%
690970159	MELOXICAM	32	1,328	39	2,832	-53.1%
666851001	AMOXICILLIN-CLAVULANATE POTASS	33	1,313	42	2,713	-51.6%
005915215	METRONIDAZOLE	34	1,291	48	2,408	-46.4%
698420900	FLUTICASONE PROPIONATE	35	1,285	NA	NA	NA
681800352	SERTRALINE HCL	36	1,255	43	2,593	-51.6%

Anthem	Continued	RX Rank	RX Count	Prev Period Rank	Prev Period Count	
572370213	MONTELUKAST SODIUM	37	1,242	36	2,929	-57.6%
293000242	AMLODIPINE BESYLATE	38	1,240	1,369	95	1,205.3%
435470353	LISINOPRIL	39	1,229	46	2,493	-50.7%
551110683	IBU	40	1,224	21	3,829	-68.0%
605052578	ATORVASTATIN CALCIUM	41	1,211	56	2,050	-40.9%
572370005	FLUCONAZOLE	42	1,186	49	2,403	-50.6%
651620627	TRAMADOL HCL	43	1,125	17	4,033	-72.1%
516721385	IBUPROFEN	44	1,099	464	383	186.9%
005740412	POLYETHYLENE GLYCOL 3350	45	1,068	50	2,340	-54.4%
684620248	RANITIDINE HCL	46	1,058	67	1,800	-41.2%
477810303	NITROFURANTOIN MONO-MACRO	47	1,046	127	1,148	-8.9%
136680115	LOSARTAN POTASSIUM	48	1,033	430	415	148.9%
005361091	FLUTICASONE PROPIONATE	49	1,030	71	1,693	-39.2%
684620180	MUPIROCIN	50	1,010	53	2,130	-52.6%

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top 50 Drugs by Paid Amount

Q3 2017	Top 50 Drugs by Paid Amount	1 of 2
Class	**Label Name**	**Claim Count**
6627001500	ELBASVIR-GRAZOPREVIR	412
1235990230	ADALIMUMAB	95
2710400300	INSULIN GLARGINE	4,328
2710400500	INSULIN LISPRO	2,253
9410003000	SOFOSBUVIR-VELPATASVIR	10,008
1235990265	GLUCOSE BLOOD	47
4420101010	ALBUTEROL SULFATE	20,546
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMID	314
1210990315	ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	332
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	531
4420990275	FLUTICASONE FUROATE-VILANTEROL	2,303
2710400200	INSULIN ASPART	1,232
6240552500	ETANERCEPT	94
1210990430	DIMETHYL FUMARATE	163
6599000220	SOMATROPIN	9,176
6110990210	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR DF	4,070
5940002310	AMPHETAMINE-DEXTROAMPHETAMINE	342
3010002000	DULAGLUTIDE	91
1210301510	DOLUTEGRAVIR SODIUM	249
7260005700	LURASIDONE HCL	778
9025058500	OXYCODONE W/ ACETAMINOPHEN	27
6629003000	PREGABALIN	76
6599170210	MOMETASONE FUROATE (INHALATION)	22,544
2770002000	LISDEXAMFETAMINE DIMESYLATE	787
6110002510	OSELTAMIVIR PHOSPHATE	1,262
5925001500	EMPAGLIFLOZIN	1,520
4440003620	ARIPIPRAZOLE	1,523
3890004000	BUPRENORPHINE HCL-NALOXONE HCL DIHYDRATE	947
2770005000	HYDROCODONE-ACETAMINOPHEN	694
6520001020	EMTRICITABINE-RILPIVIRINE-TENOFOVIR ALAFENAMIDE FUMARATE	921
8337006000	LENALIDOMIDE	727
1210990340	RIVAROXABAN	104
4420990290	CANAGLIFLOZIN	951
1210990330	ICATIBANT ACETATE	107
5907005010	USTEKINUMAB	121

Q3 2017	Top 50 Drugs by Paid Amount	2 of 2
Class	**Label Name**	**Claim Count**
2717001500	PALIPERIDONE PALMITATE	370
5250502010	APIXABAN	53
9939405000	EFAVIRENZ-EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	19
6240306045	EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	34
2710400600	CERTOLIZUMAB PEGOL	503
8337001000	EMTRICITABINE-RILPIVIRINE-TENOFOVIR DISOPROXIL FUMARATE	583
6240003010	EPINEPHRINE (ANAPHYLAXIS)	36
1210990339	DASATINIB	84
1210990227	DARUNAVIR-COBICISTAT	125
7260003000	GABAPENTIN	13,954
2153402000	SECUKINUMAB	18
6510007510	GLATIRAMER ACETATE	5,362
2717001000	PALBOCICLIB	339
1210990229	INTERFERON BETA-1A	110
4220003230	INSULIN DETEMIR	10,171

Q4 2017	Top 50 Drugs by Paid Amount	1 of 2
Class	Label Name	Claim Count
1235990230	ELBASVIR-GRAZOPREVIR	116
6627001500	ADALIMUMAB	414
2710400300	INSULIN GLARGINE	4,357
2710400500	INSULIN LISPRO	2,253
1235990265	SOFOSBUVIR-VELPATASVIR	52
9410003000	GLUCOSE BLOOD	9,673
4420101010	ALBUTEROL SULFATE	25,691
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMID	337
1210990315	ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	317
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	445
4420990275	FLUTICASONE FUROATE-VILANTEROL	2,078
2710400200	INSULIN ASPART	1,151
6629003000	ETANERCEPT	133
6240552500	DIMETHYL FUMARATE	82
3010002000	SOMATROPIN	92
1210990430	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR DF	161
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	4,068
2717001500	DULAGLUTIDE	645
1210301510	DOLUTEGRAVIR SODIUM	270
5940002310	LURASIDONE HCL	331
6599000220	OXYCODONE W/ ACETAMINOPHEN	7,897
7260005700	PREGABALIN	797
4440003620	MOMETASONE FUROATE (INHALATION)	1,743
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,291
1250406020	OSELTAMIVIR PHOSPHATE	2,583
2770005000	EMPAGLIFLOZIN	761
5925001500	ARIPIPRAZOLE	1,404
6520001020	BUPRENORPHINE HCL-NALOXONE HCL DIHYDRATE	1,050
6599170210	HYDROCODONE-ACETAMINOPHEN	20,490
1210990339	EMTRICITABINE-RILPIVIRINE-TENOFOVIR ALAFENAMIDE FUMARATE	121
9939405000	LENALIDOMIDE	20
8337006000	RIVAROXABAN	726
2770002000	CANAGLIFLOZIN	661
8582004010	ICATIBANT ACETATE	3
9025058500	USTEKINUMAB	18
5907005010	PALIPERIDONE PALMITATE	105
8337001000	APIXABAN	671
1210990330	EFAVIRENZ-EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	95
1210990229	EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	157
5250502010	CERTOLIZUMAB PEGOL	56
1210990340	EMTRICITABINE-RILPIVIRINE-TENOFOVIR DISOPROXIL FUMARATE	80
3890004000	EPINEPHRINE (ANAPHYLAXIS)	710

Q4 2017	Top 50 Drugs by Paid Amount	2 of 2
Class	**Label Name**	**Claim Count**
2153402000	DASATINIB	20
1210990227	DARUNAVIR-COBICISTAT	120
7260003000	GABAPENTIN	13,788
9025057500	SECUKINUMAB	29
6240003010	GLATIRAMER ACETATE	34
2153106000	PALBOCICLIB	17
6240306045	INTERFERON BETA-1A	28
2710400600	INSULIN DETEMIR	413

Q1 2018	Top 50 Drugs by Paid Amount	1 of 2
Class	Label Name	Claim Count
6627001500	ADALIMUMAB	380
2710400300	INSULIN GLARGINE	4,359
2710400500	INSULIN LISPRO	2,266
4420101010	ALBUTEROL SULFATE	28,236
1235990235	GLECAPREVIR-PIBRENTASVIR	89
1235990230	ELBASVIR-GRAZOPREVIR	56
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMID	344
9410003000	GLUCOSE BLOOD	9,334
1210990315	ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	329
1235990265	SOFOSBUVIR-VELPATASVIR	34
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	437
1250406020	OSELTAMIVIR PHOSPHATE	5,109
4420990275	FLUTICASONE FUROATE-VILANTEROL	1,872
2710400200	INSULIN ASPART	1,177
6629003000	ETANERCEPT	113
2717001500	DULAGLUTIDE	795
1210301510	DOLUTEGRAVIR SODIUM	302
6240552500	DIMETHYL FUMARATE	71
5940002310	LURASIDONE HCL	365
3010002000	SOMATROPIN	82
1210990430	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR DF	144
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	4,040
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,355
7260005700	PREGABALIN	781
2770005000	EMPAGLIFLOZIN	852
4440003620	MOMETASONE FUROATE (INHALATION)	1,829
5925001500	ARIPIPRAZOLE	1,434
6520001020	BUPRENORPHINE HCL-NALOXONE HCL DIHYDRATE	1,109
6599000220	OXYCODONE W/ ACETAMINOPHEN	6,496
1210990229	EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	201
9025058500	USTEKINUMAB	21
8337006000	RIVAROXABAN	746
2770002000	CANAGLIFLOZIN	619
8337001000	APIXABAN	701
5907005010	PALIPERIDONE PALMITATE	113
1210990339	EMTRICITABINE-RILPIVIRINE-TENOFOVIR ALAFENAMIDE FUMARATE	100
6599170210	HYDROCODONE-ACETAMINOPHEN	15,721
1210990330	EFAVIRENZ-EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	95
2153406020	NILOTINIB HCL	22
9939405000	LENALIDOMIDE	19
3890004000	EPINEPHRINE (ANAPHYLAXIS)	800
1210990227	DARUNAVIR-COBICISTAT	130

Q1 2018	Top 50 Drugs by Paid Amount	2 of 2
Class	Label Name	Claim Count
5250502010	CERTOLIZUMAB PEGOL	49
1210990340	EMTRICITABINE-RILPIVIRINE-TENOFOVIR DISOPROXIL FUMARATE	86
4440001500	BUDESONIDE (INHALATION)	1,019
6240407000	TERIFLUNOMIDE	34
6240306045	INTERFERON BETA-1A	31
4420990295	UMECLIDINIUM-VILANTEROL	497
7260003000	GABAPENTIN	13,594
8582004010	ICATIBANT ACETATE	2

Q2 2018	Top 50 Drugs by Paid Amount	1 of 2
Class	Label Name	Claim Count
6627001500	ADALIMUMAB	381
2710400300	INSULIN GLARGINE	4,533
2710400500	INSULIN LISPRO	2,399
1235990235	GLECAPREVIR-PIBRENTASVIR	103
4420101010	ALBUTEROL SULFATE	21,522
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMID	348
9410003000	GLUCOSE BLOOD	9,270
1210990315	ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	297
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	432
2717001500	DULAGLUTIDE	921
2710400200	INSULIN ASPART	1,152
1210301510	DOLUTEGRAVIR SODIUM	347
6629003000	ETANERCEPT	120
5940002310	LURASIDONE HCL	427
4420990275	FLUTICASONE FUROATE-VILANTEROL	1,691
6240552500	DIMETHYL FUMARATE	64
2770005000	EMPAGLIFLOZIN	947
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	4,058
1210990229	EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	262
5925001500	ARIPIPRAZOLE	1,512
1210990430	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR DF	128
7260005700	PREGABALIN	776
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,274
3010002000	SOMATROPIN	73
6520001020	BUPRENORPHINE HCL-NALOXONE HCL DIHYDRATE	1,062
8337001000	APIXABAN	771
6599000220	OXYCODONE W/ ACETAMINOPHEN	6,105
8337006000	RIVAROXABAN	726
5250502010	CERTOLIZUMAB PEGOL	57
3030001000	CORTICOTROPIN	6
9025058500	USTEKINUMAB	18
2770002000	CANAGLIFLOZIN	562
1210990339	EMTRICITABINE-RILPIVIRINE-TENOFOVIR ALAFENAMIDE FUMARATE	98
9939405000	LENALIDOMIDE	21
3890004000	EPINEPHRINE (ANAPHYLAXIS)	825
1210990227	DARUNAVIR-COBICISTAT	136
2153406020	NILOTINIB HCL	22
5907005010	PALIPERIDONE PALMITATE	105
6599170210	HYDROCODONE-ACETAMINOPHEN	14,251
1210990330	EFAVIRENZ-EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	84
1210990340	EMTRICITABINE-RILPIVIRINE-TENOFOVIR DISOPROXIL FUMARATE	80
4440003310	FLUTICASONE FUROATE (INHALATION)	1,100

Q2 2018	Top 50 Drugs by Paid Amount	2 of 2
Class	Label Name	Claim Count
6240407000	TERIFLUNOMIDE	31
6240306045	INTERFERON BETA-1A	28
7260003000	GABAPENTIN	13,330
6240003010	GLATIRAMER ACETATE	42
4016000700	AMBRISENTAN	20
1210990324	BICTEGRAVIR-EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	62
6210008020	VARENICLINE TARTRATE	435
5255705000	LINACLOTIDE	430

Top 50 Drugs by Group by Claim Amount

Q3 2017	Top 50 Drugs by Claim Amount	1 of 2
Class	Label Name	Claim Count
6599170210	HYDROCODONE-ACETAMINOPHEN	22,544
6610002000	IBUPROFEN	21,939
4420101010	ALBUTEROL SULFATE	20,546
3610003000	LISINOPRIL	15,488
2725005000	METFORMIN HCL	14,551
7260003000	GABAPENTIN	13,954
3940001010	ATORVASTATIN CALCIUM	13,273
0120001010	AMOXICILLIN	12,629
2810001010	LEVOTHYROXINE SODIUM	11,235
4927006000	OMEPRAZOLE	10,667
3400000310	AMLODIPINE BESYLATE	10,662
5710001000	ALPRAZOLAM	10,459
4220003230	FLUTICASONE PROPIONATE (NASAL)	10,171
9410003000	GLUCOSE BLOOD	10,008
4450505010	MONTELUKAST SODIUM	9,450
6599000220	OXYCODONE W/ ACETAMINOPHEN	9,176
5816007010	SERTRALINE HCL	6,880
4155003000	LORATADINE	6,877
3615004020	LOSARTAN POTASSIUM	6,514
7510005010	CYCLOBENZAPRINE HCL	6,175
5812008010	TRAZODONE HCL	6,090
6510009510	TRAMADOL HCL	6,033
0340001000	AZITHROMYCIN	5,927
3760004000	HYDROCHLOROTHIAZIDE	5,903
6610005200	MELOXICAM	5,649
6610006000	NAPROXEN	5,556
4155002010	CETIRIZINE HCL	5,431
6510007510	OXYCODONE HCL	5,362
2210004500	PREDNISONE	5,303
7720203200	CHOLECALCIFEROL	5,145
5025006500	ONDANSETRON	4,950
5915307010	QUETIAPINE FUMARATE	4,943
9720202500	LANCETS	4,939
7510009010	TIZANIDINE HCL	4,796
3320003010	METOPROLOL TARTRATE	4,767
4927007010	PANTOPRAZOLE SODIUM	4,730
5830004010	BUPROPION HCL	4,638
0210002000	CEPHALEXIN	4,555
3940007500	SIMVASTATIN	4,474

Q3 2017	Top 50 Drugs by Claim Amount	2 of 2
Class	Label Name	Claim Count
5816004000	FLUOXETINE HCL	4,454
6020408010	ZOLPIDEM TARTRATE	4,432
9055008510	TRIAMCINOLONE ACETONIDE (TOPICAL)	4,388
2710400300	INSULIN GLARGINE	4,328
1140701500	FLUCONAZOLE	4,146
7210001000	CLONAZEPAM	4,146
4920002010	RANITIDINE HCL	4,076
0199000220	AMOXICILLIN & POT CLAVULANATE	4,070
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	4,070
5816003410	ESCITALOPRAM OXALATE	4,051
6410001000	ASPIRIN	4,044

Q4 2017	Top 50 Drugs by Claim Amount	1 of 2
Class	Label Name	Claim Count
4420101010	ALBUTEROL SULFATE	25,691
6610002000	IBUPROFEN	23,621
6599170210	HYDROCODONE-ACETAMINOPHEN	20,490
0120001010	AMOXICILLIN	16,739
3610003000	LISINOPRIL	15,034
2725005000	METFORMIN HCL	14,136
3940001010	ATORVASTATIN CALCIUM	13,838
7260003000	GABAPENTIN	13,788
4220003230	FLUTICASONE PROPIONATE (NASAL)	11,646
2810001010	LEVOTHYROXINE SODIUM	11,103
3400000310	AMLODIPINE BESYLATE	10,714
4927006000	OMEPRAZOLE	10,440
4450505010	MONTELUKAST SODIUM	10,306
5710001000	ALPRAZOLAM	9,818
9410003000	GLUCOSE BLOOD	9,673
0340001000	AZITHROMYCIN	9,061
4155003000	LORATADINE	8,037
6599000220	OXYCODONE W/ ACETAMINOPHEN	7,897
5816007010	SERTRALINE HCL	6,705
3615004020	LOSARTAN POTASSIUM	6,618
2210004500	PREDNISONE	6,479
4155002010	CETIRIZINE HCL	6,275
5025006500	ONDANSETRON	6,218
7510005010	CYCLOBENZAPRINE HCL	5,972
5812008010	TRAZODONE HCL	5,891
3760004000	HYDROCHLOROTHIAZIDE	5,756
6610005200	MELOXICAM	5,559
0199000220	AMOXICILLIN & POT CLAVULANATE	5,477
6610006000	NAPROXEN	5,442
6510009510	TRAMADOL HCL	5,216
6510007510	OXYCODONE HCL	5,184
7720203200	CHOLECALCIFEROL	5,067
3320003010	METOPROLOL TARTRATE	4,827
7510009010	TIZANIDINE HCL	4,760
5915307010	QUETIAPINE FUMARATE	4,733
9720202500	LANCETS	4,687
5830004010	BUPROPION HCL	4,561
4927007010	PANTOPRAZOLE SODIUM	4,366
2710400300	INSULIN GLARGINE	4,357
5816004000	FLUOXETINE HCL	4,324
0210002000	CEPHALEXIN	4,308
3940007500	SIMVASTATIN	4,264
9055008510	TRIAMCINOLONE ACETONIDE (TOPICAL)	4,247

Q4 2017	Top 50 Drugs by Claim Amount	2 of 2
Class	Label Name	Claim Count
6410001000	ASPIRIN	4,173
5816003410	ESCITALOPRAM OXALATE	4,153
4920002010	RANITIDINE HCL	4,099
6020408010	ZOLPIDEM TARTRATE	4,098
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	4,068
4399580332	PSEUDOEPHED-BROMPHEN-DM	3,971
7210001000	CLONAZEPAM	3,892

Q1 2018	Top 50 Drugs by Claim Amount	1 of 2
Class	Label Name	Claim Count
4420101010	ALBUTEROL SULFATE	28,236
6610002000	IBUPROFEN	24,120
0120001010	AMOXICILLIN	18,649
6599170210	HYDROCODONE-ACETAMINOPHEN	15,721
3610003000	LISINOPRIL	14,633
3940001010	ATORVASTATIN CALCIUM	14,014
2725005000	METFORMIN HCL	13,601
7260003000	GABAPENTIN	13,594
4220003230	FLUTICASONE PROPIONATE (NASAL)	12,289
2810001010	LEVOTHYROXINE SODIUM	10,915
4450505010	MONTELUKAST SODIUM	10,813
0340001000	AZITHROMYCIN	10,506
3400000310	AMLODIPINE BESYLATE	10,425
4927006000	OMEPRAZOLE	10,048
9410003000	GLUCOSE BLOOD	9,334
5710001000	ALPRAZOLAM	8,483
4155003000	LORATADINE	8,425
2210004500	PREDNISONE	7,112
5816007010	SERTRALINE HCL	6,690
3615004020	LOSARTAN POTASSIUM	6,677
4155002010	CETIRIZINE HCL	6,538
6599000220	OXYCODONE W/ ACETAMINOPHEN	6,496
0199000220	AMOXICILLIN & POT CLAVULANATE	6,104
5812008010	TRAZODONE HCL	6,074
5025006500	ONDANSETRON	6,055
7510005010	CYCLOBENZAPRINE HCL	5,818
6610006000	NAPROXEN	5,642
3760004000	HYDROCHLOROTHIAZIDE	5,480
6610005200	MELOXICAM	5,406
4399580332	PSEUDOEPHED-BROMPHEN-DM	5,121
1250406020	OSELTAMIVIR PHOSPHATE	5,109
7720203200	CHOLECALCIFEROL	5,094
5915307010	QUETIAPINE FUMARATE	4,869
6510007510	OXYCODONE HCL	4,582
3320003010	METOPROLOL TARTRATE	4,560
9720202500	LANCETS	4,508
7510009010	TIZANIDINE HCL	4,496
5830004010	BUPROPION HCL	4,455
2710400300	INSULIN GLARGINE	4,359
4927007010	PANTOPRAZOLE SODIUM	4,350
9055008510	TRIAMCINOLONE ACETONIDE (TOPICAL)	4,349
5816004000	FLUOXETINE HCL	4,277

Q1 2018	Top 50 Drugs by Claim Amount	2 of 2
Class	Label Name	Claim Count
4920002010	RANITIDINE HCL	4,130
3940007500	SIMVASTATIN	4,105
0210002000	CEPHALEXIN	4,076
5816003410	ESCITALOPRAM OXALATE	4,054
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	4,040
6410001000	ASPIRIN	3,983
1140701500	FLUCONAZOLE	3,765
4310201000	BENZONATATE	3,579

Q2 2018	Top 50 Drugs by Claim Amount	1 of 2
Class	Label Name	Claim Count
4420101010	ALBUTEROL SULFATE	21,522
6610002000	IBUPROFEN	21,084
3940001010	ATORVASTATIN CALCIUM	14,814
3610003000	LISINOPRIL	14,429
6599170210	HYDROCODONE-ACETAMINOPHEN	14,251
2725005000	METFORMIN HCL	13,546
7260003000	GABAPENTIN	13,330
0120001010	AMOXICILLIN	12,945
4220003230	FLUTICASONE PROPIONATE (NASAL)	12,289
4450505010	MONTELUKAST SODIUM	11,455
2810001010	LEVOTHYROXINE SODIUM	10,873
3400000310	AMLODIPINE BESYLATE	10,514
4927006000	OMEPRAZOLE	9,986
9410003000	GLUCOSE BLOOD	9,270
4155003000	LORATADINE	8,585
5710001000	ALPRAZOLAM	7,942
4155002010	CETIRIZINE HCL	7,064
3615004020	LOSARTAN POTASSIUM	6,705
5816007010	SERTRALINE HCL	6,616
0340001000	AZITHROMYCIN	6,167
5812008010	TRAZODONE HCL	6,118
6599000220	OXYCODONE W/ ACETAMINOPHEN	6,105
7510005010	CYCLOBENZAPRINE HCL	5,739
2210004500	PREDNISONE	5,726
5025006500	ONDANSETRON	5,625
6610006000	NAPROXEN	5,444
3760004000	HYDROCHLOROTHIAZIDE	5,385
6610005200	MELOXICAM	5,361
7720203200	CHOLECALCIFEROL	5,306
5915307010	QUETIAPINE FUMARATE	4,701
9720202500	LANCETS	4,593
9055008510	TRIAMCINOLONE ACETONIDE (TOPICAL)	4,564
3320003010	METOPROLOL TARTRATE	4,562
5830004010	BUPROPION HCL	4,561
7510009010	TIZANIDINE HCL	4,550
2710400300	INSULIN GLARGINE	4,533
0199000220	AMOXICILLIN & POT CLAVULANATE	4,487
4927007010	PANTOPRAZOLE SODIUM	4,453
6510007510	OXYCODONE HCL	4,449
5816004000	FLUOXETINE HCL	4,193
0210002000	CEPHALEXIN	4,087
5816003410	ESCITALOPRAM OXALATE	4,082

Q2 2018	Top 50 Drugs by Claim Amount	2 of 2
Class	Label Name	Claim Count
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	4,058
4920002010	RANITIDINE HCL	4,019
6410001000	ASPIRIN	3,961
3940007500	SIMVASTATIN	3,959
1140701500	FLUCONAZOLE	3,666
5818002510	DULOXETINE HCL	3,348
7720203000	ERGOCALCIFEROL	3,348
3699180255	LISINOPRIL & HYDROCHLOROTHIAZIDE	3,342

Top 50 Drugs By Claim Volume- Q3 2017–Q2 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBER	RANK NAME	Specialty Indicator	CLAIM COUNT	UTILIZER COUNT
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	1	VENTOLIN HFA AER	No	5,533	2,930
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	2	IBU TAB 800MG	No	3,516	2,489
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	3	FLUTICASONE SPR 50MCG	No	3,178	1,916
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	4	GABAPENTIN CAP 300MG	No	2,825	1,044
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	5	AMOXICILLIN CAP 500MG	No	2,770	2,315
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	6	IBUPROFEN TAB 800MG	No	2,492	1,744
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	7	AZITHROMYCIN TAB 250MG	No	2,353	2,059
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	8	HYDROCO/APAP TAB 5-325MG	No	2,316	1,751
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	9	HYDROCO/APAP TAB 10-325MG	No	2,273	738
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	10	NAPROXEN TAB 500MG	No	2,181	1,404
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	11	CYCLOBENZAPR TAB 10MG	No	2,157	1,110
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	12	ATORVASTATIN TAB 20MG	No	2,063	589
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	13	MONTELUKAST TAB 10MG	No	2,027	719
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	14	AMLODIPINE TAB 10MG	No	1,959	632
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	15	ONDANSETRON TAB 4MG ODT	No	1,946	1,563
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	16	LORATADINE TAB 10MG	No	1,879	949
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	17	METFORMIN TAB 1000MG	No	1,867	553
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	18	METFORMIN TAB 500MG	No	1,866	672
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	19	ALBUTEROL NEB 0.083%	No	1,809	1,267
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	20	VITAMIN D CAP 50000UNT	No	1,754	641
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	21	TIZANIDINE TAB 4MG	No	1,751	581
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	22	OXYCOD/APAP TAB 10-325MG	No	1,744	458
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	23	ATORVASTATIN TAB 40MG	No	1,688	530
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	24	LISINOPRIL TAB 10MG	No	1,628	590
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	25	SERTRALINE TAB 100MG	No	1,593	470
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	26	OMEPRAZOLE CAP 20MG	No	1,585	650
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	27	LISINOPRIL TAB 20MG	No	1,584	564
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	28	AMOX/K CLAV TAB 875-125	No	1,537	1,360
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	29	AMOXICILLIN SUS 400/5ML	No	1,499	1,302
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	30	METRONIDAZOL TAB 500MG	No	1,481	1,277
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	31	CEPHALEXIN CAP 500MG	No	1,481	1,343
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	32	PANTOPRAZOLE TAB 40MG	No	1,452	567

Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	33	SERTRALINE TAB 50MG	No	1,445	636
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	34	PREDNISONE TAB 20MG	No	1,444	1,217
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	35	TRAZODONE TAB 50MG	No	1,437	594
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	36	AMLODIPINE TAB 5MG	No	1,422	547
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	37	OMEPRAZOLE CAP 40MG	No	1,376	466
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	38	ALPRAZOLAM TAB 1MG	No	1,366	367
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	39	TRAZODONE TAB 100MG	No	1,355	468
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	40	METHYLPRED TAB 4MG	No	1,319	1,147
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	41	TRAMADOL HCL TAB 50MG	No	1,319	883
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	42	MELOXICAM TAB 15MG	No	1,309	569
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	43	HYDROCO/APAP TAB 7.5-325	No	1,306	761
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	44	FLUCONAZOLE TAB 150MG	No	1,252	869
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	45	TRUE METRIX TES GLUCOSE	No	1,241	553
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	46	SUBOXONE MIS 8-2MG	No	1,180	167
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	47	ZOLPIDEM TAB 10MG	No	1,157	336
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	48	GABAPENTIN TAB 600MG	No	1,137	330
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	49	SMZ/TMP DS TAB 800-160	No	1,134	967
Top Drugs By Claim Volume	07/01/2017 - 06/30/2018	50	HYDROCHLOROT TAB 25MG	No	1,125	399

Top 50 Drugs By Spend- Q3 2017–Q2 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBER	RANK NAME	Specialty Indicator	CLAIM COUNT	UTILIZER COUNT
Top Drugs By Spend	07/01/2017 - 06/30/2018	1	GENVOYA TAB	No	310	71
Top Drugs By Spend	07/01/2017 - 06/30/2018	2	MAVYRET TAB 100-40MG	Yes	43	22
Top Drugs By Spend	07/01/2017 - 06/30/2018	3	TRUVADA TAB 200-300	No	339	84
Top Drugs By Spend	07/01/2017 - 06/30/2018	4	TIVICAY TAB 50MG	No	313	70
Top Drugs By Spend	07/01/2017 - 06/30/2018	5	TRIUMEQ TAB	No	172	39
Top Drugs By Spend	07/01/2017 - 06/30/2018	6	DESCOVY TAB 200/25	No	245	59
Top Drugs By Spend	07/01/2017 - 06/30/2018	7	EPCLUSA TAB 400-100	Yes	13	5
Top Drugs By Spend	07/01/2017 - 06/30/2018	8	SUBOXONE MIS 8-2MG	No	1,180	167
Top Drugs By Spend	07/01/2017 - 06/30/2018	9	VENTOLIN HFA AER	No	5,533	2,930
Top Drugs By Spend	07/01/2017 - 06/30/2018	10	STRIBILD TAB	No	86	23
Top Drugs By Spend	07/01/2017 - 06/30/2018	11	VICTOZA INJ 18MG/3ML	No	263	73
Top Drugs By Spend	07/01/2017 - 06/30/2018	12	OXYCOD/APAP TAB 10-325MG	No	1,744	458
Top Drugs By Spend	07/01/2017 - 06/30/2018	13	LANTUS INJ SOLOSTAR	No	414	179
Top Drugs By Spend	07/01/2017 - 06/30/2018	14	SYMBICORT AER 160-4.5	No	522	217
Top Drugs By Spend	07/01/2017 - 06/30/2018	15	TECFIDERA CAP 240MG	Yes	22	5
Top Drugs By Spend	07/01/2017 - 06/30/2018	16	PREZCOBIX TAB 800-150	No	85	20
Top Drugs By Spend	07/01/2017 - 06/30/2018	17	COMPLERA TAB	No	56	12
Top Drugs By Spend	07/01/2017 - 06/30/2018	18	HUMIRA PEN INJ 40MG/0.8	Yes	31	8
Top Drugs By Spend	07/01/2017 - 06/30/2018	19	ZEPATIER TAB 50-100MG	Yes	8	4
Top Drugs By Spend	07/01/2017 - 06/30/2018	20	LATUDA TAB 40MG	No	126	63
Top Drugs By Spend	07/01/2017 - 06/30/2018	21	BASAGLAR INJ 100UNIT	No	416	133
Top Drugs By Spend	07/01/2017 - 06/30/2018	22	HUMALOG KWIK INJ 100/ML	No	255	98
Top Drugs By Spend	07/01/2017 - 06/30/2018	23	JANUVIA TAB 100MG	No	269	77
Top Drugs By Spend	07/01/2017 - 06/30/2018	24	ELIQUIS TAB 5MG	No	312	107
Top Drugs By Spend	07/01/2017 - 06/30/2018	25	PRIVIGEN INJ 20GRAMS	Yes	8	1
Top Drugs By Spend	07/01/2017 - 06/30/2018	26	TECFIDERA CAP 120MG	Yes	10	3
Top Drugs By Spend	07/01/2017 - 06/30/2018	27	SUBOXONE MIS 12-3MG	No	164	26
Top Drugs By Spend	07/01/2017 - 06/30/2018	28	TAGRISSO TAB 80MG	Yes	8	1
Top Drugs By Spend	07/01/2017 - 06/30/2018	29	LENVIMA CAP 20 MG	Yes	7	1
Top Drugs By Spend	07/01/2017 - 06/30/2018	30	REVLIMID CAP 25MG	Yes	10	3
Top Drugs By Spend	07/01/2017 - 06/30/2018	31	XARELTO TAB 20MG	No	281	71
Top Drugs By Spend	07/01/2017 - 06/30/2018	32	HUMALOG INJ 100/ML	No	240	82

Top Drugs By Spend	07/01/2017 - 06/30/2018	33	LEMTRADA INJ 12/1.2ML	Yes	1	1
Top Drugs By Spend	07/01/2017 - 06/30/2018	34	NOVOLOG INJ FLEXPEN	No	203	75
Top Drugs By Spend	07/01/2017 - 06/30/2018	35	AUBAGIO TAB 14MG	Yes	16	2
Top Drugs By Spend	07/01/2017 - 06/30/2018	36	TRULICITY INJ 1.5/0.5	No	129	33
Top Drugs By Spend	07/01/2017 - 06/30/2018	37	ATRIPLA TAB	No	36	10
Top Drugs By Spend	07/01/2017 - 06/30/2018	38	ODEFSEY TAB	No	36	8
Top Drugs By Spend	07/01/2017 - 06/30/2018	39	LATUDA TAB 80MG	No	75	33
Top Drugs By Spend	07/01/2017 - 06/30/2018	40	ENBREL SRCLK INJ 50MG/ML	Yes	14	4
Top Drugs By Spend	07/01/2017 - 06/30/2018	41	ZYTIGA TAB 250MG	Yes	8	2
Top Drugs By Spend	07/01/2017 - 06/30/2018	42	LEVEMIR INJ FLEXTOUC	No	213	77
Top Drugs By Spend	07/01/2017 - 06/30/2018	43	SYNAGIS INJ 100MG/ML	Yes	28	11
Top Drugs By Spend	07/01/2017 - 06/30/2018	44	ABILIFY MAIN INJ 400MG	Yes	37	14
Top Drugs By Spend	07/01/2017 - 06/30/2018	45	ISENTRESS TAB 400MG	No	54	15
Top Drugs By Spend	07/01/2017 - 06/30/2018	46	LANTUS INJ 100/ML	No	204	93
Top Drugs By Spend	07/01/2017 - 06/30/2018	47	LYRICA CAP 150MG	No	145	34
Top Drugs By Spend	07/01/2017 - 06/30/2018	48	XYREM SOL 500MG/ML	Yes	6	1
Top Drugs By Spend	07/01/2017 - 06/30/2018	49	PREZISTA TAB 800MG	No	48	13
Top Drugs By Spend	07/01/2017 - 06/30/2018	50	NUTROPIN AQ INJ 20MG/2ML	Yes	6	1

RxTrack®

RXT6050D - Summarized DUR Activity Report

From 4/1/18 Through 6/30/18

Oct 5, 2018
2:41:53 PM

Claims Summary:

RxCLAIM Status	Total Rxs with cDUR(s)	% Total Rxs with cDUR(s)	Total Rxs with No cDURs	% Total Rxs with No cDURs	Total Rxs	% Total Rxs	Total Plan Paid	Total Member Paid
Paid	278,375	74.05%	308,921	57.52%	587,296	64.33%	$51,836,094.02	$0.00
Rejected	49,458	13.16%	169,725	31.60%	219,183	24.01%		
Reversed	48,091	12.79%	58,384	10.87%	106,475	11.66%		
Totals	**375,924**	**100.00%**	**537,030**	**100.00%**	**912,954**	**100.00%**		

cDUR Information Summary Table:

	Total cDURs			cDURs on Paid Rxs			cDURs on Rejected Rxs			cDURs on Reversed Rxs		
cDUR Type	Total cDUR Triggered Events	Count	% of All cDURs	Count	% of cDUR Type	% Total cDURs	Count	% of cDUR Type	% Total cDURs	Count	% of cDUR Type	% Total cDURs
Dosing/Duration (DOSECHEK)	83,102	56,385	15.00%	46,183	81.91%	16.59%	123	0.22%	0.25%	10,079	17.88%	20.96%
Drug Age Caution (DRUG_AGE)	34	34	0.01%	30	88.24%	0.01%	0	0.0%	0.0%	4	11.76%	0.01%
Drug-Drug Interaction (DDI-DTMS)	503,862	157,643	41.93%	136,470	86.57%	49.02%	3,374	2.14%	6.82%	17,799	11.29%	37.01%
Duplicate Rx (DUPRX)	60,919	58,610	15.59%	15,999	27.30%	5.75%	37,841	64.56%	76.51%	4,770	8.14%	9.92%
Drug Regimen Compliance (COMPLIAN)	47,315	43,773	11.64%	37,606	85.91%	13.51%	0	0.0%	0.0%	6,167	14.09%	12.82%
Duplicate Therapy (DUPTHER)	136,539	59,479	15.82%	42,087	70.76%	15.12%	8,120	13.65%	16.42%	9,272	15.59%	19.28%
Total All cDURs	**831,771**	**375,924**	**100.00%**	**278,375**	**74.05%**	**100.00%**	**49,458**	**13.16%**	**100.00%**	**48,091**	**12.79%**	**100.00%**

RXT6050D - Summarized DUR Activity Report

From 4/1/18 Through 6/30/18

* cDUR Information Summary results are sorted by Total cDUR count in descending order
* Some RxClaims could have multiple cDUR edit types
* The Count and % of cDUR Type for Paid, Rejected and Reversed Rxs are based on cDUR Type totals for each row

Fee for Service Medicaid

RXT6050D - Summarized DUR Activity Report

From 4/1/18 Through 6/30/18

DUR Service	Top Drug Drug Interaction	GPI 4	GPI 4 Description	GPI 4/ Therapy / Reason	GPI 04 Description	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per RX	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount	% Overriden	Top PPS CODE USED #1	Top PPS CODE USED #2	Top PPS CODE USED #3
Dosing/Duration (DOSECHEK)	CYCLOBENZAPRINE HCL	7510	NA	MAX DAYS THERAPY = 21	CENTRAL MUSCLE RELAXANTS**	Message	1,972	$24,065.52	$18,796.47	$0.00	62,507.0	130,361.0	0	148	$1,488.94	0.28%	ID,M0,1B		
Dosing/Duration (DOSECHEK)	ONDANSETRON ODT	5025	NA	GERIATRIC MIN DLY = 2.00UN	5-HT3 RECEPTOR ANTAGONISTS**	Message	924	$686.17	$490.02	$0.00	1,340.0	1,297.8	0	326	$112.84	0.00%			
Dosing/Duration (DOSECHEK)	SENSIPAR	3090	NA	GERIATRIC MAX DLY = 12.00UN	METABOLIC MODIFIERS**	Message	663	$258,113.68	$224,813.35	$0.00	663.0	66,213.0	0	41	$23,655.52	0.00%			
Dosing/Duration (DOSECHEK)	IPRATROPIUM BROMIDE/ALBUTEROL SULFATE	4420	NA	MIN. DAYS THERAPY = 30	SYMPATHOMIMETICS**	Message	659	$13,358.03	$9,626.72	$0.00	5,835.0	79,137.0	0	100	$1,120.97	0.19%	ID,M0,1B		
Dosing/Duration (DOSECHEK)	IPRATROPIUM BROMIDE/ALBUTEROL SULFATE	4420	NA	GERIATRIC MIN DLY = 9.00UN	SYMPATHOMIMETICS**	Message	633	$565.38	$367.43	$0.00	1,403.0	5,730.0	0	185	$70.14	0.00%			
Dosing/Duration (DOSECHEK)	KETOROLAC TROMETHAMINE	6610	NA	GERIATRIC MAX DLY = 2.00UN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)**	Message	463	$7,351.48	$4,625.86	$0.00	463.0	2,435.0	0	33	$375.11	0.00%			
Dosing/Duration (DOSECHEK)	POTASSIUM CHLORIDE ER	7970	NA	ADULT MIN DLY = 2.00 UN	POTASSIUM**	Message	432	$8,469.18	$7,021.12	$0.00	17,866.0	17,571.0	0	45	$741.50	0.19%	LD,R0,1B		
Dosing/Duration (DOSECHEK)	LISINOPRIL	3610	NA	MIN. DAYS THERAPY = 7	ACE INHIBITORS**	Message	395	$129.30	$62.57	$0.00	405.0	550.0	0	160	$35.73	0.00%			
Dosing/Duration (DOSECHEK)	HEPARIN SODIUM	8310	NA	GERIATRIC MIN DLY = 4.00UN	HEPARINS AND HEPARINOID-LIKE AGENTS**	Message	379	$2,174.54	$925.53	$0.00	469.0	747.6	0	198	$736.24	0.00%			
Dosing/Duration (DOSECHEK)	PANTOPRAZOLE SODIUM	4927	NA	MIN. DAYS THERAPY = 7	PROTON PUMP INHIBITORS**	Message	358	$114.64	$64.66	$0.00	368.0	383.0	0	223	$39.80	0.00%			
Drug Age Caution (DRUG_AGE)	ACETAMINOPHEN/CODEINE	6599	NA	AGE LESS THAN 10	OPIOID COMBINATIONS**	Message	5	$57.87	$57.87	$0.00	43.0	973.0	0	0		20.00%	PA,M0,1G		
Drug Age Caution (DRUG_AGE)	PROMETHAZINE HCL PLAIN	4140	NA	AGE LESS THAN 4	ANTIHISTAMINES - PHENOTHIAZINES**	Message	4	$40.70	$22.15	$0.00	20.0	210.0	0	2	$18.55	0.00%			
Drug Age Caution (DRUG_AGE)	NITROFURANTOIN	5300	NA	AGE LESS THAN 4	URINARY ANTI-INFECTIVES**	Message	4	$1,329.74	$1,158.88	$0.00	37.0	920.0	0	1	$170.86	0.00%			
Drug Age Caution (DRUG_AGE)	PROMETHAZINE-DM	4399	NA	AGE LESS THAN 4	COUGH/COLD/ALLERGY COMBINATIONS**	Message	4	$32.29	$32.29	$0.00	26.0	195.0	0	0		0.00%			
Drug Age Caution (DRUG_AGE)	PROMETHAZINE/CODEINE	4399	NA	AGE LESS THAN 10	COUGH/COLD/ALLERGY COMBINATIONS**	Message	3	$28.00	$28.00	$0.00	33.0	300.0	0	0		0.00%			
Drug Age Caution (DRUG_AGE)	ACETAMINOPHEN/CODEINE	6599	NA	AGE LESS THAN 4	OPIOID COMBINATIONS**	Message	2	$17.87	$17.87	$0.00	7.0	95.0	0	0		0.00%			
Drug Age Caution (DRUG_AGE)	COMPOUND CLAIM	0000	NA	ING01 AGE LESS THAN 4	-	Message	2	$27.65	$27.65	$0.00	60.0	160.0	0	0		0.00%			
Drug Age Caution (DRUG_AGE)	PHENADOZ	4140	NA	AGE LESS THAN 4	ANTIHISTAMINES - PHENOTHIAZINES**	Message	2	$88.78	$88.78	$0.00	4.0	12.0	0	0		0.00%			
Drug Age Caution (DRUG_AGE)	NITROFURANTOIN MACROCRYSTALS	5300	NA	AGE LESS THAN 4	URINARY ANTI-INFECTIVES**	Message	1	$915.76	$457.88	$0.00	90.0	90.0	0	1	$457.88	0.00%			
Drug Age Caution (DRUG_AGE)	INFANRIX	1899	NA	AGE GREATER THAN 64	TOXOID COMBINATIONS**	Message	1	$24.05	$24.05	$0.00	1.0	0.5	0	0		0.00%			
Drug Age Caution (DRUG_AGE)	PROMETHAZINE HCL	4140	NA	AGE LESS THAN 4	ANTIHISTAMINES - PHENOTHIAZINES**	Message	1	$10.99	$10.99	$0.00	7.0	60.0	0	0		0.00%			
Drug Age Caution (DRUG_AGE)	TRAMADOL HCL	6510	NA	AGE LESS THAN 10	OPIOID AGONISTS**	Message	1	$10.26	$10.26	$0.00	5.0	5.0	0	0		0.00%			
Drug Regimen Compliance (COMPLIAN)	GABAPENTIN	7260	NA	7 DAYS LATE REFILLING	ANTICONVULSANTS - MISC.**	Message	63	$1,028.60	$791.77	$0.00	1,852.0	5,671.0	0	11	$174.84	3.85%	LR,M0,1G		
Drug Regimen Compliance (COMPLIAN)	ATORVASTATIN CALCIUM	3940	NA	7 DAYS LATE REFILLING	HMG COA REDUCTASE INHIBITORS**	Message	53	$637.20	$547.13	$0.00	1,656.0	1,746.0	0	6	$63.25	13.11%	DD,M0,1B		
Drug Regimen Compliance (COMPLIAN)	GABAPENTIN	7260	NA	8 DAYS LATE REFILLING	ANTICONVULSANTS - MISC.**	Message	53	$763.72	$698.78	$0.00	1,560.0	5,162.0	0	3	$52.34	8.77%	LR,M0,1G		
Drug Regimen Compliance (COMPLIAN)	PROVENTIL HFA	4420	NA	12 DAYS LATE REFILLING	SYMPATHOMIMETICS**	Message	44	$5,272.91	$4,203.23	$0.00	955.0	328.3	0	11	$1,069.68	5.45%	ID,P0,1B		
Drug Regimen Compliance (COMPLIAN)	PROVENTIL HFA	4420	NA	8 DAYS LATE REFILLING	SYMPATHOMIMETICS**	Message	41	$5,103.92	$3,643.17	$0.00	948.0	301.5	0	13	$1,287.25	5.36%	DD,M0,1B		
Drug Regimen Compliance (COMPLIAN)	PROVENTIL HFA	4420	NA	10 DAYS LATE REFILLING	SYMPATHOMIMETICS**	Message	41	$4,520.32	$3,766.73	$0.00	919.0	294.8	0	7	$753.59	0.00%			
Drug Regimen Compliance (COMPLIAN)	PROVENTIL HFA	4420	NA	9 DAYS LATE REFILLING	SYMPATHOMIMETICS**	Message	40	$4,330.03	$3,552.90	$0.00	865.0	281.4	0	8	$690.38	2.04%	LR,M0,1B		
Drug Regimen Compliance (COMPLIAN)	LEVOTHYROXINE SODIUM	2810	NA	7 DAYS LATE REFILLING	THYROID HORMONES**	Message	38	$453.87	$412.80	$0.00	1,202.0	1,118.0	0	3	$41.07	4.88%	DD,M0,1B		
Drug Regimen Compliance (COMPLIAN)	PROVENTIL HFA	4420	NA	7 DAYS LATE REFILLING	SYMPATHOMIMETICS**	Message	37	$4,733.83	$3,380.50	$0.00	842.0	274.7	0	12	$1,266.58	0.00%			
Drug Regimen Compliance (COMPLIAN)	PROVENTIL HFA	4420	NA	14 DAYS LATE REFILLING	SYMPATHOMIMETICS**	Message	36	$4,336.07	$3,659.24	$0.00	825.0	288.1	0	7	$676.83	9.30%	DD,M0,1B		
Drug Regimen Compliance (COMPLIAN)	ATORVASTATIN CALCIUM	3940	NA	8 DAYS LATE REFILLING	HMG COA REDUCTASE INHIBITORS**	Message	35	$407.92	$320.07	$0.00	1,034.0	1,034.0	0	6	$63.36	6.98%	DD,M0,1G		
Drug-Drug Interaction (DDI-DTMS)	ALPRAZOLAM	5710	NA	HYDROCO/APAP TAB 10-325MG	BENZODIAZEPINES**	Message	970	$12,108.52	$9,663.05	$0.00	27,460.0	62,964.0	0	65	$647.73	1.04%	DA,R0,1B		
Drug-Drug Interaction (DDI-DTMS)	ATORVASTATIN CALCIUM	3940	NA	CLOPIDOGREL TAB 75MG	HMG COA REDUCTASE INHIBITORS**	Message	728	$11,589.57	$7,728.68	$0.00	34,195.0	34,646.0	0	96	$1,312.37	0.09%	ER,R0,1B		
Drug-Drug Interaction (DDI-DTMS)	HYDROCODONE/ACETAMINOPHEN	6599	NA	ALPRAZOLAM TAB 1MG	OPIOID COMBINATIONS**	Message	524	$12,835.06	$9,330.72	$0.00	13,319.0	48,052.0	0	45	$1,109.67	0.99%	ER,M0,1B		
Drug-Drug Interaction (DDI-DTMS)	ALPRAZOLAM	5710	NA	OXYCOD/APAP TAB 10-325MG	BENZODIAZEPINES**	Message	514	$6,910.88	$5,192.70	$0.00	14,744.0	33,365.0	0	36	$381.14	0.43%	ID,M0,1B		
Drug-Drug Interaction (DDI-DTMS)	HYDROCODONE/ACETAMINOPHEN	6599	NA	ALPRAZOLAM TAB 2MG	OPIOID COMBINATIONS**	Message	406	$10,002.28	$7,619.35	$0.00	10,603.0	37,475.0	0	27	$545.70	1.63%	DC,M0,1B		
Drug-Drug Interaction (DDI-DTMS)	OXYCODONE HCL	6510	NA	ALPRAZOLAM TAB 2MG	OPIOID AGONISTS**	Message	374	$14,880.05	$8,621.31	$0.00	10,419.0	38,614.0	0	22	$907.20	1.76%	DC,M0,1B		
Drug-Drug Interaction (DDI-DTMS)	GABAPENTIN	7260	NA	MORPHINE SUL TAB 15MG ER	ANTICONVULSANTS - MISC.**	Message	365	$7,106.99	$5,085.75	$0.00	11,278.0	34,851.0	0	43	$681.42	0.00%			
Drug-Drug Interaction (DDI-DTMS)	AMLODIPINE BESYLATE	3400	NA	CLOPIDOGREL TAB 75MG	CALCIUM CHANNEL BLOCKERS**	Message	355	$3,037.08	$2,242.99	$0.00	20,363.0	21,532.0	0	31	$191.66	0.00%			
Drug-Drug Interaction (DDI-DTMS)	ONDANSETRON HCL	5025	NA	HYDROCO/APAP TAB 10-325MG	5-HT3 RECEPTOR ANTAGONISTS**	Message	324	$2,971.46	$1,785.99	$0.00	1,100.0	3,134.0	0	117	$252.97	0.13%	EX,GP,1B		
Drug-Drug Interaction (DDI-DTMS)	ONDANSETRON HCL	5025	NA	HYDROCO/APAP TAB 5-325MG	5-HT3 RECEPTOR ANTAGONISTS**	Message	282	$1,049.86	$644.82	$0.00	426.0	1,169.0	0	150	$176.89	0.00%			
Duplicate Rx (DUPRX)	PROVENTIL HFA	4420	NA	PROVENTIL AER HFA	SYMPATHOMIMETICS**	Extract	227	$37,157.20	$24,238.80	$0.00	6,888.0	1,929.6	0	81	$9,942.72	0.00%	DD,M0,1B		
Duplicate Rx (DUPRX)	GABAPENTIN	7260	NA	GABAPENTIN CAP 300MG	ANTICONVULSANTS - MISC.**	Extract	204	$3,814.32	$2,789.36	$0.00	8,040.0	23,354.0	0	51	$872.19	0.00%	DA,M0,1B		
Duplicate Rx (DUPRX)	HYDROCODONE/ACETAMINOPHEN	6599	NA	HYDROCO/APAP TAB 10-325MG	OPIOID COMBINATIONS**	Hard Reject	9	$9,625.45	$179.05	$0.00	174.0	590.0	450	3	$74.09	0.00%	DA,M0,1G		
Duplicate Rx (DUPRX)	OXYCODONE/ACETAMINOPHEN	6599	NA	OXYCOD/APAP TAB 10-325MG	OPIOID COMBINATIONS**	Hard Reject	8	$12,971.42	$240.49	$0.00	166.0	630.0	402	4	$156.11	0.00%	DD,M0,1B		
Duplicate Rx (DUPRX)	SODIUM CHLORIDE	7975	NA	SOD CHLORIDE INJ 0.9%	SODIUM**	Soft Reject	0	$2,968.37					1,341	0		0.00%			
Duplicate Rx (DUPRX)	ONDANSETRON HCL	5025	NA	ONDANSETRON INJ 4MG/2ML	5-HT3 RECEPTOR ANTAGONISTS**	Soft Reject	0	$376.94					670	0		0.00%			
Duplicate Rx (DUPRX)	PROVENTIL HFA	4420	NA	PROVENTIL AER HFA	SYMPATHOMIMETICS**	Soft Reject	0	$59,135.34					539	0		0.19%	LR,M0,1B		
Duplicate Rx (DUPRX)	GABAPENTIN	7260	NA	GABAPENTIN CAP 300MG	ANTICONVULSANTS - MISC.**	Soft Reject	0	$5,485.21					419	0		0.24%	DC,R0,1G		
Duplicate Rx (DUPRX)	SERTRALINE HCL	5816	NA	SERTRALINE TAB 100MG	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	Soft Reject	0	$3,208.15					267	0		0.00%			
Duplicate Rx (DUPRX)	ALPRAZOLAM	5710	NA	ALPRAZOLAM TAB 1MG	BENZODIAZEPINES**	Hard Reject	0	$2,898.00					257	0		0.00%	DD,M0,1B		
Duplicate Therapy (DUPTHER)	QUETIAPINE FUMARATE	5915	NA	ORAL ANTIPSYCHOTICS	DIBENZAPINES**	Extract	1,399	$37,415.79	$19,374.13	$0.00	41,626.0	58,500.0	0	106	$3,705.09	0.00%	DC,R0,1B		
Duplicate Therapy (DUPTHER)	RISPERIDONE	5907	NA	ORAL ANTIPSYCHOTICS	BENZISOXAZOLES**	Extract	873	$20,081.45	$10,243.63	$0.00	25,930.0	42,581.0	0	73	$2,373.50	0.00%	AT,M0,1B		
Duplicate Therapy (DUPTHER)	MORPHINE SULFATE	6510	NA	SHORT ACTING NARCOTIC ANALGESI	OPIOID AGONISTS**	Message	692	$4,238.10	$2,049.81	$0.00	692.0	1,272.5	0	455	$1,357.37	0.00%			
Duplicate Therapy (DUPTHER)	KETOROLAC TROMETHAMINE	6610	NA	NON-STEROIDAL ANTI-INFLAMMATOR	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)**	Message	642	$4,386.89	$2,414.39	$0.00	642.0	1,318.0	0	190	$465.48	0.00%			
Duplicate Therapy (DUPTHER)	GABAPENTIN	7260	NA	GABAPENTIN AND RELATED	ANTICONVULSANTS - MISC.**	Extract	641	$20,811.00	$9,521.37	$0.00	22,961.0	71,253.0	0	71	$3,481.36	0.00%	DA,M0,1B		
Duplicate Therapy (DUPTHER)	LISINOPRIL	3610	NA	ANGIOTENSIN BLOCKERS	ACE INHIBITORS**	Extract	522	$10,674.99	$4,911.03	$0.00	32,438.0	35,189.0	0	58	$1,472.34	0.00%	DD,00,1B		
Duplicate Therapy (DUPTHER)	LEVOTHYROXINE SODIUM	2810	NA	THYROID HORMONES	THYROID HORMONES**	Extract	521	$18,155.79	$8,947.43	$0.00	26,485.0	25,912.0	0	82	$2,826.42	0.00%	DA,M0,1G		
Duplicate Therapy (DUPTHER)	ARIPIPRAZOLE	5925	NA	ORAL ANTIPSYCHOTICS	QUINOLINONE DERIVATIVES**	Extract	515	$24,380.37	$11,963.20	$0.00	15,298.0	16,668.0	0	40	$3,907.65	0.00%	DA,MR,1B		
Duplicate Therapy (DUPTHER)	QUETIAPINE FUMARATE	5915	NA	ANTIPSYCHOTICS	DIBENZAPINES**	Extract	502	$11,255.29	$7,146.26	$0.00	14,812.0	20,662.0	0	48	$1,285.07	0.00%	DC,R0,1B		
Duplicate Therapy (DUPTHER)	TRAZODONE HYDROCHLORIDE	5812	NA	ANTIDEPRESSANTS	SEROTONIN MODULATORS**	Extract	500	$9,663.06	$5,994.22	$0.00	16,425.0	22,354.0	0	38	$877.98	0.00%	AD,00,00		

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending, total Reversal Rxs descending and Top Drug/Client Rider ascending.

Total	**19,486**	**$730,395.15**	**$461,635.25**	**$0.00**	**460,794.0**	**961,960.759**	**4,345**	**3,482**	**$74,167.37**				

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending, total Reversal Rxs descending and Top Drug/Client Rider ascending.

RXT6050D - Summarized DUR Activity Report

From 4/1/18 Through 6/30/18

Selected Filters

Client(s): Nevada Medicaid - HPES

Carrier(s): NVM-NEVADA MEDICAID

Account(s): NVM-NEVADA MEDICAID

Group(s): ALL

Date Type:	Date Filled
Start Date:	2018-04-01
End Date:	2018-06-30
Relative Description:	Select Date Range
Top Values to Display:	10
cDUR Edit Types:	-, ACTMAINT, ALLERCHK, COMPLIAN, DDI-DTMS, DIAGCAUT, DINFERRD, DOSECHEK, DRUG_AGE, DRUG_SEX, DUPRX, DUPTHER, MEDLIMIT, THERDOSE
Display Report Description:	No

Anthem 3Q 2017

Rule DSC	Total CDUR Alerts	Total CDUR Successes (Rejects+Reverals)
Refill Too Soon/Stockpiling Prevention	44,498	44,235
Adverse Drug Disease Consideration	10,452	10,406
Excessive Dosing	21,154	9,392
Drug Therapy Duplication	40,678	6,051
Under Dosing	24,256	4,885
Suboptimal Patient Drug Adherence	23,633	3,771
Drug Age Consideration	9,003	1,969
Adverse Drug Interaction	5,387	814
Drug Pregnancy	482	114
Additive Toxicity	101	81
Prescriber Consultation	405	66
Drug Gender	323	54
Drug Allergy	101	15
Potential Drug Name Confusion	6	0
	180,479	**81,853**
Anthem 4Q 2017		
Refill Too Soon/Stockpiling Prevention	48,544	48,341
Drug Therapy Duplication	67,180	21,892
Adverse Drug Disease Consideration	15,602	15,544
Excessive Dosing	29,588	12,773
Under Dosing	32,346	6,296
Suboptimal Patient Drug Adherence	26,600	4,175
Drug Age Consideration	12,561	2,676
Adverse Drug Interaction	6,629	969
Drug Pregnancy	576	130
Prescriber Consultation	422	88
Drug Gender	378	71
Additive Toxicity	68	53
Drug Allergy	154	30
Potential Drug Name Confusion	10	1
	240,658	**113,039**

Anthem 1Q 2018

Rule DSC	Total CDUR Alerts	Total CDUR Successes (Rejects+Reverals)
Drug Therapy Duplication	83,757	43,509
Refill Too Soon/Stockpiling Prevention	39,812	39,600
Adverse Drug Disease Consideration	19,000	18,950
Excessive Dosing	30,067	13,668
Under Dosing	29,394	5,958
Suboptimal Patient Drug Adherence	21,883	3,440
Drug Age Consideration	12,246	2,615
Adverse Drug Interaction	6,220	842
Prescriber Consultation	363	133
Drug Pregnancy	467	121
Drug Allergy	141	47
Drug Gender	335	43
Additive Toxicity	44	28
Potential Drug Name Confusion	7	2
	243,736	**128,956**
Anthem 2Q 2018		
Refill Too Soon/Stockpiling Prevention	49,646	49,361
Drug Therapy Duplication	69,886	36,352
Adverse Drug Disease Consideration	19,614	19,532
Excessive Dosing	26,791	11,998
Suboptimal Patient Drug Adherence	22,519	3,470
Under Dosing	14,623	3,186
Drug Age Consideration	11,568	2,632
Adverse Drug Interaction	7,341	1,132
Drug Pregnancy	573	151
Drug Gender	441	75
Additive Toxicity	101	74
Prescriber Consultation	257	71
Drug Allergy	123	19
	223,483	**128,053**

C-DUR Q2 2018

SilverSummit Healthplan

Count of CLAIM PAID/REJECTED Row Labels	APRIL	MAY	JUNE	Grand Total
Apparent Drug Misuse	**784**	**912**	**873**	**2,569**
Paid	654	752	709	2,115
Rejected	63	70	74	207
Reversal	67	90	90	247
Buprenorphine with Opioid	**7**	**1**	**6**	**14**
Rejected	6	1	6	14
Cumulative APAP Check	**11**	**15**	**6**	**29**
Rejected	11	15	6	32
Cumulative Morphine Equivalent Dose	**197**	**200**	**152**	**549**
Paid	5	4	4	13
Rejected	189	194	148	531
Reversal	3	2		5
Drug-Age Precaution	**10**	**4**	**4**	**18**
Paid	9	4	4	17
Rejected				0
Reversal	1			1
Drug-Disease Precaution	**685**	**726**	**724**	**2,135**
Paid	517	529	527	1,573
Rejected	95	115	113	323
Reversal	73	82	84	239
Drug-Drug Interaction	**1,561**	**1,631**	**1,659**	**4,851**
Paid	1,132	1,146	1,211	3,489
Rejected	266	277	256	799
Reversal	163	208	192	563
Drug-Pregnancy Alert	**23**	**43**	**41**	**107**
Paid	16	28	30	74
Rejected	4	6	7	17
Reversal	3	9	4	16
Excessive Duration Alert	**523**	**560**	**608**	**1,691**
Paid	386	416	445	1,247
Rejected	104	64	67	235
Reversal	111	80	92	283
High Dose Alert	**545**	**530**	**425**	**1,500**
Paid	330	356	264	950
Rejected	104	88	69	261
Reversal	111	86	92	289
Ingredient Duplication	**2,675**	**3,243**	**2,844**	**8,762**
Paid	5	0	0	5
Rejected	2,670	3,243	2,844	8,757
Reversal				0
Low Dose Alert	**1,433**	**1,522**	**1,382**	**4,337**
Paid	981	1,083	983	3,047
Rejected	214	214	160	588
Reversal	238	225	239	702
Refill too Soon	**3,831**	**4,440**	**4,057**	**12,328**
Rejected	3,831	4,440	4,057	12,328
Therapeutic Duplication	**4,603**	**5,255**	**4,873**	**14,731**
Paid	1,494	1,583	1,562	4,639
Rejected	2,765	3,284	2,924	8,873
Reversal	344	388	351	1,083
Underuse Precaution	**2,555**	**2,859**	**3,138**	**8,552**
Paid	1,910	2,167	2,437	6,514
Rejected	213	261	257	731
Reversal	432	431	444	1,307
Grand Total	**12,437**	**13,815**	**13,392**	**39,644**

Retrospective DUR 3 Q 2017						
	List and Describe (Name/Subject) Retrospective Reviews Implemented During Reporting Month	**Type of Contact (media)**	**Unique Members Identified**	**Number of Positive Outcomes**	**Type of Outreach**	**Performed By (e.g., Subcontractor Name)**
Controlled Substance Utilization Management						
CSUM	Controlled Substance Utilization Management-Internal Prescriber fax program that identifies members with more than 10 claims for Controlled substances from three different providers in a 90-day period.	Fax/Mailing	117	67	Physician	Internal (Member Management Analytics/RHI)
Multiple Opioid Rx 3x3x3	This rule identifies adult Members over-utilizing prescribers and pharmacies having Rx supply of Three Opioid claims, from >= Three (3) distinct prescribers from AAOD-90 to AAOD AND Rx claims with supply from >= three (3) distinct pharmacies from AAOD-90 to AAOD.	Fax/Mailing	64	29	Physician	Internal (Member Management Analytics/RHI)
Triple Threat Overuse	This rule should identify members with an Rx supply for any medication in all 3 drug classes during a 30 day period of time with at least a one day overlap.	Fax/Mailing	36	21	Physician	Internal (Member Management Analytics/RHI)
Adding Therapy						
DM- No Statin	Diabetes with no Statin- Internal Prescriber fax program notifying of gap in care: Diabetic patient not on a Statin medication.	Fax/Mailing	103	21	Physician	Internal (Member Management Analytics/RHI)
Asthma	Asthma albuterol overuse with no controller medication-Internal Prescriber fax program notifying of gap in care: Asthmatic patient not on a Controller medication.	Fax/Mailing	116	4	Physician	Internal (Member Management Analytics/RHI)
ADHERENCE						
Cardiovascular	Identifies members on an ACE/ARB with an MPR(Medication Possession Ration of less than 80%	Fax/Mailing	301	78	Physician	Internal (Member Management Analytics/RHI)
Oral Diabetes	Identifies members on oral diabetes medications with an MPR of less than 80%	Fax/Mailing	151	40	Physician	Internal (Member Management Analytics/RHI)
Statins	Identifies members on Statin medication with an MPR of less than 80%	Fax/mailing	116	34	Physician	Internal (Member Management Analytics/RHI)
Asthma	Identifies members on asthma controller medications with an MPR less than 75%	Fax/mailing	998	152	Physician	Internal (Member Management Analytics/RHI)
Miscellaneous Gaps in Care						
PPI Length of Therapy	This rule identifies members who have been on a Proton Pump Inhibitor longer than the recommended length of therapy	Fax/mailing	158	52	Physician	Internal (Member Management Analytics/RHI)

Retrospective DUR 4 Q 2017						
	List and Describe (Name/Subject) Retrospective Reviews Implemented During Reporting Month	**Type of Contact (media)**	**Unique Members Identified**	**Number of Positive Outcomes**	**Type of Outreach**	**Performed By (e.g., Subcontractor Name)**
Controlled Substance Utilization Management						
CSUM	Controlled Substance Utilization Management-Internal Prescriber fax program that identifies members with more than 10 claims for Controlled substances from three different providers in a 90-day period.	Fax/Mailing	31	20	Physician	Internal (Member Management Analytics/RHI)
Multiple Opioid Rx 3x3x3	This rule identifies adult Members over-utilizing prescribers and pharmacies having Rx supply of Three Opioid claims, from >= Three (3) distinct prescribers from AAOD-90 to AAOD AND Rx claims with supply from >= three (3) distinct pharmacies from AAOD-90 to AAOD.	Fax/Mailing	18	5	Physician	Internal (Member Management Analytics/RHI)
Triple Threat Overuse	This rule should identify members with an Rx supply for any medication in all 3 drug classes during a 30 day period of time with at least a one day overlap.	Fax/Mailing	19	10	Physician	Internal (Member Management Analytics/RHI)
Adding Therapy						
DM- No Statin	Diabetes with no Statin- Internal Prescriber fax program notifying of gap in care: Diabetic patient not on a Statin medication.	Fax/Mailing	40	8	Physician	Internal (Member Management Analytics/RHI)
Asthma	Asthma albuterol overuse with no controller medication-Internal Prescriber fax program notifying of gap in care: Asthmatic patient not on a Controller medication.	Fax/Mailing	67	4	Physician	Internal (Member Management Analytics/RHI)
ADHERENCE						
Cardiovascular	Identifies members on an ACE/ARB, CCB or Thiazides and combos with an MPR(Medication Possession Ration of less than 80%	Fax/Mailing	1828	555	Physician	Internal (Member Management Analytics/RHI)
COPD	Identifies members on a COPD medication with an MPR of less than 80%.	Fax/Mailing	36	16	Physician	Internal (Member Management Analytics/RHI)
Oral Diabetes	Identifies members on oral diabetes medications with an MPR of less than 80%	Fax/Mailing	1142	269	Physician	Internal (Member Management Analytics/RHI)
Statins	Identifies members on Statin medication with an MPR of less than 80%	Fax/mailing	1092	301	Physician	Internal (Member Management Analytics/RHI)
Asthma	Identifies members on asthma controller medications with an MPR less than 75%	Fax/mailing	167	22	Physician	Internal (Member Management Analytics/RHI)
Miscellaneous Gaps in Care						
PPI Length of Therapy	This rule identifies members who have been on a Proton Pump Inhibitor longer than the recommended length of therapy	Fax/mailing	157	48	Physician	Internal (Member Management Analytics/RHI)

Retrospective DUR 1 Q 2018						
	List and Describe (Name/Subject) Retrospective Reviews Implemented During Reporting Month	**Type of Contact (media)**	**Unique Members Identified**	**Number of Positive Outcomes**	**Type of Outreach**	**Performed By (e.g., Subcontractor Name)**
Controlled Substance Utilization Management						
CSUM	Controlled Substance Utilization Management-Internal Prescriber fax program that identifies members with more than 10 claims for Controlled substances from three different providers in a 90-day period.	Fax/Mailing	55	Quarter 1 outcomes not Available until Oct 2018	Physician	Internal (Member Management Analytics/RHI)
Multiple Opioid Rx 3x3x3	This rule identifies adult Members over-utilizing prescribers and pharmacies having Rx supply of Three Opioid claims, from >= Three (3) distinct prescribers from AAOD-90 to AAOD AND Rx claims with supply from >= three (3) distinct pharmacies from AAOD-90 to AAOD.	Fax/Mailing	22	Quarter 1 outcomes not Available until Oct 2018	Physician	Internal (Member Management Analytics/RHI)
Triple Threat Overuse	This rule should identify members with an Rx supply for any medication in all 3 drug classes during a 30 day period of time with at least a one day overlap.	Fax/Mailing	23	Quarter 1 outcomes not Available until Oct	Physician	Internal (Member Management Analytics/RHI)
Adding Therapy						
DM- No Statin	Diabetes with no Statin- Internal Prescriber fax program notifying of gap in care: Diabetic patient not on a Statin medication.	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
Asthma	Asthma albuterol overuse with no controller medication-Internal Prescriber fax program notifying of gap in care: Asthmatic patient not on a Controller medication.	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
ADHERENCE						
Cardiovascular	Identifies members on an ACE/ARB with an MPR(Medication Possession Ration of less than 80%	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
COPD	Identifies members on a COPD medication with an MPR of less than 80%.	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
Oral Diabetes	Identifies members on oral diabetes medications with an MPR of less than 80%	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
Statins	Identifies members on Statin medication with an MPR of less than 80%	Fax/mailing	0		Physician	Internal (Member Management Analytics/RHI)
Asthma	Identifies members on asthma controller medications with an MPR less than 75%	Fax/mailing	0		Physician	Internal (Member Management Analytics/RHI)
Miscellaneous Gaps in Care						
Drug Drug Interaction	These rules are designed to target members with specific drug drug interactions.	Fax/Mailing	1	Quarter 1 outcomes not Available until Oct	Physician	Internal (Member Management Analytics/RHI)

PPI Length of Therapy	This rule identifies members who have been on a Proton Pump Inhibitor longer than the recommended length of therapy	Fax/mailing	53	Quarter 1 outcomes not Available until Oct 2018	Physician	Internal (Member Management Analytics/RHI)
Polypharmacy 10	This rule seeks to identify members with at least 10 distinct medications from at least 3 distinct providers in the past 90 days	Fax/mailing	236	Quarter 1 outcomes not Available until Oct 2018	Physician	Internal (Member Management Analytics/RHI)

**Some Programs were turned off due to NV rebranding and program maintenance*

Retrospective DUR 2 Q 2018						
	List and Describe (Name/Subject) Retrospective Reviews Implemented During Reporting Month	**Type of Contact (media)**	**Unique Members Identified**	**Number of Positive Outcomes**	**Type of Outreach**	**Performed By (e.g., Subcontractor Name)**
Controlled Substance Utilization Management						
CSUM	Controlled Substance Utilization Management-Internal Prescriber fax program that identifies members with more than 10 claims for Controlled substances from three different providers in a 90-day period.	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
Multiple Opioid Rx 3x3x3	This rule identifies adult Members over-utilizing prescribers and pharmacies having Rx supply of Three Opioid claims, from >= Three (3) distinct prescribers from AAOD-90 to AAOD AND Rx claims with supply from >= three (3) distinct pharmacies from AAOD-90 to AAOD.	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
Triple Threat Overuse	This rule should identify members with an Rx supply for any medication in all 3 drug classes during a 30 day period of time with at least a one day overlap.	Fax/Mailing	0		Physician	Internal (Member Management Analytics/RHI)
Adding Therapy						
DM- No Statin	Diabetes with no Statin- Internal Prescriber fax program notifying of gap in care: Diabetic patient not on a Statin medication.	Fax/Mailing	47	Outcomes available Jan 2019	Physician	Internal (Member Management Analytics/RHI)
Asthma	Asthma albuterol overuse with no controller medication-Internal Prescriber fax program notifying of gap in care: Asthmatic patient not on a Controller medication.	Fax/Mailing	50	Outcomes available Jan 2019	Physician	Internal (Member Management Analytics/RHI)
Post MI No Beta Blocker	Identifying members that had a myocardial infarction but do not have a claim for a beta blocker	Fax/mailing	1	Outcomes available Jan 2019		
ADHERENCE						
Cardiovascular	Identifies members on an ACE/ARB, CCB or thiazides with an MPR(Medication Possession Ration of less than 80%	Fax/Mailing	907	Outcomes available Jan 2019	Physician	Internal (Member Management Analytics/RHI)
COPD	Identifies members on a COPD medication with an MPR of less than 80%.	Fax/Mailing	15	Outcomes available Jan 2019	Physician	Internal (Member Management Analytics/RHI)
Oral Diabetes	Identifies members on oral diabetes medications with an MPR of less than 80%	Fax/Mailing	394	Outcomes available Jan 2019	Physician	Internal (Member Management Analytics/RHI)
Statins	Identifies members on Statin medication with an MPR of less than 80%	Fax/mailing	390	Outcomes available Jan 2019	Physician	Internal (Member Management Analytics/RHI)
Asthma	Identifies members on asthma controller medications with an MPR less than 75%	Fax/mailing	352	Outcomes available Jan 2019	Physician	Internal (Member Management Analytics/RHI)
Miscellaneous Gaps in Care						

PPI Length of Therapy	This rule identifies members who have been on a Proton Pump Inhibitor longer than the recommended length of therapy	Fax/mailing	0		Physician	Internal (Member Management Analytics/RHI)
Polypharmacy 10	This rule seeks to identify members with at least 10 distinct medications from at least 3 distinct providers in the past 90 days	Fax/mailing	0		Physician	Internal (Member Management Analytics/RHI)

**Some Programs were turned off due to NV rebranding and program maintenance*

RETRO DUR

SilverSummith Healthplan

	Jan-18	Feb-18	Mar-18	Apr-18	May-18	Jun-18
Retrospective Drug Utilization Review (Retro DUR)						
Drug-Use Reports						
Report Name	**Members Identified**	**Members Identified**	**Members Identified**	**Members Identified**	**Members Identified**	**Members Identified**
Therapeutic Duplication	7	6	10	14	18	22
Medication Dose In Elderly	0	0	0	0	0	0
Medication Duration In Elderly	0	0	0	0	0	0
Drug Drug Interaction	360	399	445	497	484	524