BRIAN SANDOVAL
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CODY PHINNEY
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DEPARTMENT OF HEALTH AND HUMAN SERVICES
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NOTICE OF PUBLIC MEETING – DRUG USE REVIEW BOARD

Date of Posting:	December 17, 2018
Date of Meeting:	January 24, 2019 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
Webinar Registration	https://optum.webex.com/optum/onstage/g.php?MTID=ee918c1d5525b1309d1687d7fc75b1eca Or go to www.webex.com and enter the Event Number listed below. Once you have registered for the meeting, you will receive an email message confirming your registration. This message will provide the information that you need to join the meeting.
Event Number:	641 918 363 Click "Join Now" Follow the instructions that appear on your screen to join the audio portion of the meeting. Audio will be transmitted over the internet.

A password should not be necessary, but if asked use: Medicaid1!

For Audio Only:

Phone: 1-763-957-6300
Event: 641 918 363

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 October 18, 2018

b. Status Update by the DHCFP

4. Clinical Presentations

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

1. Public comment on proposed clinical prior authorization criteria.
2. Presentation of utilization and clinical information.
3. Discussion by Board and review of utilization data.
4. Proposed adoption of updated prior authorization criteria.

b. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for Inhaled Short-Acting Beta Agonists

1. Public comment on proposed clinical prior authorization criteria.
2. Presentation of utilization and clinical information.
3. Discussion by Board and review of utilization data.
4. Proposed adoption of updated prior authorization criteria.

c. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for compounded medications

1. Public comment on proposed clinical prior authorization criteria.
2. Presentation of utilization and clinical information.
3. Discussion by Board and review of utilization data.
4. Proposed adoption of updated prior authorization criteria.

d. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for baloxavir marboxil (Xofluza®)

1. Public comment on proposed clinical prior authorization criteria.
2. Presentation of utilization and clinical information.
3. Discussion by Board and review of utilization data.
4. Proposed adoption of updated prior authorization criteria.

e. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for sacubitril/valsartan (Entresto®)

1. Public comment on proposed clinical prior authorization criteria.
2. Presentation of utilization and clinical information.
3. Discussion by Board and review of utilization data.
4. Proposed adoption of updated prior authorization criteria.

f. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for cannabidiol (Epidiolex®)

1. Public comment on proposed clinical prior authorization criteria.
2. Presentation of utilization and clinical information.
3. Discussion by Board and review of utilization data.
4. Proposed adoption of updated prior authorization criteria.

g. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for pulmonary arterial hypertension agents

1. Public comment on proposed clinical prior authorization criteria.
2. Presentation of utilization and clinical information.
3. Discussion by Board and review of utilization data.
4. 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

1. Discussion by the Board and review of utilization data.
2. **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

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

c. Antibiotic Utilization

1. Discussion by the Board and review of utilization data.

2. **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

1. Top 10 Therapeutic Classes for Q1 2018, Q2 2018 and Q3 2018 (by Payment and by Claims).
2. Top 50 Drugs of Q1 2018, Q2 2018 and Q3 2018 (by Payment and by Claims).

b. Concurrent Drug Utilization Review (ProDUR)

1. Review of Q3 2018.
2. Review of Top Encounters by Problem Type.

c. Retrospective Drug Utilization Review (RetroDUR)

1. Status of previous quarter.
2. Status of current quarter.
3. Review and discussion of responses.

9. Closing Discussion

a. Public comments on any subject

b. Date and location of the next meeting

1. 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.

Notice of this public workshop meeting and draft copies of the changes will be available on or after the date of this notice at the DHCFP Web site at http://dhcfp.nv.gov. The agenda posting of this meeting can be viewed at the follow locations: Carson City Central Office; Las Vegas District Office; Reno District Office; Elko District Office; Nevada State Library; Carson City Library; Churchill County Library; Las Vegas Library; Douglas County Library; Elko County Library; Esmeralda 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 Holly Long at the Division of Health Care Financing and Policy, 1100 E. William Street, Suite 101, Carson City, Nevada 89701, at least three days before the public meeting.

All persons that have requested in writing to receive the Public Meetings 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 hlong@dhcfp.nv.gov in writing, at 1100 East William Street, Suite 101, Carson City, Nevada 89701 or call Holly Long at (775) 684-3150.

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DRUG USE REVIEW BOARD

Meeting Minutes

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

ATTENDEES

Board Members Present
Paul Oesterman, Pharm.D.
James Marx, MD
Michael Owens, MD
Jennifer Wheeler, Pharm.D.
Yvette Kaunismaki, MD
David England, Pharm.D
Netochi Adeolokun, Pharm.D.

Board Member Absent
Marta Bunuel, MD

DHCFP
Holly Long, Social Services Program Specialist
Beth Slamowitz, Pharm.D., Social Service Pharmacy/DME Program Chief
Amy Crowe, Senior Deputy Attorney General

DXC
Camilla Hauck, RPh

OptumRx
Carl Jeffery, Pharm.D

Managed Care Organizations
Thomas Beranek, RPh – Silver Summit Health Plan
Ryan Bitton, Pharm.D. – Health Plan of Nevada
Jeannine Murray, RPh – Anthem

Public
Mark Schwartz, GSK
Deron Grothe, Teva
Sandy Sierawski, Pfizer
Marc Rueckert, Pfizer
Don Moran, Teva

Public On-line
Jill Carroll, BMS
Lisa Wilson, Biogen
Tony Wang, BMS
Lori Howarth, Bayer
Joanna Jacob, Ferrari Public Affairs
Judy Stein, Amgen
Alice Swett, Alexion
Micah Johnson, BMS

AGENDA

1. Call to Order and Roll Call

Camilla Hauck, RPh, DXC
Beth Slamowitz, Pharm.D., DHCFP
Holly Long, DHCFP
Carl Jeffery, Pharm.D., OptumRx
Paul Oesterman, Pharm.D.
James Marx, MD
Yvette Kaunismaki, MD
Netochi Adeolokun, Pharm.D.
Michael Owens, MD
Jennifer Wheeler, Pharm.D.
Ryan Bitton, Pharm.D.
Thomas Beranek, RPh

Via phone:
David England, Pharm.D.
Amy Crowe – Senior Deputy Attorney General

2. Public Comment on Any Matter on the Agenda

Paul Oesterman: Is there any public comment?

No public comment.

3. Administrative

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

Motion to approve the meeting minutes as presented. Second. Voting: Ayes are unanimous, the motion carries.

b. Status Update by DHCFP

Holly Long: We are working on the antibiotic policy that was approved at the July 26 meeting. We've been making quite a bit of progress. I'll go over that when we get to that item on the agenda today. As far as just general updates, we have had the federal qualified health centers or FQHC section has been relocated in the Medicaid Services Manual from chapter 600 which is physicians services now it has its's own chapter, it's going to be chapter 2900. This was effective on October 1, 2018.

Beth Slamowitz: This is the first meeting I am with DHCFP, no longer with DXC. I just wanted to make sure everyone was aware. My official title is Pharmacy Programs Chief. Any questions for the State would be directed toward me.

4. Clinical Presentations

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

Paul Oesterman: Is there any public comment?

Sandy Sierawski: I'm Sandy Sierawski. I'm a pharmacist here in Nevada and I work for Pfizer in the medical division. I'm here to just make a couple of comments about Xeljanz. Xeljanz XR in the immunomodulator class of drugs. You are looking at that PA criteria and we have rheumatoid arthritis indications, psoriatic arthritis indications falls in line with the criteria they already have established, but we have newly added an indication for ulcerative colitis for the treatment of adult patients with moderately to severe colitis disease. Take note that this is the first line of therapy for that so if you look at the criteria established for ulcerative colitis, the criteria says the recipient failed to adequately respond one or more of the following standard therapies for having a prior failure before getting this medication. I just wanted you to be aware that this medication is the first line of therapy. It's a novel mechanism of action and is available orally so you get some additional treatment options for UC in your patient population. Just kind of to give you the whole picture, I just want to comment on the recommended dose for ulcerative colitis is 10mg twice daily for 8 weeks and then 5 to 10 mg daily. Discontinue therapy after 16 weeks at 10mg twice daily if they don't get adequate response or benefit. Just to offer balanced information, I do want to let you know that here is a box warning on Xeljanz and that is for serious infections and malignancy and when studied in the UC population, the Xeljanz treatment was 10 mg twice a day and it was associated with greater risk of infection compared to 5 mg twice a day. I have complete package insert information and complete all the safety and warnings. If you want me to go through anymore of those, I just wanted to give you a brief overview. Any questions for me?

Carl Jeffery: A lot of what is in the binder and I think the Board is going to revamp this; I think we're going to talk about it later after the meeting to see if we can kind of narrow this process

down, but what Optum is recommending is just the addition of the new drugs. There are two new agents in this class that we're including and then going through the reviews, there's a couple new products that have been introduced recently that weren't included previously so these are now included into the criteria. I propose we just add the names of the drugs. We have them all listed out here and then the unique criteria because they come and go. They get new indications all the time so the easiest way is just to add these new ones on there. All the subsequent pages are all the different criteria from the MCOs and they have a lot of pages of criteria in there.

Paul Oesterman: I know we're dealing with different MCOs but it is possible to try to consolidate into a…

Holly Long: Yeah, we're going to talk about that later. We have a proposition to solve that.

Paul Oesterman: Going back to Sandy's presentation on the Xeljanz for ulcerative colitis, with the current PA criteria, if a patient has ulcerative colitis and they want to use that, what kind of process would they have to go through for that particular indication?

Carl Jeffery: Well, and the criteria's on there, so we have criteria for the ulcerative colitis already and so the recipient with the diagnosis of moderate to severe ulcerative colitis, they are appropriate age, but this is what Sandy was talking about was the fail first corticosteroids or 5-aminosalicylic acid or immunosuppressant or thiopurines. I'm not prepared to discuss changes to the criteria at this time but we can bring it back for a future meeting. Ryan and Tom what do you think about bringing this back and maybe you can modify this criteria. I was just reading through the HPN criteria to see if you guys address it.

Ryan Bitton: We normally cover conventional therapy first and that is pretty standard.

Carl Jeffery: So maybe in the future we can bring this back and do some more research and find out what's best standard therapy.

Paul Oesterman: Just for clarification purposes, what we have in front of us is the proposal to add the new agents that have not been previously been included in the class? So what we're looking at is the addition of agents?

Carl Jeffery: That's right.

Paul Oesterman: Do we have motion to add these newer products that have come to market and their inclusion in this class of agents?

Motion to accept criteria as presented. Second. Voting: Ayes are unanimous, the motion carries.

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.

Holly Long: The proposed criteria didn't make it into the DUR binder, but this is what the state was proposing and was suggested. This mirrors what we already have for opioids. The differences are in bold so you'll see everywhere where it says 7 day has been changed to 3 day and of course the age and the change there. I also added chiropractic treatment as an example for where pain cannot be controlled through the use of non-opioid therapies. It was that because Medicaid does

pay for chiropractic treatment for those under 20 years old, so that was as an example and then I also on the second page added the HHS reference because it's specific to opioids in adolescents. Otherwise, it's mirroring what we already have.

Paul Oesterman: So, the primary difference is the change from 7 down to 3 days and there are the exceptions for post-op and others. Just for reminder purposes, we already have separate criteria for cough syrups.

Holly Long: Right. Tramadol there will be a few more specific for under 18, but this will be blanketed for opioids in general.

James Marx: What about medication treatment like your Suboxone?

Holly Long: Suboxone has its own criteria, so it would be different.

Paul Oesterman: Were you able to send Dave a copy of this?

Holly Long: I'm not sure if he has a copy of this.

James Marx: I'm kind of confused. How is this being impacted by let's say, 14-year-old who had complicated complex spine surgery where there's rods and instrumentation?

Paul Oesterman: Post-surgery with prolonged recovery, there's an exception.

James Marx: How does that get conveyed to the call center?

Carl Jeffery: The way the call center works, that would be one of the first questions they ask for it to be approved.

James Marx: I think medication assisted treatment should be in here too under the exceptions. So, it doesn't get confused.

Beth Slamowitz: Medication assisted treatment is also part of behavioral health. It is it's own program and doesn't necessarily fall under the pharmacy program. They have their own policy they are developing. Because it is in combination with behavioral health treatments as well. It is not something included in our standard therapy criteria.

James Marx: I'm concerned someone with a prescription for Suboxone who is 16 or 17 years old, they go to the pharmacy…

Beth Slamowitz: This policy is based on pain treatment. If they were getting treatment with Suboxone, and we wouldn't pay for it for the treatment of pain, that diagnosis would have to be on the prescription.

James Marx: So, they would pick up the ICD-10 code? They saw an opioid dependence and accept that?

Beth Slamowitz: This isn't for those medications, so this is separate criteria from what we are discussing.

James Marx: So, you are not considering Suboxone under the opioids?

Beth Slamowitz: No, they have their own criteria within the chapter.

James Marx: Ok, that answers my question.

Holly Long: This is what we would do. This criteria would be put in with opioid preparations at the last meeting in July and then incorporating that into the existing opioid criteria that we have. It got tagged onto the very bottom of it and there is a reference to where it is, so if it is approved, it would also be put in there within that opioid criteria. I got this information that was recommended by the state of Washington as one of their recommendations that they're taking to their DUR board.

Ryan Bitton: This is the criteria that we put in place as well, but we have the age at 20 years old for three days max. HPN is in support of this criteria.

Holly Long: Washington did 20 years of age too, is there a big difference between 18 and 20? I was looking at the age group that is most at risk. Ages 13-17 seem to show as the most at-risk age group. If it is helpful to do 20 and under, we can do that.

James Marx: I am a little concerned with 60 mg morphine equivalent. That is a lot for a 4 year-old. Hopefully it wouldn't be prescribed, but I have seen cases of high doses. It was written in error and the pharmacist didn't catch it.

Beth Slamowitz: It says "Or less" per day. This was made to limit the initial prescriptions when there are alternatives. Hopefully they won't reach that amount for a three-day supply.

Carl Jeffery: We have the utilization starting on page 421 in your binder. You can see the different programs. For the fee for service side, scroll down into the MCOs and we can address those, too. I broke it down by age group so we can see what ages and under one methadone as our highest one and those are probably babies who are born to addicted mothers and then just a couple of claims, and we're talking about a couple of claims with less than 1. If you get to the 1 to 4-year olds, we're still looking at the total claim count not over 15 claims for any of those. We're not talking about very many claims that these are going to be impacting. All of these claim numbers climb from ages 5 to 9. From 10 to 17, and even in the past year, we've seen a pretty good decline in the amount of hydrocodone that has been prescribed, too. That tells a good story, too.

Paul Oesterman: I say looking at all the graphs, there's a general trending down. Excellent. We have in front of us, the proposed prior authorization criteria for the opioids prescribed to patients under the age of 18, mirrors the over 18 with the exception of changing from a 7-day prescription for initial prescriptions to 3 days and total of 13 3-day prescriptions in any rolling 12 month period.

Motion to accept criteria as presented. Second. Voting: Ayes are unanimous, the motion carries.

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

Don Moran: I'm a pharmacist and also a member of the medical affairs team. Our company is the manufacturer of one of these CGRP products. We were the second drug to be approved on September 14 by the FDA for episodic and chronic migraine, essentially preventative therapy. The drug does not appear in the agenda materials because I think the materials were prepared prior to our launch so I just wanted to say that on behalf of the company, we are hoping that you will consider this as part of the CGRP class. Now, what makes our molecule unique, especially compared to oral preventative agents which have been standard of therapy for many years, it's an injectable product and unlike others, it can be injected once a month subcutaneously or injected once every 3 months. So, issues of compliance can really be controlled by the clinician who chooses to administer the product in his or her office or in a patient who can self-administer the product at home, having some flexibility treating the disease, and also flexibility by monthly or quarterly dosing should improve patient compliance with therapy. In looking at the DUR class review that you were given, the thing that caught my attention was probably the second to the last paragraph in the entire document. It's the conclusion that the CGRP have a role in the subset of patients with migraine, unable to tolerate and establish oral prophylactic therapy. It goes so far as to say that these agents have been specifically designed to treat migraines. Their value is not in just patients who can't tolerate oral therapies but those patients who failed to respond to oral therapies, so take a look at the universe of patients with migraines who have disease severe enough who need preventative therapy, about 35%, 1/3 of migraine patients suffering migraines are candidates for an oral or some kind of preventative therapy. Of that third of the population, 25%, 1 of 4 patients who are eligible for preventative therapy actually seek care or continue to use it. Why is that? The number one reason for not using preventative therapy, 43% of the patients, inadequate response; 43% of the patients can't tolerate therapy side effects which means that over a period of time, probably by the end of the year, fewer than 10% of those eligible for therapy actually are using as preventative so this class actually offers an alternative and an innovation for the treatment. What I've seen in your DUR, unlike your colleagues, at United Healthcare, you put one more step in the road before the patient can have access to this medication, so physicians prescribing on behalf of Blue Cross patients, on behalf of the UHC patients, they have to demonstrate patients had at least 2 trials of prophylactic therapy, you're actually asking patients to demonstrate through the clinician, they've had at least 3 different trials over a 6-month period of time. So, you're a little more delayed compared to other clinicians in the state of Nevada. One other thing to think about is if I look at your population of 460,000 people. There's probably 2000 patients who have criteria that were going to run up against your prior authorizations. There's 125 pain specialists who are part of the criteria, there's 325 neurologists dividing 2000 prescriptions by your population of neurologists. That's between 7 and 17 new prior authorizations every 6 months with clinicians that evaluate these patients. I ask today that one, Ajovy be included in your DUR criteria in your prior authorization criteria. Two, consider aligning criteria to more consistent with that of Amerigroup and the United Healthcare providers and various clinicians are following uniformity. Those prior authorizations could use leverage to power some of your primary care doctors who can make a diagnosis and maybe take on a decision. Then you can think about automating your prior authorization process so that your processes, looking at the prescription history and background, you're looking to see if patients have a history of preventative use and then based on that preventative use, you have a profile for a patient who should in fact manually trigger a prior authorization. Are there any questions?

Paul Oesterman: I think one thing that you mentioned is something that we've been trying to do is focus on drug classes more than specific products. Otherwise, we end up going through the same class every single time.

Carl Jeffery: You mentioned you are not in favor of the specialist requirement. Is there another one outside of a neurologist or pain specialist that would be best to limit these to?

Don Moran: I'm sensitive for two reasons. I'm familiar with the recent American Medical Association survey doctors who are reporting that performed about 29 prior authorizations per week in their office, about 14 hours of time, imaging studies, diagnostic studies, access to medications. This is now incremental to that. I understand the need for a neurologist to be involved but I think primary care docs, certainly have the power to diagnose a migraine and they can certainly prescribe every other migraine treatments to date other than this for your prior authorization. I'm sensitive to prior authorization requesting physicians, nurse practitioners who have now discovered that they can't continue to care for their patients with migraines with this therapy because they now must involve a neurologist in the patient's care and in the state of Nevada, I don't know how easy patient access is to neurologists across the entire spectrum. So my request is just being sensitive to primary care doctors who might be able to leverage, might be able to simplify the process and use prescription claims history, and you know your community has 325 neurologists and if they will welcome an additional number of prior authorizations.

Holly Long: What is the reason for the 14 headache days per month?

Carl Jeffery: This is the standard criteria for the diagnosis of episodic migraines. This just confirms that yes, they have episodic migraines and its similar criteria for the chronic migraine. It has 15 headaches per month and at least 8 must be migraines. As Paul had eluded to, we're not calling out just any single agent in there because there are, as Don mentioned, there's three products now. Don's exactly right, the other two products came out after we had our clinical review done so the next, future reviews will include those but we're not making any distinction about which product has which criteria so I think it's fair to add some criteria for the general class and include all three agents in that criteria.

Paul Oesterman: I guess I need to make one comment. I appreciate your concern for the neurologists and pain specialists and the potential for work load; however, in the past, we have, as you can imagine, seen inappropriate prescribing and one of our duties as the DUR board is to make sure that the prescriptions that are dispensed are appropriate. When something like this is new and available, there is a very good potential for multiple primary care practitioners to be detailed on these products and all the sudden we see a spike where it may not always be appropriate, so I see both sides.

James Marx: The vast majority of headaches are treated at the primary care level, and I know that particularly the family practitioners that really done a good job and they incorporated it into their certification and maintenance. The average time to get a patient to a neurologist in Las Vegas is 3 to 4 months and most of the pain specialists really don't do much in the way of headaches, it is pretty limited to Botox. In this day and age, I don't think there's any need for neurologists to see patients for migraines. Migraines have become such a well described, well included in all the residencies. I don't see any reason to require pain specialists or neurologists who would be responsible for this, and I think we just need to take a look at the utilization. I don't think that will be that much of a problem because I hope that the Pharma would do a good job in detailing this. Migraine headache is a real problem and it's a tremendous deterrent to productivity and quality of life and I think that it's really important that we get, this is really a very dramatic improvement in the lifestyles because basically other than Botox perhaps, there really hasn't been anything. I think this is going to be more effective than Botox, but there's really very little that's really giving these

patients any sort of quality of life. And to deny this medication for a neurology consult I think is detrimental. I don't see it as being reasonable to include in the criteria.

Holly Long: So I looked up quite a few other states are jumping right on board with this, and they were drug-specific. They're obviously already talking updating to do a class instead but the little bit of difference that I saw, they did say that the prescriber has to be a specialist or consulted with a specialist such as a neurologist, and they just did a blank statement instead of putting in an exact age, I kind of liked it. They did a patient is within the age range as recommended by the FDA label so we don't have to go back in and change it when they change the age later as that's a good possibility. As far as the number of migraines, they said the patient is experiencing at least 4 migraines a day per month requiring acute pharmacological management so they didn't go specific into the differences between acute and chronic, and they didn't limit it with the definitions like you're explaining it, they just did 4. Another one that they put was the failure statement. They did a 3-month trial of at least one agent from each of the following classes and they gave the list of beta-blockers and antidepressants or anticonvulsants.

Carl Jeffery: Right and this is what Don was talking about. We've got the 3 different classes so either Elavil or Effexor or Depakote or Topamax or a beta-blocker.

Holly Long: They limited the initial approval to 3 months.

David England: Even though we may not use a neurologist initially, could we amend the criteria that states within a year, they would have to see a neurologist?

Holly Long: So do like a continuation to continue therapy after a certain amount of time and it would require that?

Paul Oesterman: Initial prescription doesn't require…

Beth Slamowitz: I would say after the initial prior auth. If the initial prior auth was for six months, then after the initial prior auth and then would have to be in consult or by a neurologist.

Michael Owens: I think when you start using injection medications, I really like the opinion of a specialist. Because if things go wrong, I always imagine myself in a courtroom, are you specialized enough to be giving this medication and then it goes back to standard care and what's expected in your community. Medications like Prolia, but it has taken me a long time to get there. It's one of those things where I think if a patient has failed everything else, then if it's my patient, I would have said, well, with migraine medication is not working, we'll just have to keep chugging away and I'll get you in to see a neurologist. My usual spiel is if the neurologist said that this is okay and they're on board with this, and I have their blessing, you don't need to see the neurologist ever again. I want that stamp of approval. My practice is varied enough that so that if there's anything new that I'm looking at introducing, then I typically will have a consult on this.

Beth Slamowitz: This isn't first-line therapy. You have to fail other oral therapies. If they got to the point where those are not working, then at that point those primary care prescribers would have some consultation with a specialist, does this make sense. Maybe it isn't a migraine.

James Marx: I can speak from a legal perspective, if you have gone through those other medications, that you met the standard of care. I am much more concerned with triptans than I am

with CGRP's. I would take the opposite, I would put someone on this before starting Imitrex injections. We all are very cognoscente of the risks and benefits we have to practice, but I think if you go through the algorithm of care, basically you are going to meet the standard of care and there's going to be a lot of doctors that are in situations who really can't get a neurological consultation. I don't think we should design the criteria because of that. You don't want to make those prior authorizations so hard that they won't actually do it. Our prior authorization criteria is so difficult because when you have to go to a neurologist or a pain specialist, you know what do you need, you want an okay for someone else to give a medication. That isn't going to make a real impact in terms of moving that patient in the priority of being seen. I think we are going to make it unreasonably difficult to get this medication.

Beth Slamowitz: Remember a consultation can be a phone call or chart review. It isn't always that a patient needs to be seen at an appointment. There is difficulty with the number of specialists, that is why the consultation is not meant to be in person.

James Marx: Again, speaking from an insurance standpoint, I can tell you that if you call a neurologist and say we have this patient, even though it's just a phone call, that's considered a consultation and there's a much higher level. It doesn't meet the standard of care. They are called "Curb-side consult" and they're very dangerous and you're not going to find a neurologist who is wanting to give you a phone okay.

Yvette Kaunismaki: I agree. I mean, as a specialist myself, if somebody calls me and asks about this, I would say I need to see the patient.

Beth Slamowitz: A consult doesn't necessarily mean I'm calling you up, I have this patient with this, what should I give them? I would hope the provider on the line would want to see a chart or medical record or see that person.

Yvette Kaunismaki: Just a note on that consultation, they still need to get on the schedule.

Michael Owens: It is the same with pain consult. By the time a patient has failed other migraine treatments, you can see that coming down the road. It is one of those things you can tell they are not doing well. If you have a patient with diabetes and their A1c keeps climbing to 11 or 12, no matter what you're doing, I'm going to send them to an endocrinologist. You see those scenarios coming. It is the same with getting patients into pain management. It sometimes takes two or three months. That is one of those things you are aware of. I don't think you are putting the patient through a lot of undue pain and suffering by having them wait to see a neurologist. That is the way I practice and it my comfort level with introducing new medications, it just takes a while.

Paul Oesterman: What I'm hearing, you have this proposed criteria in front of us and the primary question revolves around bullet point number 4, the episodic migraine, as to whether these products need to be prescribed by or in consultation with one of the following specialists, either a neurologist or pain specialist. Ignoring that point for the moment, are there any other concerns with the criteria of that as presented?

Netochi Adeolokun: The criteria from other states, does the criteria require three step therapies or two?

Holly Long: The patient has failed a 3-month trial of at least one agent from each of the following classes of preventative medications and they have in parenthesis unless contraindicated and they have listed beta-blockers with a list of examples, antidepressants and a list of examples, and anticonvulsants.

Paul Oesterman: They have had to fail one from each class, similar to the criteria here.

Ryan Bitton: For HPN, we have a failure of two agents, it is just a matter of how you write it. We have an initial authorization for three months like those other states. Some of the trials were built around a three-month endpoint to see efficacy. Some others have six months. HPN proposes three months and then 12 months after that.

Holly Long: Virginia said additional approval will be for 3 months. Additional therapy may be approved only with the clinical documentation showing a 50% reduction in either the number of headaches per month or the overall symptom severity as measured by MIDIS or HIT-6 compared to baseline.

Ryan Bitton: We are not as prescriptive as the percentage of decrease.

Paul Oesterman: Hearing everything, it sounds like there could be a compromise here where we make our initial approval for 3 months not requiring a specialist and then if it appears to be effective for the patient that for the next year, prior authorization would require.

Carl Jeffery: Are there primary care doctors who have specialized in migraine who maybe would have an advantage of treating that over another primary care who focuses on lipids or is that worth including in there?

James Marx: There are a few. One of the things that will chill your enthusiasm a little, the fact that these are injectable, not a lot of patients are going to be gung ho about this. I think only the most severe patients are going to be willing to do the injections. There is a tremendous resistance to injections. The next step of this therapy will be an oral or nasal delivery.

Paul Oesterman: I agree with your point there and I think that's one factor that I don't think the neurologists and pain specialists are going to get hit with, 2000 patients or something like that, there's that many that don't want to self-inject but it's not going to be as big a burden as potentially could be.

Holly Long: Could we maybe be a little bit more general with the specialists. Instead of saying that it has to be prescribed by or in consultation with one of the following neurology or pain specialists if we said something along the lines of the prescriber is a specialist or has consulted a specialists such as a neurologist so that it leaves it more open or should it just be a neurologist or pain specialist?

Beth Slamowitz: I think it should probably be one way or the other, but I also want to caution, it sounds like a good compromise to say that you agree with a three month prior auth and then you would switch to allow them to have a consultation or have a specialist write it at that time but you have a risk of that individual having access to care if that provider is giving them the initial prescription and they have a 3-month or 6-month prior authorization is not a good communicator and doesn't indicate to them that this is the only time you're going to get from me and you're going

to have to go get an appointment with a specialist at that time. There could be a break in treatment and you could have recurrence or it could get worse or who knows and they're still going to have to go see that specialist as an initial patient and they're still going to have to go through a workup. I can't imagine any specialist will take it at face value at that point even if they have already been on this medication. I just want to caution that it should be one way or another for continuity of care.

James Marx: Personally, for a patient like that, after three or six months, they tell me it is successful, I would wonder why I'm seeing them. Not realizing there was prior authorization criteria. Where is the meat? What is the consultation about? It is for pro-active treatment not looking back.

Beth Slamowitz: So maybe if you want to take out that requirement in the criteria, and we can bring this back with some utilization to see who is prescribing it and how much is being used and then we can determine at that time if it makes sense to go another route.

James Marx: I think that is the way to go.

David England: I did a quick search, most recommendations state to refer to a neurologist or pain specialist to assess comorbidities.

Ryan Bitton: Once we let the cat out of the bag, it is going to be difficult to reign back in. These are great therapies, these are block-buster good quality drugs. I'm concerned with opening them to everyone.

Beth Slamowitz: You have the failure criteria, so it won't be used first-line.

Paul Oesterman: In the interest of time, I'm going to do a couple of things here. I'm going to ask for a motion to approve the criteria as it has been presented. Hearing none and seeing none, secondarily ask for a motion to approve the criteria with the elimination of bullet point 4 under episodic migraine and bullet point 5 under chronic migraine with the understanding that we will bring this back in 2 meetings and look at utilization numbers.

Carl Jeffery: Also, change the initial approval to 3 months?

Paul Oesterman: I'm not familiar with these products. What's the usual onset for determination of efficacy?

Beth Slamowitz: Some are 3 months and some are 6 months to see if there's any improvement over that time period.

Carl Jeffery: I think they started seeing effects almost immediately.

Paul Oesterman: I say the approval length to be 3 months. We'll make a formal motion to approve the presented criteria with the elimination of bullet point 4 for episodic migraines, bullet point 5 for chronic migraines, and the approval length would be for initial 3-month period and then in 2 meetings, we will look at the utilization criteria.

Carl Jeffery: Under the reauthorization criteria, it does have a requirement for the specialist.

Paul Oesterman: Do we have a motion to approve that criteria?

Motion to approve. Second. Voting: Ayes are unanimous, the motion carries as amended.

5. Public Comment on any DUR Board Requested Report

James Marx: I have encountered this recently with management care organizations where we have initial requests for prior authorization for Suboxone for medication-assisted treatment and I know that the pharmacies theoretically are supposed to give you a 3-day fill on them but apparently they're not. I'm not even sure why we need a prior authorization for Suboxone or any of the other Suboxone variants. It seems to me, when the patient presents and they need medication-assisted treatment that prior authorization should be pretty obvious. I can see where you have to prove that they actually were abusing it. I'm not sure why there would be a prior authorization criteria. I think it's really a deterrent to therapy.

Ryan Bitton: HPN doesn't have prior authorization criteria.

James Marx: Right, it wasn't HPN.

Ryan Bitton: We used to, but it has been removed.

James Marx: I think we need to get the word out, it is a deterrent to therapy. There is one manufacture that has voucher for 15 days supply, but I don't know how long those are going to last.

Carl Jeffery: Your request is for us to bring this back to future meetings?

Beth Slamowitz: It would help to know which MCO you're referring to.

James Marx: It was Amerigroup.

Beth Slamowitz: I know that for fee for service, we allow seven days' worth without prior authorization.

Holly Long: So, do you want to email me that information and I will get in communication with Eric Sanchez and Jeanine Murray and we kind of clarify exactly what it was. Will that help?

James Marx: Well, what is the.. Is there a prior authorization criteria now? Do we have that? Fee for service doesn't.

Carl Jeffery: Yeah, after the 7 days we have a prior authorization criteria.

James Marx: So what are the rules?

Carl Jeffery: I don't remember all the rules off the top of my head, but basically they're not finding any other opioids, and they're under treatment for…

Beth Slamowitz: So if there are specific criteria or specific issues or components, you can certainly bring it to Holly or myself and we can see if maybe at a future meeting we can bring that back and have the MCOs address the criteria that they have and see if we have that conversation.

6. DUR Board Requested Reports

a. Prior Authorizations on High Dollar Claims

Carl Jeffery: This was just put into place August 6. We don't have very much data. For fee for service, anyway. The MCOs had some form of a limit on before that, so just for fee for service. What you have in your binders there is the number of PAs that are approved or rejected based on what was requested. There's a foreshadowing on what's to come. We've got a lot of oncology drugs on here, too, so those have a 10,000 dollar limit. We don't apply the 10,000-dollar limit to physician-administered drug claims. This is only POS.

Paul Oesterman: On the second one, the aminoglycoside antibiotic, Tobi Podhaler capsules, there are alternatives to that particular product.

Carl Jeffery: The P&T has addressed these and they've got the class of tobramycin inhaled for CF and I think the Tobi is preferred. We work with the manufacturer on that one.

Paul Oesterman: There's a lot more rejected than are approved.

Carl Jeffery: What's kind of interesting going through some of these claims, I can't just look at the PA requests, I have to look at the claims that were submitted for over 10,000 dollars to see because sometimes they'll get that reject and they'll never submit a PA for it, and so we'll never see it in our PA system because they never submitted it because they know they don't meet criteria. Trying to track those down is a challenge.

Paul Oesterman: I think this is a good report and it's providing the information that we were interested in. Is there anybody on the board who wants any drilled down information on anything in this report? This is a 60-day almost…

Carl Jeffery: Yes, from October 3.

b. Opioid Utilization – top prescribers and members

Carl Jeffery: This is a running report we've been watching for a long time so it is kind of our standard. We've got the fee for service side and I'll let the MCOs speak in turn for their own reports but for the fee for service side, we've got the top utilizing by member, by different claims. I think we've seen this member in here before.

Paul Oesterman: The first encrypted member 747. Again, caution is the amount of acetaminophen that the patient may be ingesting.

Carl Jeffery: This is over the course of a year. A lot of these members have a lot of quantity and a lot of claims. It's deceptive and I didn't tease it out, but some of them may be long-term care where they're getting like 7 days at a time and so there would be a claim every 7 days so it's a little deceptive.

Paul Oesterman: Okay, so instead of looking at the count of claims, look at the sum of quantity. Is there a correlation between these top 15 members and the top prescribers?

Carl Jeffery: I didn't match those up.

Paul Oesterman: For the next meeting, can we take a look and see if there is any correlation between the top opioid member utilization and the top prescriber? It's not to say it's necessarily inappropriate to have an oncologist or pain specialist who is the prescriber. It has been known that patients will seek out those people who are willing to write prescriptions more leniently than others.

Carl Jeffery: When you look at the general trends starting on page 470, the general trends here, and again tells a good story about the numbers decreasing, I think. Even by count of, almost in all metrics, count of members, count of claims decreasing, quantities decreasing, the supply is decreasing so I think the message is getting out.

Paul Oesterman: One more calculation to add to this would be number of doses per member. Quantity divided by the number of members.

James Marx: One thing that catches my eye is the Methadone.

Paul Oesterman: We have on page 472, the top 10 prescribers by count of claims for the fee for service model.

Carl Jeffery: It was kind of the same, our number one nurse practitioner that we got the letter of response to and moved down to number 2 a while ago and now it's got a new number 1 anesthesiologist in Henderson and is eclipsing everybody else by quite a bit.

Paul Oesterman: We have a similar-type letter to what we sent in the past, it might be worth sending.

Carl Jeffery: Yeah, I'll have to check to see if they got one before, because they've been in the top 10 here for a while. They probably got one but kind of wanted to give some updated standings. Maybe they are proud of that.

Paul Oesterman: Anthem, what do we have here?

Jeanine Murray: These are the top 10 prescribers for the opioid utilization and then the top 10 members.

Paul Oesterman: Is it at all possible to see if the top 10 prescribers for the different MCOs are one in the same?

Carl Jeffery: We looked at that at the last meeting and there was one prescriber that crossed over but it wasn't real big. We can do that again. It just takes some coordination. We need the real NPIs and we'd have to disguise that.

Jeanine Murray: But we can share that on the pre-DUR meeting that we have right?

Carl Jeffery: Right.

Ryan Bitton: I don't have much to say, that is the data. It is broken down by member count by quarter.

Paul Oesterman: What happened to prescriber ID A who's number 1 in the third quarter of 2017 dropped to second and then disappeared completely off the list?

Ryan Bitton: I'm not sure. I can look into that.

Paul Oesterman: Silver Summit?

Thomas Beranek: I don't have any additional comments. We will try to get everything in the same format for the next meeting.

c. Antibiotic Utilization

Holly Long: I just wanted to give everybody an update as far as where we're at with the antibiotic policy that was recommended to the state at the last meeting in July. We asked for letters to go out with provider education regarding the antibiotic policy. Those went out starting September 18 and there were a few different avenues that were used. We were faxing, we were mailing, we were e-mailing. We had it provided to the board of pharmacy and to the board of medical examiners for them to turn around and provide to whomever they deemed necessary. I also provided it to Dr. Capurro, the Nevada State Dental Health Officer and she is over the DPBH oral health program and she agreed to assist us with providing it as far as outreach to the dental providers. We also did a lot of mailing and emailing to directors of pharmacy, anybody that we can pretty much Google and find. We tried to make sure that we got to everybody. We were more specific with rural areas when we were sending that out. We also attended a tribal consultation in order to do some outreach to the tribal community, and I got a lot of feedback with the consultation. The letter was provided to them and they had information about what the policy included. We have an initial web announcement that is going to be going out but hasn't been posted yet. We also have a flyer or sort of like a newsletter that we're creating that is going to have almost like a fact sheet specific to the policy. A lot of the feedback that we've been getting so far pretty much is telling us that people don't understand that it's specific to the fluoroquinolones and third generation cephalosporins so we're being specific to what antibiotics it is and then to the exception criteria that was approved, as well. We were going over that and the fact sheet or newsletter. That should be provided I think within the next week. We'll start posting that and we'll have numerous locations where we're going to try to post that as far as the DHCFP's pharmacy site, Medicaid site, and then all the outreach that I did as far as the Board of Medical Examiners and the Board of Pharmacy again doing all that again. We're doing a project kickoff which will be internal for the state so that we can develop a list of who is going forward with workshop or work group, and we're going to do a webinar with Dr. James Wilson that was here that presented when we were at the July DUR Board Meeting. We're looking the earliest it would possibly be would be early February but because of what we're doing, we're actually seeing that that might get pushed out. It will be a while but eventually after implementation, we can definitely look at utilization.

Paul Oesterman: In anticipation of that, word of mouth is getting out. I would really be interested like Dr. Marx has asked, just look at our utilization knowing that it hasn't been fully implemented.

Carl Jeffery: There's some utilization numbers in the binder here and so you can see, even in the top 10, we've got several products in there so we've got some high utilization of the classes that we're first addressing here. These include some of the physician-administered drug claims, too, so some of the ceftriaxone, those won't be impacted and actually they're exempt anyway. Some of these won't be included in here but a lot of the Cipro, Cefdinir, the levofloxacin. There's some pretty big numbers for the last year so this will be a pretty big impact.

Holly Long: One of the major concerns that came up that I'm looking for help with is that people were concerned since we are requiring culture and sensitivity wondering if that would be paid for by Medicaid and yes it will be. The other is if that's going to have a hold-up or other issues and so really what I'm looking for is information, if anybody has any contacts with the major lab corporations in Nevada? I don't have that so Lab Corps or Quest or any of those that would be good contacts in order for me just to get into communication with them and give them a heads up of what we're looking at implementing so that I can get information from them to be able to provide to the community.

Paul Oesterman: Okay, so we'll get some utilization from this and this report is complete antibiotic utilization. If we can just limit it to the targeted fluoroquinolones and the third generation cephalosporins, I think that would be helpful.

d. Oncology Medication Utilization

Carl Jeffery: The Board may not have asked for this one; this may be one we prompted trying to prime you guys because I think where we're going is probably some utilization management for some oncology medications. We've got the list of drugs on here listed by claim count. The Avastin is a little deceptive because they also use the injection into the eye for macular degeneration so that one is probably a bit skewed but the other ones… With the oncology drugs, I saw a TV commercial and I think half the commercial was listing the indication. The indications are so specific and right now without any kind of controls on them, you never know if they're being used off label. I don't think Medicaid should be responsible for footing the bill for the drugs studies. If they are off label, then Medicaid shouldn't be reimbursing for them.

Paul Oesterman: So, the proposal would be to bring back some PA criteria that is maybe simple as FDA approved indications?

Carl Jeffery: Yeah, we're working on some options.

Ryan Bitton: HPN has criteria that states it has to be FDA approved indication or reference recommendations that are 2B or above. So, no experimental treatment is covered. We have a lot of specific criteria in place.

7. Public Comment on any Standard DUR Report

Holly Long: I have one more thing to talk about. There is a form that we're going to use, it's my consolidation proposition going forward. I'll talk about that after the report review.

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).

Carl Jeffery: Nothing outstanding here. As we've seen the trends, the hep-C antivirals just keep ticking down. It seems like to me that we've treated most of the people in Nevada that have hepatitis-C so I think that's a good trend, as well, and nothing else. We have the antihaemophilia products that are always number 1 on here. We've approved some criteria for those so I think it's not implemented yet but I think there may be some trend with that eventually.

Ryan Bitton: Our utilization is also included.

Carl Jeffery: It looks like HPN has antivirals are increasing.

Ryan Bitton: That includes flu treatments as well, so there was a spike for flu season.

Carl Jeffery: We also have the top 50 in here and nothing to write home about with those, either. Pretty standard. Another primer for what we're thinking about for the next meeting is some criteria around albuterol utilization so get your mind thinking about how maybe we can control some of that utilization. On page 550 here, it's our standard report. This is the updated report for ProDUR.

Paul Oesterman: If we're going to be looking at albuterol at our next meeting, then we should get some stats in terms of all the asthma and COPD medications. Does anyone on the board have other requests for the next meeting?

Holly Long: I'd like to recommend that we bring compounds back. I know we just reviewed that and made a decision in July.

Beth Slamowitz: I attended a conference in DC with the FDA to go over the final rules for compounds. There was a lot of interesting information and I'll bring some of that forward, as well, so you can kind of see. There were representatives from every state.

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.

Holly Long: Instead of asking everyone to submit prior authorization criteria, we're proposing that we use this form instead. So, this would be provided by myself and Optum to each of the MCOs when we're developing the DUR binder. In lieu of providing pages and pages of prior

authorization criteria and asking everyone to hurry up and go through all that, we're going to do the forms. In the past, I've tried to go through and provide a spreadsheet of comparisons and it's too difficult to be able to do that so we're hoping this will work. I thought we would try this. It's very a simple form and if anybody has any suggestions for changes that we need to make. This will take the place of all the prior authorization criteria from each of the MCOs, what we would do is provide the criteria of what Optum is proposing or proposed changes to what exists, ask them to review it, compare it to what they have, and then provide this back. This will go in the binder with any comments or suggested changes or approve whatever is proposed and this will go in the binder instead of all the pages and pages of criteria. Where it says managed care organization, that is a drop-down in the form. I'll put what the prior authorization criteria being reviewed is and then provide one for each of the drugs or drug classes that we're looking at.

Beth Slamowitz: All the board will see in the binder is the exceptions. It will state they either approve of the Optum proposed criteria or they will provide what changes they would like to see.

Holly Long: So, for example, if everybody is looking at HPN and we really, really like that one and we would have those documents supplied as attachments with it but otherwise it will just be this form.

James Marx: How much notice are they going to get with this?

Holly Long: It is a few months out from when we request the information from them. We provide them with information and Carl has developed this spreadsheet in order to make the binders as efficient as possible in getting that information from each of the MCOs. We'll provide the criteria and the template and spreadsheet for them, and when they provide it back to us, this will be in place of all their prior authorization criteria including all their reports and it will go into the binder.

Paul Oesterman: I like it.

Beth Slamowitz: We are hoping to eliminate the 600 page binders.

Holly Long: Let me know if there are any comments or changes.

Ryan Bitton: I think getting the reports consistent is the biggest benefit. Making the reports more meaningful.

Paul Oesterman: Do you want the date on this?

Beth Slamowitz: Sure, we'll add the meeting date. It will be part of the binder going forward.

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 is January 24 back at the Hyatt.

c. Adjournment.

Meeting adjourned at 7:06 PM

Prior Authorization Guideline

Guideline Name Oral Oncology Medications

Coverage and Limitations:

This criteria applies only if other product-specific criteria are not available in Medicaid Services Manual Chapter 1200.

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

Prior Authorization will be granted if all of the following are met:

1. The member has a diagnosis that is indicated in the Food and Drug Administration (FDA) approved package insert, or listed in nationally recognized compendia, for the determination of medically-accepted indications

   AND

2. If not indicated as a first line agent, either in the FDA approved package insert or nationally recognized compendia, documentation of previous therapies tried and failed

   AND

3. Prescribed by, or in consultation with an oncologist or hematologist

   AND

4. Must be used in combination with other chemotherapeutic or adjuvant agents according to the FDA approved prescribing information

   AND

5. One of the following:

a. If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was preformed to confirm the diagnosis

OR

b. If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis

AND

6. The member does not have any contraindications to the requested oral oncology medication

AND

7. The requested quantity and dosing regimen falls within the manufacturer's published dosing guidelines or nationally recognized compendia and is appropriate for the member's age

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient is responding satisfactorily to the treatment.

*Members currently receiving oral oncology treatment will be grandfathered in to avoid treatment interruption.

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Oral Oncology Medications

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Anthem will maintain its own criteria for this category. Anthem only has drug specific PA criteria and each align with FDA approved labeling/package insert and is not more restrictive than the proposed therapeutic class policy.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: Jeannine M Murray

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Oral Oncology Medications

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

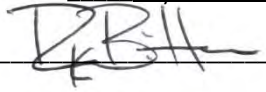
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

HPN does not maintain a clinical protocol for oncology agents not listed on the Preferred Drug List (PDL). Reviews for drugs that are not on the PDL have a standard non-formulary review, which for oncology includes referring to the National Comprehensive Cancer Network (NCCN) to insure the use is supported and not investigational or experimental. So while the clinical protocol may be operationally unnecessary for HPN operations, clinically the criteria is sound and appropriate for such reviews.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Ryan Bitton

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Oral Oncology Medications

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: ____Tom Beranek_____

Signature of individual completing this form: Tom Beranek

Prior Authorization Guideline

Guideline Name Afinitor, Afinitor Disperz (everolimus)

1 . Indications

Drug Name: Afinitor (everolimus)

Indications

Advanced Neuroendocrine Tumors of Pancreatic Origin (PNET) Indicated for the treatment of progressive PNET in patients with unresectable, locally advanced or metastatic disease. Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.

Advanced Renal Cell Carcinoma (RCC) Indicated for the treatment of patients with advanced RCC after failure of treatment with sunitinib or sorafenib.

Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC) Indicated for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.

Subependymal Giant Cell Astrocytoma (SEGA) Indicated for the treatment of adult and pediatric patients aged 1 year and older with TSC who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

Advanced Hormone Receptor-Positive, HER2-Negative Breast Cancer (Advanced HR + BC) Indicated for the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane, after failure of treatment with letrozole or anastrozole.

Neuroendocrine Tumors of Gastrointestinal or Lung Origin Indicated for the treatment of adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic. AFINITOR is not indicated for the treatment of patients with functional carcinoid tumors.

Drug Name: Afinitor Disperz (everolimus)

Indications

Subependymal Giant Cell Astrocytoma (SEGA) Indicated for the treatment of adult and pediatric patients aged 1 year and older with TSC who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected. The effectiveness of Afinitor Disperz is based on demonstration of durable objective response, as evidenced by reduction in SEGA tumor volume. Improvement in disease-related symptoms and overall survival in patients with SEGA and TSC has not been demonstrated.

Tuberous Sclerosis Complex (TSC) Associated Partial-onset Seizures Indicated for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures

2 . Criteria

Product Name: Afinitor

Diagnosis	Advanced Neuroendocrine Tumors of Pancreatic Origin (PNET)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of progressive neuroendocrine tumors of pancreatic origin

   AND

1. Disease is one of the following:
   a. Unresectable, locally advanced
   b. Metastatic

   AND

2. Prescribed by or in consultation with an oncologist

Product Name: Afinitor

Diagnosis	Advanced Neuroendocrine Tumors of Pancreatic Origin (PNET)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Advanced Renal Cell Carcinoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of advanced/metastatic renal cell carcinoma.

   AND

2. Trial and failure with one of the following:
   a. Sutent (sunitinib)
   b. Nexavar (sorafenib)

   AND

3. Prescribed by or in consultation with an oncologist

Product Name: Afinitor

Diagnosis	Advanced Renal Cell Carcinoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery

   AND

2. Prescribed by or in consultation with a nephrologist

Product Name: Afinitor

Diagnosis	Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor, Afinitor Disperz

Diagnosis	Subependymal Giant Cell Astrocytoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS)

   AND

2. Patient is not a candidate for curative surgical resection

   AND

3. Prescribed by or in consultation with an oncologist.

Product Name: Afinitor, Afinitor Disperz

Diagnosis	Subependymal Giant Cell Astrocytoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Breast cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of hormone receptor positive, HER-2 negative advanced breast cancer

   AND

2. Trial and failure, contraindication, or intolerance to one of the following:
   a. Femara (letrozole)
   b. Arimidex (anastrozole)

   AND

3. Used in combination with Aromasin (exemestane)

   AND

4. Prescribed by or in consultation with an oncologist

Product Name: Afinitor

Diagnosis	Breast cancer
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Neuroendocrine tumors of gastrointestinal or lung origin
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of progressive, well-differentiated, non-functional neuroendocrine tumors of gastrointestinal or lung origin

   AND

2. One of the following:
   a. Unresectable, locally advanced disease
   b. Metastatic disease

   AND

3. Prescribed by or in consultation with an oncologist

Product Name: Afinitor

Diagnosis	Neuroendocrine tumors of gastrointestinal or lung origin
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Neuroendocrine tumors of gastrointestinal or lung origin
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor Disperz

Diagnosis	TSC-associated Partial-onset Seizures
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of TSC-associated partial-onset seizures

   AND

2. Used as adjunctive therapy

   AND

3. Prescribed by or in consultation with a neurologist

Product Name: Afinitor Disperz

Diagnosis	TSC-associated Partial-onset Seizures
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient shows reduction in seizure frequency while on therapy

3 . References

1. Afinitor and Afinitor Disprerz Prescribing Information. Novartis Pharmaceuticals Corporation. East Hanover, NJ. April 2018.

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Afinitor®

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Anthem criteria aligns well with proposed criteria and is not more restrictive than proposed.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting. If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: Jeannie M Murray

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Afinitor®

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: _____Ryan Bitton_____

Signature of individual completing this form: _____

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Afinitor®

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Addition of Quantity Limits/Dose Verification:

a. Dose does not exceed 10 mg/day (1 tablet/day); Or
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Rationale: To ensure appropriate drug use and prevent unsubstantiated dosing regimens.

Reduction of initial approval duration to 6 months.

Require re-authorization at this time - 12 months of continued therapy pending approval.

See continued recommendations on page 2:

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: ____Tom Beranek_____

Signature of individual completing this form: Tom Beranek

Meets one of the following (a or b): a. For RCC with predominant clear cell histology both of the following (i and ii): i. Failure of one of the following, unless contraindicated or clinically significant adverse effects are experienced: Sutent®, Votrient®, Inlyta®, Avastin® in combination with Intron®-A, Proleukin®, Cabometyx®, or Torisel®;

ii. Failure of a trial of Opdivo® or Cabometyx® (if not previously used as first- line therapy), unless contraindicated or clinically significant adverse effects are experienced;

Renal Cell Carcinoma

Meets one of the following (a or b):
a. For RCC with predominant clear cell histology both of the following (i and ii):
i. Failure of one of the following, unless contraindicated or clinically significant adverse effects are experienced: Sutent®, Votrient®, Inlyta®, Avastin® in combination with Intron®-A, Proleukin®, Cabometyx®, or Torisel®;
ii. Failure of a trial of Opdivo® or Cabometyx® (if not previously used as first- line therapy), unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for all of the above agents*
b. RCC with non-clear cell histology (off-label);

Continued Therapy
A. All Indications (must meet all)**:**
1. Member meets one of the following:
a. Currently receiving medication via Plan benefit or member has previously met initial approval criteria;
b. Documentation supports that member is currently receiving Afinitor or Afinitor Disperz 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 of Afinitor or Afinitor Disperz, request meets one of the following (a or b):
a. New dose does not exceed 10 mg/day (1 tablet/day);
b. 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 – 12 months

Prior Authorization Guideline

Guideline Name Ibrance (palbociclib)

1 . Indications

Drug Name: Ibrance (palbociclib) **<u>Indications</u>** **Breast Cancer** Indicated for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with: (1) an aromatase inhibitor as initial endocrine based therapy in postmenopausal women, or (2) fulvestrant in women with disease progression following endocrine therapy.

2 . Criteria

Product Name: Ibrance

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of advanced or metastatic breast cancer

   AND

2. Disease is hormone-receptor (HR)-positive [2]

AND

3. Disease is human epidermal growth factor receptor 2 (HER2)-negative

AND

4. One of the following:
    a) Both of the following:
        i. Used in combination with an aromatase inhibitor (e.g., anastrozole, letrozole, exemestane)
        ii. Patient is a postmenopausal woman

OR

    b) Both of the following:
        i. Used in combination with Faslodex (fulvestrant)
        ii. Disease has progressed following endocrine therapy

AND

5. Prescribed by or in consultation with an oncologist

Product Name: Ibrance

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Ibrance therapy

3 . References

1. Ibrance prescribing information. Pfizer Inc. New York, NY. February 2018.
2. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Breast Cancer. v.1.2018. Available by subscription at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Accessed July 10, 2018.

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Ibrance®

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

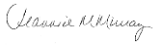
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Anthem will maintain its own criteria as it is less restrictive allowing also for diagnosis of Soft Tissue Sarcoma With Differentiated/Dedifferentiated Liposarcoma of the retroperitoneum (NCCN 2A

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Ibrance®

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: _____Ryan Bitton_____

Signature of individual completing this form: _____

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Ibrance®

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Addition of Quantity Limits/Dose Verification:

a. Dose does not exceed 125 mg/day (1 tablet/day for 21 days);

OR

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Rationale: To ensure appropriate drug use and prevent unsubstantiated dosing regimens.

Reduction of initial approval duration to 6 months.

a) Require re-authorization at this time 12 months of continued therapy pending approval.

See continued recommendations on page 2:

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Tom Beranek

Signature of individual completing this form: Tom Beranek

Continued recommendations:

Breast Cancer Continuation: (must meet all):

1.Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Ibrance for breast cancer and has received this medication for at least 30 days;

2. Member is responding positively to therapy without the following reasons to discontinue (a or b):

a. Disease progression or unacceptable toxicity;

b. Required dose reduction to < 75 mg/day;

3. Request meets one of the following (a or b):

a. Dose does not exceed 125 mg/day (1 tablet/day for 21 days);

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

Rationale: Increase involvement and oversight of MCO in patient care. Ensure appropriate use, safety, and tolerability of medication regimen.

Other recommendations:

Prior Authorization Guideline

Guideline Name Sprycel (dasatinib)

1 . Indications

Drug Name: Sprycel (dasatinib)

Indications

Newly diagnosed Chronic Myelogenous Leukemia Indicated for the treatment of adults with newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.

Resistant or intolerant Chronic Myelogenous Leukemia Indicated for the treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.

Acute Lymphoblastic Leukemia (ALL) Indicated for the treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.

Pediatric Patients with Ph+ CML Indicated for the treatment of pediatric patients with Ph+ CML in chronic phase.

2 . Criteria

Product Name: Sprycel

Diagnosis	Philadelphia chromosome-positive/BCR ABL positive (Ph+/BCR ABL+) Acute Lymphoblastic Leukemia/Acute Lymphoblastic Lymphoma (ALL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of Ph+/BCR ABL+ acute lymphoblastic leukemia (ALL)

   AND

2. Resistance or intolerance to any prior therapy

   AND

3. Prescribed by or in consultation with an oncologist and/or hematologist

Product Name: Sprycel

Diagnosis	Ph+/BCR ABL+ Acute Lymphoblastic Leukemia/Acute Lymphoblastic Lymphoma (ALL)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

Product Name: Sprycel

Diagnosis	Ph+/BCR ABL+ Chronic Myelogenous/Myeloid Leukemia (CML)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of Ph+/BCR ABL+ chronic myelogenous/myeloid leukemia (CML)

   AND

2. Patient does not have the T315I, F317L, and V299L mutation [2]

   AND

3. Prescribed by or in consultation with an oncologist and/or hematologist

Product Name: Sprycel

Diagnosis	Ph+/BCR ABL+ Chronic Myelogenous/Myeloid Leukemia (CML)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Patient does not show evidence of progressive disease while on therapy

3 . Endnotes

A. According to National Comprehensive Cancer Network (NCCN) recommendations, imatinib, dasatinib, and nilotinib are all first-line therapies for chronic myelogenous/myeloid leukemia. Since all 3 agents are appropriate as a first-line option, a step through any of the 3 products is inappropriate. [2]
B. According to NCCN recommendations, patients with disease that is resistant to first-line imatinib should be treated with nilotinib, dasatinib, or bosutinib in the second-line setting. Patients with disease that is resistant to first-line nilotinib or dasatinib could be treated with an alternate TKI (other than imatinib) in the second-line setting. Dasatinib and nilotinib are effective against a majority of mutations resistant to imatinib, except for the T315I mutation. Consider clinical trial, ponatinib, omacetaxine, or hematopoietic cell transplantation (HCT) for patients with a T315I mutation. [2]

4 . References

1. Sprycel Prescribing Information. Bristol-Myers Squibb Company. Princeton, NJ. November 2017.
2. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Chronic Myelogenous Leukemia v.4.2018. Available by subscription at: https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. (Accessed July 9, 2018).

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Sprycel®

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Anthem proposes adding these items to criteria:

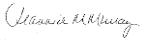
Individual has a diagnosis of CML in accelerated phase and has one of the following mutations: Y253H, E255K/V, or F359V/C/I and results are confirmed (NCCN 2A- The NCCN Drugs & Biologics Compendium (NCCN Compendium™) © 2018 National Comprehensive Cancer Network, Inc. Available at: NCCN.org.);

Individual has a diagnosis of Ph+ CML in chronic phase in children and adolescents weighing at least 10 kg (22 pounds).

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Sprycel®

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: _____Ryan Bitton_____

Signature of individual completing this form: _____

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Sprycel®

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Recommend adding dosage limitations:

Dose does not exceed 180 mg/day.

Initial approval duration: 6 months.

Continued approval/reauthorization:

Recommend adding dosage limitations:

If request is for a dose increase, request meets one of the following (a or b):

a. New dose does not exceed 180 mg/day;

b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: ____Tom Beranek_____

Signature of individual completing this form: Tom Beranek _____

Oncology Utilization

Fee for Service Medicaid

October 1, 2017 - September 30, 2018

Point of Sale Pharmacy Claims by Amount Paid

Q4 2017

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
AFINITOR	18	26	710	794	$ 370,657.65
IBRANCE	20	22	609	441	$ 230,447.79
ACTIMMUNE	3	4	112	24	$ 190,474.92
SPRYCEL	12	13	420	420	$ 154,325.76
POMALYST	4	4	98	70	$ 52,817.68
XTANDI	5	5	150	600	$ 51,539.00
IMATINIB MESYLATE	12	13	450	450	$ 50,036.64
ZYTIGA	5	7	210	570	$ 43,176.98
TAGRISSO	3	3	90	90	$ 42,602.76
TASIGNA	3	3	84	336	$ 34,792.65
IMBRUVICA	2	3	90	270	$ 33,339.27
ICLUSIG	2	2	60	60	$ 33,142.34
VOTRIENT	3	3	90	360	$ 33,087.12
NEXAVAR	2	2	60	240	$ 32,979.20
BOSULIF	2	2	60	60	$ 27,098.10
RITUXAN	3	3	132	290	$ 25,220.78
TYKERB	4	4	120	510	$ 23,149.71
CAPECITABINE	21	30	620	2,264	$ 17,535.71
TARCEVA	2	2	60	60	$ 15,671.08
STIVARGA	1	1	28	84	$ 14,891.66
TRETINOIN	4	5	143	532	$ 14,358.19
CALQUENCE	1	1	30	60	$ 14,074.17
ALECENSA	1	1	60	240	$ 13,323.78
METHOTREXATE	312	344	11,221	10,465	$ 13,128.75
OPDIVO	1	2	56	48	$ 12,237.06
AVASTIN	2	2	42	40	$ 7,605.74
RYDAPT	1	1	31	56	$ 7,505.17
PURIXAN	2	2	70	600	$ 6,833.82
TEMOZOLOMIDE	4	5	126	77	$ 6,220.66
EXEMESTANE	44	44	1,680	1,680	$ 6,033.14
CYCLOPHOSPHAMIDE	4	7	85	18	$ 5,994.36
MEGESTROL ACETATE	157	175	4,710	53,313	$ 5,397.40
TAMOXIFEN CITRATE	151	159	6,690	6,930	$ 5,020.36
TAFINLAR	2	2	60	72	$ 4,303.60
FASLODEX	2	2	56	20	$ 3,803.30
MERCAPTOPURINE	50	56	1,834	2,806	$ 3,789.51
LYNPARZA	1	2	30	120	$ 3,390.84
LUPRON DEPOT (3-MONTH)	1	1	90	1	$ 3,243.44
HERCEPTIN	1	2	14	2	$ 2,958.26
HYDROXYUREA	95	98	3,154	6,454	$ 2,896.43
ANASTROZOLE	175	186	8,132	7,338	$ 2,769.14
LUPRON DEPOT (1-MONTH)	2	2	60	2	$ 2,177.50
LETROZOLE	107	112	3,925	3,940	$ 1,697.72

PACLITAXEL	8	8	161	642	$	1,455.16
TABLOID	2	2	21	45	$	1,157.82
GLEOSTINE	1	1	42	4	$	1,083.60
LEUCOVORIN CALCIUM	23	23	524	346	$	1,035.56
CARBOPLATIN	3	3	77	420	$	560.71
DEPO-PROVERA	1	1	90	3	$	488.48
TREXALL	2	2	56	8	$	339.56
METHOTREXATE SODIUM	13	13	406	64	$	250.93
DOXORUBICIN HCL	2	3	42	175	$	241.74
BICALUTAMIDE	8	9	375	375	$	170.28
Grand Total	**1,310**	**1,428**	**48,346**	**104,889**	**$**	**1,632,532.98**

Q1 2018

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid	
AFINITOR	16	23	646	730	$	374,876.17
IBRANCE	25	28	770	574	$	308,931.12
SPRYCEL	14	15	450	450	$	186,791.74
ACTIMMUNE	3	3	84	18	$	156,995.91
POMALYST	7	9	217	154	$	116,200.93
TASIGNA	6	8	224	896	$	100,810.45
XTANDI	6	8	240	960	$	86,715.32
HERCEPTIN	8	12	203	36	$	54,591.12
ICLUSIG	3	3	90	90	$	49,713.51
TAGRISSO	3	3	90	90	$	43,879.92
ZYTIGA	6	6	180	630	$	42,055.47
IMATINIB MESYLATE	11	12	480	480	$	37,997.08
VOTRIENT	3	3	90	360	$	36,359.73
NEXAVAR	2	4	60	240	$	34,647.48
OPDIVO	3	9	154	124	$	32,124.81
BOSULIF	2	2	60	60	$	28,451.98
RITUXAN	2	3	84	270	$	24,421.77
LUPRON DEPOT (3-MONTH)	6	6	534	6	$	21,692.79
AVASTIN	4	6	106	108	$	20,948.55
TARCEVA	4	4	120	135	$	20,038.22
BENDEKA	2	2	56	32	$	19,422.74
CAPECITABINE	25	34	774	2,722	$	18,898.46
ALIMTA	2	3	24	5	$	16,683.34
PERJETA	2	2	42	42	$	14,620.02
CALQUENCE	1	1	30	60	$	14,074.17
METHOTREXATE	327	347	11,361	10,600	$	12,464.21
IMBRUVICA	1	1	30	90	$	12,190.07
TYKERB	2	2	60	240	$	11,971.78
NERLYNX	1	1	30	180	$	11,455.17
GLEEVEC	1	1	30	30	$	9,853.02
TAFINLAR	3	3	90	120	$	7,314.20
LUPRON DEPOT (1-MONTH)	4	5	150	5	$	5,894.99
FASLODEX	3	3	84	30	$	5,704.95
EXEMESTANE	41	42	1,476	1,476	$	4,962.83
MEGESTROL ACETATE	155	168	4,642	46,096	$	4,730.70

MERCAPTOPURINE	52	59	1,863	3,013	$	3,942.35
TEMOZOLOMIDE	3	3	84	30	$	3,408.12
TAMOXIFEN CITRATE	106	108	4,530	4,740	$	3,265.71
CYCLOPHOSPHAMIDE	2	3	42	9	$	2,997.18
HYDROXYUREA	83	88	2,899	5,696	$	2,605.11
DOCETAXEL	3	4	64	56	$	2,472.51
ANASTROZOLE	157	162	7,526	6,607	$	2,442.33
LETROZOLE	112	120	4,175	4,270	$	1,828.26
PACLITAXEL	4	7	126	551	$	1,225.48
GLEOSTINE	1	1	42	4	$	1,083.60
CARBOPLATIN	4	6	133	570	$	990.02
METHOTREXATE SODIUM	25	25	786	136	$	572.86
TREXALL	3	3	84	12	$	528.51
LEUCOVORIN CALCIUM	10	10	342	246	$	286.58
GEMCITABINE HCL	1	1	1	2	$	280.00
DEPO-PROVERA	1	1	84	1	$	219.56
BICALUTAMIDE	9	10	509	509	$	178.92
DOXORUBICIN HCL	1	1	14	75	$	100.70
FLUOROURACIL	1	1	1	12	$	11.28
TABLOID	1	1	14	33	$	10.47
Grand Total	**1,283**	**1,396**	**47,080**	**94,711**	**$**	**1,976,934.27**

Q2 2018

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty		Sum of Amt Paid
AFINITOR	16	23	652	764	$	389,202.14
IBRANCE	25	25	658	504	$	271,260.81
SPRYCEL	11	13	390	390	$	163,050.28
ACTIMMUNE	3	3	84	18	$	156,995.91
ZYTIGA	7	9	270	1,020	$	89,384.25
RITUXAN	6	8	321	870	$	78,675.42
HERCEPTIN	10	15	273	46	$	69,751.93
IMBRUVICA	5	6	170	230	$	69,080.47
ICLUSIG	2	2	60	120	$	66,264.34
TASIGNA	4	5	140	560	$	63,723.50
OPDIVO	3	10	168	192	$	50,445.62
TAGRISSO	3	3	90	90	$	43,879.92
XTANDI	4	4	120	480	$	43,661.44
BOSULIF	3	3	90	90	$	42,677.97
POMALYST	3	3	77	56	$	42,041.00
IMATINIB MESYLATE	19	19	690	690	$	38,884.86
VOTRIENT	3	3	90	360	$	36,359.73
NERLYNX	3	3	90	540	$	34,365.51
PERJETA	3	4	84	98	$	34,106.60
VERZENIO	3	3	84	168	$	33,874.11
GLEEVEC	3	3	90	90	$	29,559.06
CALQUENCE	2	2	60	120	$	28,148.34
KISQALI	2	2	56	126	$	27,900.78
LUPRON DEPOT (3-MONTH)	6	6	534	6	$	21,284.22
NEXAVAR	2	2	45	120	$	18,007.23

SUTENT	1	1	42	28	$	17,029.37
TARCEVA	2	2	60	60	$	16,923.14
VENCLEXTA	2	3	90	180	$	16,756.32
AVASTIN	3	4	84	80	$	15,590.68
CAPECITABINE	22	30	664	2,526	$	13,030.26
METHOTREXATE	338	368	12,608	11,399	$	12,635.41
TYKERB	1	2	60	240	$	11,971.78
ZELBORAF	1	1	28	224	$	10,137.59
BENDEKA	1	1	28	16	$	9,905.37
GILOTRIF	1	1	30	30	$	8,164.94
LUPRON DEPOT (1-MONTH)	6	6	178	6	$	7,209.36
COTELLIC	1	1	28	63	$	7,015.14
TEMOZOLOMIDE	5	7	196	50	$	6,907.38
FASLODEX	3	3	84	30	$	5,761.71
MEGESTROL ACETATE	156	169	4,543	51,372	$	5,332.51
EXEMESTANE	33	35	1,560	1,560	$	4,998.23
TAMOXIFEN CITRATE	129	133	5,970	6,480	$	4,304.18
MERCAPTOPURINE	54	60	1,990	3,303	$	4,072.66
ERBITUX	1	1	1	300	$	3,566.34
DOCETAXEL	2	3	63	48	$	2,903.31
ANASTROZOLE	170	178	8,071	7,392	$	2,677.72
VENCLEXTA STARTING PACK	1	1	28	42	$	2,416.83
HYDROXYUREA	72	79	2,564	4,953	$	2,178.62
XATMEP	1	1	56	120	$	1,906.17
LETROZOLE	113	117	4,390	4,455	$	1,790.65
TREXALL	5	5	140	52	$	1,102.19
PACLITAXEL	5	7	140	384	$	796.19
CYCLOPHOSPHAMIDE	1	1	21	2	$	669.43
MESNEX	1	1	4	8	$	638.90
PURIXAN	1	1	30	50	$	629.06
METHOTREXATE SODIUM	24	28	945	174	$	619.32
DEPO-PROVERA	1	1	30	3	$	533.63
LEUCOVORIN CALCIUM	13	13	480	348	$	402.24
BICALUTAMIDE	9	10	660	660	$	212.58
CARBOPLATIN	1	1	21	75	$	124.67
IRINOTECAN HYDROCHLORIDE	2	2	2	6	$	47.70
CISPLATIN	1	1	7	100	$	40.17
Grand Total	**1,334**	**1,457**	**51,282**	**104,566**	**$**	**2,143,587.19**

Q3 2018

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty		Sum of Amt Paid
AFINITOR	12	16	452	592	$	301,209.51
IBRANCE	26	27	728	539	$	290,101.05
ACTIMMUNE	3	4	112	24	$	209,327.88
ZYTIGA	11	11	330	1,200	$	99,280.69
ICLUSIG	3	4	120	150	$	82,845.68
TASIGNA	6	6	168	672	$	76,468.20
IMBRUVICA	6	6	170	168	$	68,268.48
HERCEPTIN	10	12	245	40	$	62,458.84

SPRYCEL	5	5	150	150	$	62,270.90
RITUXAN	5	8	263	560	$	52,694.48
NERLYNX	3	4	120	720	$	45,820.68
BOSULIF	3	3	90	90	$	42,677.97
ZEJULA	2	2	60	180	$	39,524.34
XTANDI	2	3	90	360	$	32,746.08
LUPRON DEPOT (3-MONTH)	9	9	804	9	$	32,638.83
POMALYST	2	2	56	42	$	32,478.20
TYKERB	5	5	130	590	$	29,431.48
TAGRISSO	2	2	60	60	$	29,253.28
OPDIVO	2	2	56	96	$	25,192.30
VOTRIENT	2	2	60	240	$	24,239.82
JAKAFI	2	2	60	120	$	23,119.57
VERZENIO	2	2	56	112	$	22,582.74
CAPECITABINE	31	47	1,049	3,908	$	20,992.47
GLEEVEC	2	2	60	60	$	19,706.04
IMATINIB MESYLATE	19	19	630	630	$	18,703.25
NEXAVAR	1	1	30	120	$	18,680.54
TARCEVA	2	2	60	60	$	16,923.14
GILOTRIF	2	2	60	60	$	16,329.88
AVASTIN	4	5	85	80	$	16,054.48
PERJETA	3	3	63	42	$	14,922.19
KISQALI	1	1	28	63	$	14,356.41
CALQUENCE	1	1	30	60	$	14,074.17
TEMOZOLOMIDE	5	12	344	220	$	11,650.52
VENCLEXTA	2	2	60	120	$	11,170.88
METHOTREXATE	296	326	11,126	10,558	$	10,455.95
CYCLOPHOSPHAMIDE	6	6	154	20	$	8,338.34
AZACITIDINE	1	1	28	20	$	6,235.77
FASLODEX	2	3	90	30	$	5,761.71
RYDAPT	1	1	28	40	$	5,684.97
TAMOXIFEN CITRATE	137	141	6,047	6,407	$	4,299.61
MEGESTROL ACETATE	134	139	4,184	41,732	$	4,237.92
MERCAPTOPURINE	48	54	1,794	3,061	$	3,817.92
EXEMESTANE	23	24	1,200	1,200	$	3,805.06
PURIXAN	3	4	120	250	$	3,135.13
ANASTROZOLE	174	196	8,488	7,716	$	2,946.46
XATMEP	3	3	112	152	$	2,432.11
LUPRON DEPOT (1-MONTH)	2	2	60	2	$	2,403.12
VECTIBIX	1	1	1	10	$	2,374.88
HYDROXYUREA	81	82	2,785	4,926	$	2,199.34
LETROZOLE	100	108	4,137	4,100	$	1,687.77
LEUCOVORIN CALCIUM	15	15	492	426	$	1,166.12
TABLOID	2	2	39	38	$	980.87
TREXALL	3	3	84	44	$	749.85
DEPO-PROVERA	1	1	84	3	$	533.63
METHOTREXATE SODIUM	16	18	579	102	$	460.41
BICALUTAMIDE	9	10	540	540	$	192.42
CARBOPLATIN	1	1	21	60	$	76.25
OXALIPLATIN	1	1	1	10	$	50.00
Grand Total	**1,256**	**1,376**	**49,073**	**93,584**	**$**	**1,952,220.58**

Oncology Utilization

Fee for Service Medicaid
October 1, 2017 - September 30, 2018
Point of Sale Pharmacy Claims

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
AFINITOR	62	88	2,460	2,880	$ 1,435,945.47
201710	8	12	318	346	$ 161,693.30
201711	5	7	196	224	$ 104,773.05
201712	5	7	196	224	$ 104,191.30
201801	6	9	252	280	$ 143,606.01
201802	5	6	168	196	$ 100,585.09
201803	5	8	226	254	$ 130,685.07
201804	4	5	142	170	$ 87,664.15
201805	6	9	256	284	$ 144,952.95
201806	6	9	254	310	$ 156,585.04
201807	5	8	226	282	$ 143,995.30
201808	4	5	140	224	$ 113,200.15
201809	3	3	86	86	$ 44,014.06
IBRANCE	96	102	2,765	2,058	$ 1,100,740.77
201710	6	7	196	140	$ 73,158.19
201711	6	6	168	126	$ 65,839.32
201712	8	9	245	175	$ 91,450.28
201801	8	10	273	210	$ 113,021.10
201802	7	7	189	140	$ 75,350.79
201803	10	11	308	224	$ 120,559.23
201804	9	9	238	182	$ 97,955.01
201805	8	8	210	161	$ 86,652.90
201806	8	8	210	161	$ 86,652.90
201807	8	9	238	175	$ 94,191.03
201808	9	9	245	182	$ 97,955.01
201809	9	9	245	182	$ 97,955.01
SPRYCEL	42	46	1,410	1,410	$ 566,438.68
201710	5	5	180	180	$ 59,927.88
201711	4	4	120	120	$ 46,967.68
201712	3	4	120	120	$ 47,430.20
201801	5	6	180	180	$ 73,458.22
201802	4	4	120	120	$ 50,205.64
201803	5	5	150	150	$ 63,127.88
201804	4	5	150	150	$ 62,480.72
201805	3	4	120	120	$ 50,284.78
201806	4	4	120	120	$ 50,284.78
201807	2	2	60	60	$ 24,908.36
201808	2	2	60	60	$ 24,908.36
201809	1	1	30	30	$ 12,454.18
Grand Total	200	236	6,635	6,348	$ 3,103,124.92

Anthem Oncology Utilization

Quarter Serviced	**4th Quarter 2017**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
AFINITOR 10 MG TABLET	2	4	105	105
AFINITOR 2.5 MG TABLET	1	1	15	15
AFINITOR 5 MG TABLET	1	5	120	120
ALECENSA 150 MG CAPSULE	1	2	60	480
ANASTROZOLE 1 MG TABLET	51	128	3473	2889
BICALUTAMIDE 50 MG TABLET	4	10	195	195
CAPECITABINE 500 MG TABLET	4	7	172	784
CYCLOPHOSPHAMIDE 50 MG CAPSULE	1	2	60	60
EXEMESTANE 25 MG TABLET	12	29	735	735
HYDROXYUREA 500 MG CAPSULE	9	19	525	1080
IBRANCE 125 MG CAPSULE	3	6	168	126
IMATINIB MESYLATE 100 MG TAB	1	2	60	60
IMATINIB MESYLATE 400 MG TAB	5	13	375	375
IMBRUVICA 140 MG CAPSULE	1	2	60	240
LENVIMA 18 MG DAILY DOSE	1	4	120	360
LETROZOLE 2.5 MG TABLET	33	74	1954	1846
LEUCOVORIN CALCIUM 25 MG TAB	1	3	84	12
LEUCOVORIN CALCIUM 5 MG TAB	5	14	356	208
LONSURF 15 MG-6.14 MG TABLET	1	1	28	40
LONSURF 20 MG-8.19 MG TABLET	1	1	28	40
LUPRON DEPOT 11.25 MG 3MO KIT	4	4	286	4
LUPRON DEPOT 22.5 MG 3MO KIT	1	1	90	1
LUPRON DEPOT 3.75 MG KIT	6	9	262	9
LUPRON DEPOT 45 MG 6MO KIT	3	3	213	3
MEGESTROL 20 MG TABLET	5	10	280	530
MEGESTROL 40 MG TABLET	9	15	419	879
MEGESTROL ACET 40 MG/ML SUSP	39	69	2004	18843
MERCAPTOPURINE 50 MG TABLET	12	31	831	1263
METHOTREXATE 2.5 MG TABLET	114	270	7562	6642
METHOTREXATE 250 MG/10 ML VIAL	1	1	30	10
METHOTREXATE 50 MG/2 ML VIAL	8	11	312	52
NERLYNX 40 MG TABLET	2	4	120	720
POMALYST 2 MG CAPSULE	1	3	84	63
SPRYCEL 100 MG TABLET	1	2	60	60
SUTENT 50 MG CAPSULE	1	1	42	21
TAMOXIFEN 10 MG TABLET	2	4	120	180
TAMOXIFEN 20 MG TABLET	38	90	2694	2634
TARCEVA 150 MG TABLET	1	3	90	90
TASIGNA 150 MG CAPSULE	2	7	196	784
TEMOZOLOMIDE 100 MG CAPSULE	1	2	56	15
TEMOZOLOMIDE 180 MG CAPSULE	1	1	5	5
TEMOZOLOMIDE 250 MG CAPSULE	1	2	56	10
TREXALL 5 MG TABLET	1	2	58	28
ZYDELIG 150 MG TABLET	1	1	15	30
Grand Total	**362**	**873**	**24578**	**42646**

Quarter Serviced	**1st Quarter 2018**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
AFINITOR 10 MG TABLET	1	3	90	90
AFINITOR 2.5 MG TABLET	1	2	60	60
AFINITOR 5 MG TABLET	1	3	90	90
ALECENSA 150 MG CAPSULE	1	1	30	240
ANASTROZOLE 1 MG TABLET	55	138	3574	2835

BICALUTAMIDE 50 MG TABLET	2	5	120	120
CAPECITABINE 150 MG TABLET	1	2	48	140
CAPECITABINE 500 MG TABLET	7	16	361	1276
CYCLOPHOSPHAMIDE 50 MG CAPSULE	1	1	30	30
EXEMESTANE 25 MG TABLET	12	27	720	720
FIRMAGON 2 X 120 MG KIT	1	1	28	2
HYDROXYUREA 500 MG CAPSULE	12	24	520	1052
IBRANCE 100 MG CAPSULE	1	2	56	42
IBRANCE 125 MG CAPSULE	3	7	196	147
IMATINIB MESYLATE 100 MG TAB	1	2	60	60
IMATINIB MESYLATE 400 MG TAB	6	15	435	435.002
IMBRUVICA 140 MG CAPSULE	1	4	60	180
LENVIMA 18 MG DAILY DOSE	1	3	90	270
LETROZOLE 2.5 MG TABLET	26	63	1729	1621
LEUCOVORIN CALCIUM 25 MG TAB	2	4	99	72
LEUCOVORIN CALCIUM 5 MG TAB	6	15	413	198
LONSURF 15 MG-6.14 MG TABLET	1	3	84	120
LONSURF 20 MG-8.19 MG TABLET	1	3	84	120
LUPRON DEPOT 11.25 MG 3MO KIT	6	6	348	6
LUPRON DEPOT 3.75 MG KIT	8	12	350	12
MEGESTROL 20 MG TABLET	7	9	270	450
MEGESTROL 40 MG TABLET	16	20	560	1075
MEGESTROL ACET 40 MG/ML SUSP	45	75	2075	17930
MERCAPTOPURINE 50 MG TABLET	12	26	757	1132
METHOTREXATE 2.5 MG TABLET	91	214	6083	5209
METHOTREXATE 250 MG/10 ML VIAL	1	1	30	10
METHOTREXATE 50 MG/2 ML VIAL	10	15	421	66
NERLYNX 40 MG TABLET	1	1	15	90
NEXAVAR 200 MG TABLET	1	4	60	240
POMALYST 2 MG CAPSULE	1	1	28	21
RYDAPT 25 MG CAPSULE	1	1	30	120
SPRYCEL 100 MG TABLET	2	6	165	165
TABLOID 40 MG TABLET	2	2	44	44
TAMOXIFEN 10 MG TABLET	2	7	150	420
TAMOXIFEN 20 MG TABLET	35	82	2488	2468
TARCEVA 150 MG TABLET	1	3	90	90
TASIGNA 150 MG CAPSULE	2	5	140	560
TEMOZOLOMIDE 100 MG CAPSULE	1	2	56	15
TEMOZOLOMIDE 250 MG CAPSULE	2	3	77	31
TREXALL 5 MG TABLET	1	1	30	24
VOTRIENT 200 MG TABLET	1	2	60	240
XALKORI 250 MG CAPSULE	1	1	30	60
Grand Total	**368**	**843**	**23334**	**40398.002**

Quarter Serviced	**2nd Quarter 2018**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
AFINITOR 10 MG TABLET	2	2	45	45
AFINITOR 5 MG TABLET	1	3	90	90
ALECENSA 150 MG CAPSULE	1	1	30	240
ANASTROZOLE 1 MG TABLET	53	136	3533	2696
BICALUTAMIDE 50 MG TABLET	5	12	255	255
CAPECITABINE 150 MG TABLET	1	1	21	28
CAPECITABINE 500 MG TABLET	6	13	272	1020
CYCLOPHOSPHAMIDE 50 MG CAPSULE	1	1	30	120
EXEMESTANE 25 MG TABLET	11	29	720	720
FIRMAGON 2 X 120 MG KIT	2	2	56	4

HYDROXYPROGESTERONE 1.25 G/5ML	1	1	28	5
HYDROXYUREA 500 MG CAPSULE	10	23	526	975
IBRANCE 100 MG CAPSULE	1	4	112	84
IBRANCE 125 MG CAPSULE	3	6	168	126
IMATINIB MESYLATE 100 MG TAB	1	2	60	60
IMATINIB MESYLATE 400 MG TAB	7	17	495	495
IMBRUVICA 140 MG CAPSULE	1	3	58	146
IMBRUVICA 420 MG TABLET	1	1	28	28
LENVIMA 18 MG DAILY DOSE	1	3	90	270
LETROZOLE 2.5 MG TABLET	29	78	1819	1777
LEUCOVORIN CALCIUM 10 MG TAB	1	1	2	12
LEUCOVORIN CALCIUM 25 MG TAB	2	6	174	27
LEUCOVORIN CALCIUM 5 MG TAB	5	14	412	188
LUPRON DEPOT 11.25 MG 3MO KIT	6	6	504	6
LUPRON DEPOT 22.5 MG 3MO KIT	1	1	30	1
LUPRON DEPOT 3.75 MG KIT	9	17	486	17
LUPRON DEPOT 45 MG 6MO KIT	1	1	30	1
MEGESTROL 20 MG TABLET	3	8	240	420
MEGESTROL 40 MG TABLET	11	22	560	1495
MEGESTROL ACET 40 MG/ML SUSP	43	75	2156	20870
MERCAPTOPURINE 50 MG TABLET	9	22	605	1072
METHOTREXATE 2.5 MG TABLET	102	235	6624	5581
METHOTREXATE 250 MG/10 ML VIAL	1	1	30	10
METHOTREXATE 50 MG/2 ML VIAL	13	17	471	68
NERLYNX 40 MG TABLET	2	4	75	450
NEXAVAR 200 MG TABLET	2	4	90	360
ODOMZO 200 MG CAPSULE	1	1	30	30
SPRYCEL 100 MG TABLET	2	4	105	105
TABLOID 40 MG TABLET	2	2	28	28
TAMOXIFEN 10 MG TABLET	3	9	195	510
TAMOXIFEN 20 MG TABLET	32	76	2280	2280
TARCEVA 150 MG TABLET	1	3	90	90
TASIGNA 150 MG CAPSULE	1	3	84	336
TEMOZOLOMIDE 140 MG CAPSULE	1	2	42	30
TEMOZOLOMIDE 5 MG CAPSULE	1	2	42	60
TRETINOIN 10 MG CAPSULE	1	1	15	112
TREXALL 5 MG TABLET	1	1	30	24
TREXALL 7.5 MG TABLET	1	1	28	4
VOTRIENT 200 MG TABLET	2	7	178	670
XALKORI 250 MG CAPSULE	1	1	30	60
Grand Total	**377**	**885**	**24102**	**44101**

Quarter Serviced	**3rd Quarter 2018**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
AFINITOR 10 MG TABLET	1	2	60	60
AFINITOR 5 MG TABLET	1	2	60	60
ALECENSA 150 MG CAPSULE	1	2	30	240
ANASTROZOLE 1 MG TABLET	50	122	2927	2256
BENDEKA 100 MG/4 ML VIAL	1	3	84	48
BICALUTAMIDE 50 MG TABLET	6	20	385	385
BOSULIF 400 MG TABLET	1	5	105	105
CAPECITABINE 150 MG TABLET	2	3	55	140
CAPECITABINE 500 MG TABLET	6	16	349	1352
CYCLOPHOSPHAMIDE 500 MG VIAL	3	4	112	22
DECITABINE 50 MG VIAL	1	2	56	10
ELIGARD 22.5 MG SYRINGE KIT	1	1	84	1

Anthem Oncology Utilization Q3 continued

ETOPOSIDE 50 MG CAPSULE	1	1	7	7
EXEMESTANE 25 MG TABLET	10	34	735	735
FIRMAGON 2 X 120 MG KIT	1	1	28	2
FLUTAMIDE 125 MG CAPSULE	1	1	15	15
GILOTRIF 20 MG TABLET	1	2	45	45
HYDROXYUREA 500 MG CAPSULE	13	30	657	1357
IBRANCE 100 MG CAPSULE	2	4	105	77
IBRANCE 125 MG CAPSULE	2	7	196	147
IMATINIB MESYLATE 100 MG TAB	1	2	60	60
IMATINIB MESYLATE 400 MG TAB	6	15	450	450
IMBRUVICA 140 MG CAPSULE	1	1	28	56
IMBRUVICA 420 MG TABLET	2	4	112	112
LENVIMA 18 MG DAILY DOSE	1	2	60	180
LETROZOLE 2.5 MG TABLET	27	72	1630	1560
LEUCOVORIN CALCIUM 25 MG TAB	1	3	84	12
LEUCOVORIN CALCIUM 5 MG TAB	5	11	326	125
LUPRON DEPOT 11.25 MG 3MO KIT	2	2	174	2
LUPRON DEPOT 3.75 MG KIT	6	11	320	11
MEGESTROL 20 MG TABLET	5	8	240	450
MEGESTROL 40 MG TABLET	11	17	494	1364
MEGESTROL ACET 40 MG/ML SUSP	52	91	2567	26879
MERCAPTOPURINE 50 MG TABLET	18	44	1126	1790
MESNEX 400 MG TABLET	2	2	6	32
METHOTREXATE 2.5 MG TABLET	100	241	6663	5713
METHOTREXATE 50 MG/2 ML VIAL	11	16	455	58
NERLYNX 40 MG TABLET	1	2	60	360
ODOMZO 200 MG CAPSULE	1	3	90	90
RITUXAN 10 MG/ML VIAL	1	3	84	240
SPRYCEL 100 MG TABLET	2	7	210	210
STIVARGA 40 MG TABLET	2	4	112	336
TABLOID 40 MG TABLET	1	1	14	42
TAMOXIFEN 10 MG TABLET	3	9	195	480
TAMOXIFEN 20 MG TABLET	33	82	2460	2460
TASIGNA 150 MG CAPSULE	1	3	84	336
TRETINOIN 10 MG CAPSULE	2	5	121	710
TREXALL 5 MG TABLET	1	3	86	74
TREXALL 7.5 MG TABLET	1	2	56	8
TRISENOX 12 MG/6 ML VIAL	1	2	56	240
VENCLEXTA STARTING PACK	1	1	28	42
VOTRIENT 200 MG TABLET	1	3	90	360
Grand Total	**381**	**934**	**24636**	**51906**

Anthem Afinitor, Ibrance, Sprycel Utilization

Afinitor

Month-Year	Distinct Count of Mbr ID	Claim Count	Sum of Total Days of Therapy	Sum of Total Quantity
Oct-2017	3	4	75	75
Nov-2017	2	3	90	90
Dec-2017	3	3	75	75
Jan-2018	3	3	90	90
Feb-2018	3	3	90	90
Mar-2018	2	2	60	60
Apr-2018	2	2	60	60
May-2018	1	1	30	30
Jun-2018	2	2	45	45
Jul-2018	2	2	60	60
Aug-2018	1	1	30	30
Sep-2018	1	1	30	30
Grand Total	**5**	**27**	**735**	**735**

Ibrance

Row Labels	Distinct Count of Mbr ID	Claim Count	Sum of Total Days of Therapy	Sum of Total Quantity
Oct-2017	1	1	28	21
Nov-2017	2	3	84	63
Dec-2017	2	2	56	42
Jan-2018	2	3	84	63
Feb-2018	3	3	84	63
Mar-2018	3	3	84	63
Apr-2018	3	3	84	63
May-2018	3	4	112	84
Jun-2018	3	3	84	63
Jul-2018	3	4	112	84
Aug-2018	3	3	84	63
Sep-2018	3	4	105	77
Grand Total	**4**	**36**	**1001**	**749**

Sprycel

Row Labels	Distinct Count of Mbr ID	Claim Count	Sum of Total Days of Therapy	Sum of Total Quantity
Oct-2017	1	1	30	30
Nov-2017	0	0	0	0
Dec-2017	1	1	30	30
Jan-2018	1	1	30	30
Feb-2018	2	3	75	75
Mar-2018	1	2	60	60

Anthem Afinitor, Ibrance, Sprycel Utilization continued

Apr-2018	1	1	30	30
May-2018	2	2	45	45
Jun-2018	1	1	30	30
Jul-2018	2	3	90	90
Aug-2018	2	3	90	90
Sep-2018	1	1	30	30
Grand Total	**3**	**19**	**540**	**540**

Grand Total	**12**	**82**	**2276**	**2024**

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
AFINITOR	**30**	**38**	**756**	**868**	**NA**
201710	0	0	0	0	NA
201711	2	2	42	42	NA
201712	3	3	56	56	NA
201801	3	5	84	84	NA
201802	3	4	70	70	NA
201803	1	2	28	28	NA
201804	2	3	56	56	NA
201805	4	5	98	112	NA
201806	3	4	84	112	NA
201807	3	3	70	84	NA
201808	4	5	112	168	NA
201809	2	2	56	56	NA
IBRANCE	**53**	**60**	**1,680**	**1,260**	**NA**
201710	6	6	168	126	NA
201711	7	9	252	189	NA
201712	2	2	56	42	NA
201801	3	4	112	84	NA
201802	5	6	168	126	NA
201803	4	4	112	84	NA
201804	4	4	112	84	NA
201805	4	5	140	105	NA
201806	4	4	112	84	NA
201807	5	6	168	126	NA
201808	4	4	112	84	NA
201809	5	6	168	126	NA

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
SPRYCEL	**41**	**45**	**1,260**	**2,040**	**NA**
201710	8	9	270	330	NA
201711	5	6	150	210	NA
201712	4	5	150	210	NA
201801	4	5	150	270	NA
201802	3	3	90	150	NA
201803	3	3	75	135	NA
201804	2	2	60	120	NA
201805	3	3	75	135	NA
201806	2	2	45	105	NA
201807	3	3	75	135	NA
201808	2	2	60	120	NA
201809	2	2	60	120	NA
Grand Total	**124**	**143**	**3,696**	**4,168**	**NA**

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
AFINITOR TAB 10MG	3	3	14	42
AFINITOR TAB 7.5MG	1	2	28	56
ANASTROZOLE TAB 1MG	108	229	135	5,529
BICALUTAMIDE TAB 50MG	6	16	58	474
BOSULIF TAB 100MG	1	1	15	60
BOSULIF TAB 500MG	1	3	30	90
CAPECITABINE TAB 150MG	2	9	35	504
CAPECITABINE TAB 500MG	10	26	93	2,390
CYCLOPHOSPH CAP 50MG	3	3	58	190
ERIVEDGE CAP 150MG	1	3	30	90
EXEMESTANE TAB 25MG	11	21	30	613
GILOTRIF TAB 30MG	1	3	30	90
HYDROXYUREA CAP 500MG	23	45	83	2,589
IBRANCE CAP 100MG	2	3	28	63
IBRANCE CAP 125MG	6	12	28	252
IBRANCE CAP 75MG	1	2	28	42
IMATINIB MES TAB 400MG	5	14	30	420
IMBRUVICA CAP 140MG	3	6	30	600
INTRON A INJ 10MU	2	5	42	16
LETROZOLE TAB 2.5MG	65	156	88	4,515
LEUCOVOR CA TAB 10MG	1	1	3	30
LEUCOVOR CA TAB 25MG	3	4	58	42
LEUCOVOR CA TAB 5MG	13	27	58	279
LUPRON DEPOT INJ 11.25MG	1	1	90	1
LUPRON DEPOT INJ 3.75MG	1	2	30	2
MEGESTROL AC SUS 40MG/ML	69	88	214	28,850
MEGESTROL AC TAB 20MG	11	18	35	725
MEGESTROL AC TAB 40MG	16	23	55	1,380
MEKINIST TAB 2MG	1	3	30	90
MERCAPTOPUR TAB 50MG	25	47	101	2,440
METHOTREXATE INJ 25MG/ML	11	19	145	154
METHOTREXATE INJ 50MG/2ML	5	9	58	52
METHOTREXATE TAB 2.5MG	294	567	238	14,439
NEXAVAR TAB 200MG	4	7	45	375
SPRYCEL TAB 100MG	3	6	30	180
SPRYCEL TAB 140MG	3	8	45	210
SPRYCEL TAB 20MG	1	3	30	270

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
SPRYCEL TAB 70MG	2	3	30	90
STIVARGA TAB 40MG	2	3	28	252
SUTENT CAP 50MG	1	2	28	56
TAFINLAR CAP 75MG	1	3	30	360
TAGRISSO TAB 40MG	1	3	30	90
TAMOXIFEN TAB 10MG	4	6	30	210
TAMOXIFEN TAB 20MG	53	116	30	3,480
TARCEVA TAB 100MG	1	3	30	90
TARCEVA TAB 150MG	2	5	30	150
TASIGNA CAP 150MG	6	17	42	1,624
TEMOZOLOMIDE CAP 100MG	2	4	33	20
TEMOZOLOMIDE CAP 140MG	1	1	5	10
TEMOZOLOMIDE CAP 180MG	1	3	28	30
TRETINOIN CAP 10MG	2	2	44	410
VENCLEXTA TAB 100MG	1	2	30	240
VOTRIENT TAB 200MG	1	3	15	180
XTANDI CAP 40MG	3	6	30	720
ZEJULA CAP 100MG	1	1	30	90
ZYTIGA TAB 250MG	1	3	30	360
Total	803	1,581	2,731	76,606

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
01/01/18 - 03/31/18 - Q1				
AFINITOR TAB 7.5MG	1	2	28	56
ANASTROZOLE TAB 1MG	106	232	230	5,826
BICALUTAMIDE TAB 50MG	11	24	58	714
BOSULIF TAB 100MG	1	1	15	60
CAPECITABINE TAB 150MG	7	14	63	770
CAPECITABINE TAB 500MG	17	32	63	2,920
CYCLOPHOSPH CAP 50MG	3	5	83	224
EXEMESTANE TAB 25MG	10	25	30	750
GILOTRIF TAB 30MG	1	3	30	90
HYDROXYUREA CAP 500MG	28	55	90	3,461
IBRANCE CAP 100MG	2	4	28	84
IBRANCE CAP 125MG	5	10	28	210
ICLUSIG TAB 45MG	1	2	30	60
IMATINIB MES TAB 400MG	7	17	30	540
IMBRUVICA CAP 140MG	4	9	30	840
JAKAFI TAB 10MG	1	3	30	180
LENVIMA CAP 14 MG	1	3	30	180
LETROZOLE TAB 2.5MG	58	124	89	3,621
LEUCOVOR CA TAB 25MG	2	5	28	20
LEUCOVOR CA TAB 5MG	10	21	58	216
LONSURF TAB 20-8.19	1	2	28	120
LUPRON DEPOT INJ 3.75MG	2	2	30	2
MEGESTROL AC SUS 40MG/ML	43	66	153	19,790
MEGESTROL AC TAB 20MG	7	14	55	560
MEGESTROL AC TAB 40MG	17	26	54	1,559
MEKINIST TAB 2MG	2	4	30	120
MERCAPTOPUR TAB 50MG	26	50	117	2,402
METHOTREXATE INJ 25MG/ML	9	14	174	132
METHOTREXATE INJ 50MG/2ML	7	13	104	52
METHOTREXATE TAB 2.5MG	273	522	193	13,398
NEXAVAR TAB 200MG	2	2	45	90
POMALYST CAP 4MG	1	1	28	21
SPRYCEL TAB 100MG	1	1	30	30
SPRYCEL TAB 140MG	2	5	30	150
SPRYCEL TAB 20MG	1	4	30	360
SPRYCEL TAB 50MG	1	1	15	15
SUTENT CAP 50MG	1	1	28	28

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
01/01/18 - 03/31/18 - Q1				
TABLOID TAB 40MG	1	1	14	12
TAFINLAR CAP 75MG	2	4	30	420
TAMOXIFEN TAB 10MG	2	2	30	60
TAMOXIFEN TAB 20MG	54	130	30	3,960
TARCEVA TAB 100MG	1	3	30	90
TARCEVA TAB 150MG	1	3	30	90
TASIGNA CAP 150MG	9	20	42	1,988
TASIGNA CAP 200MG	1	2	28	224
TRETINOIN CAP 10MG	1	1	28	112
VOTRIENT TAB 200MG	2	5	15	300
XTANDI CAP 40MG	2	4	30	480
Total	751	1,503	2,536	67,513

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
04/01/18 - 06/30/18 - Q2				
AFINITOR TAB 7.5MG	1	3	28	84
AFINITOR DIS TAB 3MG	1	3	14	84
ANASTROZOLE TAB 1MG	110	250	191	6,150
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	2,836
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	2,380
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	3,854
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	25,670
MEGESTROL AC TAB 20MG	7	11	30	480
MEGESTROL AC TAB 40MG	18	29	94	1,663
MEKINIST TAB 2MG	2	4	30	120
MERCAPTOPUR TAB 50MG	23	48	123	2,541
METHOTREXATE INJ 25MG/ML	14	18	175	72
METHOTREXATE INJ 50MG/2ML	8	11	79	60
METHOTREXATE TAB 2.5MG	279	551	240	13,487
NERLYNX TAB 40MG	1	1	30	180

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
04/01/18 - 06/30/18 - Q2				
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
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	4,032
TARCEVA TAB 100MG	2	5	45	120
TARCEVA TAB 150MG	2	6	45	120
TASIGNA CAP 150MG	8	20	35	1,904
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
Total	763	1,565	3,045	73,209

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/1/18 - 09/30/18 - Q3				
AFINITOR TAB 7.5MG	1	3	28	84
AFINITOR DIS TAB 3MG	1	3	28	84
ANASTROZOLE TAB 1MG	2	4	42	140
BICALUTAMIDE TAB 50MG	108	247	72	5,835
CAPECITABINE TAB 150MG	11	25	30	750
CAPECITABINE TAB 500MG	2	5	21	252
COTELLIC TAB 20MG	18	31	104	3,178
CYCLOPHOSPH CAP 50MG	1	1	28	63
ETOPOSIDE INJ 20MG/ML	3	5	30	270
EXEMESTANE TAB 25MG	1	1	11	26
HYDROXYUREA CAP 500MG	16	33	30	990
IBRANCE CAP 100MG	23	41	75	2,369
IBRANCE CAP 125MG	2	6	28	126
IBRANCE CAP 75MG	4	6	28	126
ICLUSIG TAB 45MG	1	4	28	84
IMATINIB MES TAB 400MG	1	2	30	60
IMBRUVICA CAP 140MG	5	13	30	405
IMBRUVICA TAB 420MG	1	1	30	120
IMBRUVICA TAB 560MG	3	4	28	112
JAKAFI TAB 10MG	2	3	28	84
JAKAFI TAB 5MG	1	1	30	60
KISQALI TAB 600DOSE	1	1	30	60
LENVIMA CAP 14 MG	2	3	28	189
LETROZOLE TAB 2.5MG	1	3	30	180
LEUCOVOR CA TAB 15MG	58	140	79	4,050
LEUCOVOR CA TAB 25MG	1	1	30	90
LEUCOVOR CA TAB 5MG	6	11	58	46
LONSURF TAB 15-6.14	8	19	79	281
LONSURF TAB 20-8.19	1	3	28	300
LUPRON DEPOT INJ 11.25MG	1	2	28	120
LUPRON DEPOT INJ 22.5MG	2	2	90	2
LUPRON DEPOT INJ 3.75MG	1	1	90	1
LYNPARZA TAB 150MG	2	4	30	4
MEGESTROL AC SUS 40MG/ML	2	5	30	600
MEGESTROL AC TAB 20MG	59	96	185	28,662
MEGESTROL AC TAB 40MG	7	9	44	283
MEKINIST TAB 2MG	21	35	76	2,206

Oncology (Oral) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/1/18 - 09/30/18 - Q3				
MERCAPTOPUR TAB 50MG	1	3	30	90
METHOTREXATE INJ 25MG/ML	22	46	77	2,438
METHOTREXATE INJ 50MG/2ML	18	30	218	162
METHOTREXATE TAB 2.5MG	12	17	110	72
NERLYNX TAB 40MG	285	547	252	13,509
NINLARO CAP 2.3MG	1	1	30	180
SPRYCEL TAB 140MG	1	2	28	6
SPRYCEL TAB 20MG	1	3	30	90
SPRYCEL TAB 50MG	1	3	30	270
STIVARGA TAB 40MG	1	1	15	15
SUTENT CAP 50MG	1	1	28	84
TABLOID TAB 40MG	2	4	29	59
TAFINLAR CAP 75MG	4	4	27	72
TAGRISSO TAB 80MG	1	3	30	360
TAMOXIFEN TAB 10MG	1	3	30	90
TAMOXIFEN TAB 20MG	1	1	30	60
TARCEVA TAB 100MG	52	121	51	3,678
TARCEVA TAB 150MG	1	4	30	120
TASIGNA CAP 150MG	1	3	15	45
TEMOZOLOMIDE CAP 140MG	8	21	28	2,100
TEMOZOLOMIDE CAP 180MG	2	4	49	20
TEMOZOLOMIDE CAP 20MG	1	1	28	5
TEMOZOLOMIDE CAP 5MG	1	1	21	5
TRETINOIN CAP 10MG	1	3	28	30
VENCLEXTA TAB 100MG	1	1	30	330
XTANDI CAP 40MG	2	4	30	360
ZELBORAF TAB 240MG	3	9	45	720
ZYTIGA TAB 250MG	1	1	28	224
ZYTIGA TAB 500MG	1	3	30	360
Total	810	1,621	3,131	77,966
Grand Total	**3,127**	**6,270**	**11,443**	**295,294**

Oncology Utilization

SilverSummit Healthplan

October 1, 2017 - September 30, 2018

Point of Sale Pharmcy Claims

Drug Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
AFINITOR	**1**	**2**	**60**	**60**	**$ 25,875.78**
201710	0	0	0	0	$ 0.00
201711	0	0	0	0	$ 0.00
201712	0	0	0	0	$ 0.00
201801	0	0	0	0	$ 0.00
201802	0	0	0	0	$ 0.00
201803	0	0	0	0	$ 0.00
201804	0	0	0	0	$ 0.00
201805	0	0	0	0	$ 0.00
201806	0	0	0	0	$ 0.00
201807	1	2	60	60	$ 25,875.78
201808	0	0	0	0	$ 0.00
201809	0	0	0	0	$ 0.00
IBRANCE	**0**	**0**	**0**	**0**	**$ 0.00**
201710	0	0	0	0	$ 0.00
201711	0	0	0	0	$ 0.00
201712	0	0	0	0	$ 0.00
201801	0	0	0	0	$ 0.00
201802	0	0	0	0	$ 0.00
201803	0	0	0	0	$ 0.00
201804	0	0	0	0	$ 0.00
201805	0	0	0	0	$ 0.00
201806	0	0	0	0	$ 0.00
201807	0	0	0	0	$ 0.00
201808	0	0	0	0	$ 0.00
201809	0	0	0	0	$ 0.00
SPRYCEL	**0**	**0**	**0**	**0**	**$ 0.00**
201710	0	0	0	0	$ 0.00
201711	0	0	0	0	$ 0.00
201712	0	0	0	0	$ 0.00
201801	0	0	0	0	$ 0.00
201802	0	0	0	0	$ 0.00
201803	0	0	0	0	$ 0.00
201804	0	0	0	0	$ 0.00
201805	0	0	0	0	$ 0.00
201806	0	0	0	0	$ 0.00
201807	0	0	0	0	$ 0.00
201808	0	0	0	0	$ 0.00
201809	0	0	0	0	$ 0.00
Grand Total	**1**	**2**	**60**	**60**	**$ 25,875.78**

Oncology Utilization – Q4 2017 – Q3 2018

SilverSummit Healthplan

Report Type	Report Date Range	Medication Name	Total Claims	Unique Members	Number of Units	Days Supply
Oncology Utilization	10/01/2017 - 09/30/2018	ANASTROZOLE TAB 1MG	126	35	2476	3674
Oncology Utilization	10/01/2017 - 09/30/2018	BICALUTAMIDE TAB 50MG	16	2	480	480
Oncology Utilization	10/01/2017 - 09/30/2018	CAPECITABINE TAB 150MG	4	4	232	92
Oncology Utilization	10/01/2017 - 09/30/2018	CAPECITABINE TAB 500MG	9	5	1020	228
Oncology Utilization	10/01/2017 - 09/30/2018	CYCLOPHOSPH CAP 50MG	3	1	30	69
Oncology Utilization	10/01/2017 - 09/30/2018	CYCLOPHOSPH INJ 500MG	1	1	2	21
Oncology Utilization	10/01/2017 - 09/30/2018	DOXORUBICIN INJ 50MG	1	1	50	21
Oncology Utilization	10/01/2017 - 09/30/2018	EXEMESTANE TAB 25MG	23	4	690	690
Oncology Utilization	10/01/2017 - 09/30/2018	HYDROXYUREA CAP 500MG	14	11	864	381
Oncology Utilization	10/01/2017 - 09/30/2018	IMATINIB MES TAB 400MG	4	2	120	120
Oncology Utilization	10/01/2017 - 09/30/2018	IMBRUVICA TAB 560MG	4	1	112	112
Oncology Utilization	10/01/2017 - 09/30/2018	LENVIMA CAP 20 MG	5	1	300	150
Oncology Utilization	10/01/2017 - 09/30/2018	LETROZOLE TAB 2.5MG	12	3	360	360
Oncology Utilization	10/01/2017 - 09/30/2018	LEUCOVOR CA TAB 5MG	4	1	16	112
Oncology Utilization	10/01/2017 - 09/30/2018	LONSURF TAB 15-6.14	2	1	80	56
Oncology Utilization	10/01/2017 - 09/30/2018	LONSURF TAB 20-8.19	3	2	140	84
Oncology Utilization	10/01/2017 - 09/30/2018	LUPRON DEPOT INJ 11.25MG	4	2	4	336
Oncology Utilization	10/01/2017 - 09/30/2018	LUPRON DEPOT INJ 3.75MG	5	2	5	140
Oncology Utilization	10/01/2017 - 09/30/2018	MEGESTROL AC SUS 40MG/ML	70	27	27660	1917
Oncology Utilization	10/01/2017 - 09/30/2018	MEGESTROL AC TAB 20MG	8	4	460	190
Oncology Utilization	10/01/2017 - 09/30/2018	MEGESTROL AC TAB 40MG	7	5	418	164

Oncology Utilization	10/01/2017 - 09/30/2018	MERCAPTOPUR TAB 50MG	10	3	387	237
Oncology Utilization	10/01/2017 - 09/30/2018	METHOTREXATE INJ 25MG/ML	15	5	72	414
Oncology Utilization	10/01/2017 - 09/30/2018	METHOTREXATE INJ 50MG/2ML	9	5	40	224
Oncology Utilization	10/01/2017 - 09/30/2018	METHOTREXATE TAB 2.5MG	189	57	4261	5297
Oncology Utilization	10/01/2017 - 09/30/2018	NEXAVAR TAB 200MG	1	1	120	30
Oncology Utilization	10/01/2017 - 09/30/2018	RITUXAN INJ 500MG	1	1	200	30
Oncology Utilization	10/01/2017 - 09/30/2018	SPRYCEL TAB 100MG	2	1	60	60
Oncology Utilization	10/01/2017 - 09/30/2018	SUTENT CAP 50MG	1	1	28	42
Oncology Utilization	10/01/2017 - 09/30/2018	TAGRISSO TAB 40MG	2	1	60	60
Oncology Utilization	10/01/2017 - 09/30/2018	TAGRISSO TAB 80MG	9	1	270	270
Oncology Utilization	10/01/2017 - 09/30/2018	TAMOXIFEN TAB 10MG	3	1	70	70
Oncology Utilization	10/01/2017 - 09/30/2018	TAMOXIFEN TAB 20MG	86	16	2580	2580
Oncology Utilization	10/01/2017 - 09/30/2018	TARCEVA TAB 150MG	3	1	90	90
Oncology Utilization	10/01/2017 - 09/30/2018	TASIGNA CAP 150MG	7	1	784	196
Oncology Utilization	10/01/2017 - 09/30/2018	TRETINOIN CAP 10MG	3	1	360	90
Oncology Utilization	10/01/2017 - 09/30/2018	TREXALL TAB 15MG	1	1	4	30
Oncology Utilization	10/01/2017 - 09/30/2018	TREXALL TAB 5MG	3	1	12	88
Oncology Utilization	10/01/2017 - 09/30/2018	VOTRIENT TAB 200MG	1	1	120	30
Oncology Utilization	10/01/2017 - 09/30/2018	XATMEP SOL 2.5MG/ML	2	1	24	56
Oncology Utilization	10/01/2017 - 09/30/2018	ZEJULA CAP 100MG	2	1	180	60
Oncology Utilization	10/01/2017 - 09/30/2018	ZYTIGA TAB 250MG	12	3	1440	360

INTRODUCTION

- Breast cancer is the most frequently diagnosed cancer globally and is the leading cause of cancer-related death in women. Long-term survival outcomes are related to disease stage at diagnosis *(National Comprehensive Cancer Network [NCCN] 2017)*.
  - Most patients presenting with localized disease will have long-term disease-free survival (*Rugo et al 2016*).
  - Systemic treatment of breast cancer recurrence or metastatic disease prolongs survival and quality of life, but is generally not curative. Treatments associated with minimal toxicity are preferred *(Rugo et al 2016, NCCN 2017).*
- Biologic markers such as hormone receptor (HR) status (estrogen receptor [ER] and progesterone receptor [PR] status), human epidermal growth factor receptor 2 (HER2) overexpression, and tumor burden have both prognostic and predictive value of treatment response. Treatment selection should be based upon these markers *(UpToDate 2017).*
- Chronic myelogenous leukemia (CML) is an uncommon type of cancer of the blood cells.
- Afinitor is a kinase inhibitor of mammalian target of rapamycin (mTOR), a serine-threonine kinase, downstream of the PI3K/AKT pathway.
- Ibrance is an inhibitor of cyclin-dependent kinases (CDK) 4 and 6.
- Sprycel is a kinase inhibitor for: BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGRFβ.

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Afinitor® (Everolimus)	–
Ibrance® (Palbociclib)	–
Sprycel® (Dasatinib)	–

(*Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Everolimus	Palbociclib	Dasatinib
Postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole.	X		
Adults with progressive neuroendocrine tumors of pancreatic origin (PNET) and adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic.	X		
Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.	X		
Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.	X		
Treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • an aromatase inhibitor as initial endocrine based therapy in postmenopausal women; or • fulvestrant in women with disease progression following endocrine therapy.		X	
Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.			X
Adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.			X
Adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.			X
Pediatric patients with Ph+ CML in chronic phase			X

(*Prescribing information: Afinitor 2018, Ibrance 2018, Sprycel 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 GUIDELINES

- **National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines: Breast Cancer (v2.2017)**
  - For initial treatment of postmenopausal patients with ER-positive, HER2-negative, recurrent or metastatic disease, NCCN recommends aromatase inhibitors (anastrozole or letrozole), serum ER modulators (tamoxifen or toremifene), selective ER down-regulator (fulvestrant), progestin, androgens, high-dose estrogen, or newer combination therapies (see Table 4 for a complete list of recommended regimens).
    - The combination of palbociclib or ribociclib with letrozole is included as a category 1, first-line endocrine therapy option for postmenopausal women with HR-positive, HER2-negative metastatic breast cancer.
    - The combination of palbociclib with fulvestrant is included as a category 1 option for premenopausal women receiving ovarian suppression or postmenopausal women with HR-positive, HER2-negative metastatic breast cancer who have progressed on endocrine therapy.
  - Women who respond to endocrine therapy should receive additional endocrine therapy at disease progression. Chemotherapy should be reserved for patients who have demonstrated no clinical benefit after 3 sequential endocrine therapy regimens or those with symptomatic visceral disease.

- **American Society of Clinical Oncology (ASCO) Clinical Practice Guideline: Endocrine Therapy for Hormone Receptor-Positive Metastatic Breast Cancer *(Rugo et al 2016)***
  - Sequential hormone therapy is the preferential treatment for most women with HR-positive metastatic breast cancer. Except in cases of immediately life-threatening disease, hormone therapy, alone or in combination, should be used as initial treatment.
  - For postmenopausal women, aromatase inhibitors are the preferred first-line treatment, with or without palbociclib.
  - Premenopausal women should be offered ovarian suppression or ablation and hormone therapy; current hormonal agents have not been studied in premenopausal women.
  - Fulvestrant plus palbociclib may be utilized in pre- or postmenopausal patients experiencing progression during prior treatment with aromatase inhibitors with or without 1 line of prior chemotherapy.
  - Sequential hormone therapy should be offered to patients with endocrine-responsive disease, except in the case of rapid progression with organ dysfunction; no specific order of agents is recommended.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Afinitor	Tablets: 2.5mg 5mg 7.5mg 10mg Disperz: 2mg 3mg 5mg	PO	Breast Cancer, NET, RCC: 10mg PO once daily	Also used for certain seizure disorders.
Ibrance	Capsules: 125mg 100mg 75mg	PO	125mg PO once daily	Taken with food. Given for 21 days followed by 7 days off treatment.
Sprycel	Tablets: 20mg 50mg 70mg 80mg 100mg 140mg	PO	Adults: Chronic Phase CML: Starting 100mg PO once daily Others: Starting 140mg PO once daily Pediatric: Based on body weight	Follow dose escalation per package insert. Tablets must be swallowed whole, do not crush, cut or chew. Adjustment necessary for Strong CYP3A4 Inducers and Inhibitors.

REFERENCES

- Ibrance [package insert], New York, NY: Pfizer; September 2018
- Afinitor [package insert], East Hanover, NJ: Novartis, April 2018
- Sprycel [package insert], Princeton, NJ: Bristol-Myers Squibb Company; November 2018
- Rugo HS, Rumble RB, Macrae E, et al. Endocrine therapy for hormone receptor-positive metastatic breast cancer: American Society of Clinical Oncology Guideline. *J Clin Oncol*. 2016; 34:3069-103.
- National Comprehensive Cancer Network Clinical Practice Guideline: Breast Cancer (v.2.2017). http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed April 11, 2017.

Prior Authorization Guideline

Guideline Name Short-Acting Bronchodilators

1 . Indications

Drug Name: Proventil HFA, ProAir HFA, ProAir RespiClick, Ventolin HFA (albuterol sulfate inhalation aerosol) or albuterol nebulizer solution.

Indications

Bronchospasm Indicated in adults and children 4 years of age and older for the treatment or prevention of bronchospasm with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm.

2 . Criteria

Product Name: Proventil HFA, ProAir HFA, ProAir RespiClick, Ventolin HFA, Albuterol nebulizer solution

Approval Length	12 months
Guideline Type	Quantity Limit

Approval Criteria

Quantity Limit:

Albuterol Metered Dose Inhalers (MDI): Two units per month
Albuterol Nebulizer Solution: 3 bottles of 20ml each or 125 nebulizer units per month.

1. **To exceed the quantity, all of the following must be met:**

a. Member has a diagnosis of asthma

AND

b. Member has been assessed for causes of asthma and external triggers have been removed or reduced where possible.

AND

c. Member has been trained on appropriate use of short-acting inhaler or nebulizer.

AND

d. Member is currently also receiving maximally tolerated long-acting medications (inhaled corticosteroids, inhaled antimuscarinics or long-acting beta agonists) or has been assessed and treatment is not appropriate.

OR

2. To exceed the quantity, all of the following must be met:

a. Member has a diagnosis of asthma

AND

b. Member is 18 years of age or under and requires an additional inhaler unit for school or equivalent program.

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Short-Acting Bronchodilators

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Anthem agrees with the criteria to exceed the quantity limit; however Anthem has preferred and nonpreferred products in the category and proposes this criteria be added for nonpreferred products:

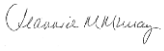
I. Individual has had a trial and inadequate response or intolerance to one preferred agent;

OR II. If all dry powder inhalers (DPIs)^ are designated non-preferred agents, the requested agent may be approved for individuals who lack effective hand-breath coordination

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Short-Acting Bronchodilators

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

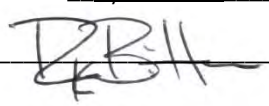
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

HPN feels the criteria is uneeded per existing processes. HPN reviews all requests for exceptions for quantity limitations against the FDA label and published compendia resources such as DrugDex by Micromedex to ensure clinical support for the increased dose.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Ryan Bitton

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Short-Acting Bronchodilators

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: _____Tom Beranek_____

Signature of individual completing this form: Tom Beranek _____

Short-Acting Beta Agonists

Summary of Utilization

October 1, 2017 - September 30, 2018

Fee for Service Medicaid

Drug Name	Count of Members	Count of Claims	Claims per member	Sum of Days	Sum of Qty	Sum of Amt Paid
PROVENTIL AER HFA	14,335	41,694	3	1,031,865	321,747	$ 3,971,773.85
ALBUTEROL NEB 0.083%	7,371	15,702	2	252,575	2,919,372	$ 231,880.05
VENTOLIN HFA AER	3,144	9,651	3	246,796	198,966	$ 125,149.46
PROAIR HFA AER	1,167	3,556	3	92,342	35,692	$ 146,777.54
ALBUTEROL NEB 0.5%	986	1,221	1	2,874	6,354	$ 4,471.47
ALBUTEROL NEB 0.63MG/3	372	676	2	11,296	119,727	$ 34,226.71
ALBUTEROL NEB 1.25MG/3	443	653	1	9,407	100,746	$ 30,323.34
LEVALBUTEROL NEB 0.63MG	158	475	3	7,368	78,873	$ 30,679.27
LEVALBUTEROL AER 45/ACT	79	313	4	7,860	6,105	$ 21,284.63
XOPENEX HFA AER	51	191	4	5,678	3,585	$ 11,504.29
LEVALBUTEROL NEB 1.25MG	40	150	4	2,946	31,407	$ 9,076.33
PROAIR RESPI AER	29	86	3	2,253	108	$ 3,883.91
XOPENEX NEB 0.63MG	10	38	4	567	5,688	$ 18,624.76
XOPENEX NEB 1.25/3ML	10	23	2	455	5,130	$ 8,352.67
LEVALBUTEROL NEB 0.31MG	9	14	2	317	2,376	$ 1,086.93
ALBUTEROL TAB 4MG ER	5	12	2	880	1,770	$ 1,688.14
LEVALBUTEROL NEB 1.25/0.5	7	9	1	24	96	$ 35.91
XOPENEX CONC NEB 1.25/0.5	7	8	1	8	11	$ 57.65
XOPENEX NEB 0.31MG	1	1	1	1	3	$ 3.00

Short-Acting Beta Agonists

Count of Members and Claims per year
October 1, 2017 - September 30, 2018
Fee for Service Medicaid

Drug Name	Count of Members
1 Claim	
ALBUTEROL NEB 0.083%	4,453
ALBUTEROL NEB 0.5%	842
ALBUTEROL NEB 0.63MG/3	267
ALBUTEROL NEB 1.25MG/3	351
ALBUTEROL SYP 2MG/5ML	89
ALBUTEROL TAB 2MG	2
ALBUTEROL TAB 4MG	10
ALBUTEROL TAB 4MG ER	1
LEVALBUTEROL AER 45/ACT	25
LEVALBUTEROL NEB 0.31MG	6
LEVALBUTEROL NEB 0.63MG	73
LEVALBUTEROL NEB 1.25/0.5	6
LEVALBUTEROL NEB 1.25MG	13
PROAIR HFA AER	562
PROAIR RESPI AER	17
PROVENTIL AER HFA	6,917
VENTOLIN HFA AER	1,401
XOPENEX NEB 0.31MG	1
XOPENEX NEB 0.63MG	2
XOPENEX NEB 1.25/3ML	6
XOPENEX CONC NEB 1.25/0.5	6
XOPENEX HFA AER	9
2-5 Claims	
ALBUTEROL NEB 0.083%	2,380
ALBUTEROL NEB 0.5%	139
ALBUTEROL NEB 0.63MG/3	85
ALBUTEROL NEB 1.25MG/3	81
ALBUTEROL SYP 2MG/5ML	16
ALBUTEROL TAB 2MG	2
ALBUTEROL TAB 4MG	7
ALBUTEROL TAB 4MG ER	4
LEVALBUTEROL AER 45/ACT	35
LEVALBUTEROL NEB 0.31MG	3
LEVALBUTEROL NEB 0.63MG	65
LEVALBUTEROL NEB 1.25/0.5	1
LEVALBUTEROL NEB 1.25MG	20
PROAIR HFA AER	416
PROAIR RESPI AER	7
PROVENTIL AER HFA	5,311
VENTOLIN HFA AER	1,229
XOPENEX NEB 0.63MG	7
XOPENEX NEB 1.25/3ML	4
XOPENEX CONC NEB 1.25/0.5	1

XOPENEX HFA AER	31
6-12 Claims	
ALBUTEROL NEB 0.083%	479
ALBUTEROL NEB 0.5%	5
ALBUTEROL NEB 0.63MG/3	17
ALBUTEROL NEB 1.25MG/3	10
ALBUTEROL TAB 2MG	4
ALBUTEROL TAB 4MG	1
LEVALBUTEROL AER 45/ACT	14
LEVALBUTEROL NEB 0.63MG	15
LEVALBUTEROL NEB 1.25MG	4
PROAIR HFA AER	155
PROAIR RESPI AER	3
PROVENTIL AER HFA	1,820
VENTOLIN HFA AER	462
XOPENEX NEB 0.63MG	1
XOPENEX HFA AER	10
>12 Claims	
ALBUTEROL NEB 0.083%	59
ALBUTEROL NEB 0.63MG/3	3
ALBUTEROL NEB 1.25MG/3	1
LEVALBUTEROL AER 45/ACT	5
LEVALBUTEROL NEB 0.63MG	5
LEVALBUTEROL NEB 1.25MG	3
PROAIR HFA AER	34
PROAIR RESPI AER	2
PROVENTIL AER HFA	287
VENTOLIN HFA AER	52
XOPENEX HFA AER	1
Grand Total	**28,355**

Anthem SABA Utilization

Quarter Serviced	**4th Quarter 2017**			
Row Labels	**Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
ALBUTEROL 2.5 MG/0.5 ML SOL	10	10	97	345
ALBUTEROL 5 MG/ML SOLUTION	4	4	80	80
ALBUTEROL SUL 0.63 MG/3 ML SOL	173	173	2556	23880
ALBUTEROL SUL 1.25 MG/3 ML SOL	252	252	3459	33720
ALBUTEROL SUL 2.5 MG/3 ML SOLN	4814	4814	79795	707543
ALBUTEROL SULF 2 MG/5 ML SYRUP	135	135	1848	20215
ALBUTEROL SULFATE 2 MG TAB	2	2	9	32
ALBUTEROL SULFATE 4 MG TAB	2	2	33	36
ALBUTEROL SULFATE ER 4 MG TAB	3	3	90	180
LEVALBUTEROL 0.31 MG/3 ML SOL	2	2	16	144
LEVALBUTEROL 0.63 MG/3 ML SOL	15	15	359	2448
LEVALBUTEROL 1.25 MG/3 ML SOL	7	7	210	1368
LEVALBUTEROL CONC 1.25 MG/0.5	1	1	10	30
LEVALBUTEROL TAR HFA 45MCG INH	28	28	716	465
PROAIR HFA 90 MCG INHALER	108	108	2388	935
PROAIR RESPICLICK INHAL POWDER	5	5	112	5
PROVENTIL HFA 90 MCG INHALER	36	36	789	241.2
VENTOLIN HFA 90 MCG INHALER	10425	10425	224047	190628
XOPENEX 1.25 MG/3 ML SOLUTION	2	2	48	432
XOPENEX HFA 45 MCG INHALER	3	3	48	45
Grand Total	**16027**	**16027**	**316710**	**982772.2**

Quarter Serviced	**1st Quarter 2018**			
Row Labels	**Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
ALBUTEROL 2.5 MG/0.5 ML SOL	6	6	82	270
ALBUTEROL 5 MG/ML SOLUTION	5	5	110	220
ALBUTEROL SUL 0.63 MG/3 ML SOL	261	261	3620	30555
ALBUTEROL SUL 1.25 MG/3 ML SOL	353	353	5406	47970
ALBUTEROL SUL 2.5 MG/3 ML SOLN	5781	5781	95874	832448
ALBUTEROL SULF 2 MG/5 ML SYRUP	141	141	1855	21544
ALBUTEROL SULFATE 2 MG TAB	3	3	23	79
ALBUTEROL SULFATE 4 MG TAB	2	2	13	36
ALBUTEROL SULFATE ER 4 MG TAB	4	4	120	240
LEVALBUTEROL 0.31 MG/3 ML SOL	3	3	42	216
LEVALBUTEROL 0.63 MG/3 ML SOL	11	11	166	1152
LEVALBUTEROL 1.25 MG/3 ML SOL	6	6	140	1152
LEVALBUTEROL TAR HFA 45MCG INH	24	24	597	375
PROAIR HFA 90 MCG INHALER	143	143	3151	1241
PROAIR RESPICLICK INHAL POWDER	4	4	115	4
PROVENTIL HFA 90 MCG INHALER	60	60	1299	402
VENTOLIN HFA 90 MCG INHALER	11146	11146	240786	203498
XOPENEX 1.25 MG/3 ML SOLUTION	1	1	24	216
XOPENEX HFA 45 MCG INHALER	4	4	78	60

Grand Total	**17958**	**17958**	**353501**	**1141678**

Anthem SABA Utilization **2nd Quarter 2018**
Quarter Serviced

Row Labels	Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
ALBUTEROL 2.5 MG/0.5 ML SOL	3	3	37	90
ALBUTEROL 5 MG/ML SOLUTION	2	2	30	40
ALBUTEROL SUL 0.63 MG/3 ML SOL	150	150	2359	18960
ALBUTEROL SUL 1.25 MG/3 ML SOL	206	206	3117	27045
ALBUTEROL SUL 2.5 MG/3 ML SOLN	3269	3269	56730	490672
ALBUTEROL SULF 2 MG/5 ML SYRUP	50	50	712	7994
ALBUTEROL SULFATE 4 MG TAB	2	2	60	120
ALBUTEROL SULFATE ER 4 MG TAB	4	4	97	194
LEVALBUTEROL 0.63 MG/3 ML SOL	10	10	221	1464
LEVALBUTEROL 1.25 MG/3 ML SOL	2	2	40	360
LEVALBUTEROL TAR HFA 45MCG INH	31	31	756	525
PROAIR HFA 90 MCG INHALER	108	108	2414	926.5
PROAIR RESPICLICK INHAL POWDER	5	5	135	5
PROVENTIL HFA 90 MCG INHALER	34	34	808	227.8
VENTOLIN HFA 90 MCG INHALER	9515	9515	206903	173570
XOPENEX HFA 45 MCG INHALER	1	1	16	15
Grand Total	**13392**	**13392**	**274435**	**722208.3**

Quarter Serviced **3rd Quarter 2018**

Row Labels	Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
ALBUTEROL 2.5 MG/0.5 ML SOL	5	5	110	345
ALBUTEROL 5 MG/ML SOLUTION	2	2	20	40
ALBUTEROL SUL 0.63 MG/3 ML SOL	104	104	1679	13395
ALBUTEROL SUL 1.25 MG/3 ML SOL	162	162	2672	22050
ALBUTEROL SUL 2.5 MG/3 ML SOLN	2701	2701	47538	419148
ALBUTEROL SULF 2 MG/5 ML SYRUP	38	38	481	6328
ALBUTEROL SULFATE 2 MG TAB	1	1	14	56
ALBUTEROL SULFATE 4 MG TAB	3	3	90	180
ALBUTEROL SULFATE ER 4 MG TAB	3	3	90	180
LEVALBUTEROL 1.25 MG/3 ML SOL	1	1	30	21
LEVALBUTEROL TAR HFA 45MCG INH	26	26	585	420
PROAIR HFA 90 MCG INHALER	157	157	3536	1360
PROAIR RESPICLICK INHAL POWDER	13	13	327	13
PROVENTIL HFA 90 MCG INHALER	61	61	1394	408.7
VENTOLIN HFA 90 MCG INHALER	9073	9073	199311	166578
XOPENEX HFA 45 MCG INHALER	2	2	46	30
Grand Total	**12352**	**12352**	**257923**	**630552.7**

Short-Acting Beta Agonists HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
ALBUTEROL NEB 0.083%	5,749	6,467	498	1,187,121
ALBUTEROL NEB 0.5%	26	30	123	1,050
ALBUTEROL NEB 0.63MG/3	214	220	300	28,500
ALBUTEROL NEB 1.25MG/3	349	367	371	52,800
ALBUTEROL SYP 2MG/5ML	182	192	316	28,822
ALBUTEROL TAB 2MG	1	1	30	90
ALBUTEROL TAB 4MG	1	3	30	360
ALBUTEROL TAB 4MG ER	1	2	30	240
ALBUTEROL TAB 8MG ER	1	1	30	60
LEVALBUTEROL AER 45/ACT	26	38	151	645
LEVALBUTEROL NEB 0.63MG	9	9	79	1,737
LEVALBUTEROL NEB 1.25/0.5	1	1	30	90
LEVALBUTEROL NEB 1.25MG	6	7	79	801
PROAIR HFA AER	308	355	355	3,222
PROAIR RESPI AER	6	7	92	7
PROVENTIL AER HFA	78	95	153	670
VENTOLIN HFA AER	12,740	17,951	438	348,714
XOPENEX HFA AER	5	9	35	135
Total	19,703	25,755	3,140	1,655,064
01/01/18 - 03/31/18 - Q1				
ALBUTEROL NEB 0.083%	6,988	7,802	561	1,375,977
ALBUTEROL NEB 0.5%	24	30	98	1,250
ALBUTEROL NEB 0.63MG/3	268	281	287	35,415
ALBUTEROL NEB 1.25MG/3	578	611	397	80,430
ALBUTEROL SYP 2MG/5ML	190	199	269	26,487
LEVALBUTEROL AER 45/ACT	24	37	163	630
LEVALBUTEROL NEB 0.31MG	3	4	28	288
LEVALBUTEROL NEB 0.63MG	14	15	101	2,046
LEVALBUTEROL NEB 1.25MG	10	14	124	2,133
PROAIR HFA AER	318	354	283	3,171
PROAIR RESPI AER	10	11	68	11
PROVENTIL AER HFA	127	154	212	1,065
VENTOLIN HFA AER	13,535	18,794	546	358,280
XOPENEX HFA AER	4	8	65	120
Total	22,093	28,314	3,202	1,887,303

Short-Acting Beta Agonists HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
04/01/18 - 06/30/18 - Q2				
ALBUTEROL NEB 0.083%	3,933	4,578	496	850,488
ALBUTEROL NEB 0.5%	30	34	132	1,190
ALBUTEROL NEB 0.63MG/3	144	150	294	19,110
ALBUTEROL NEB 1.25MG/3	231	247	349	36,780
ALBUTEROL SYP 2MG/5ML	79	82	226	10,361
ALBUTEROL TAB 4MG	2	2	40	150
LEVALBUTEROL AER 45/ACT	26	45	169	705
LEVALBUTEROL NEB 0.31MG	2	2	13	144
LEVALBUTEROL NEB 0.63MG	7	7	101	1,017
LEVALBUTEROL NEB 1.25MG	10	16	79	2,229
PROAIR HFA AER	239	282	344	2,516
PROAIR RESPI AER	10	10	71	10
PROVENTIL AER HFA	83	108	133	744
VENTOLIN HFA AER	10,963	16,029	564	304,982
XOPENEX HFA AER	4	9	50	135
Total	15,763	21,601	3,061	1,230,561
07/01/18 - 09/30/18 - Q3				
ALBUTEROL NEB 0.083%	3,319	3,872	527	703,536
ALBUTEROL NEB 0.5%	30	34	88	1,197
ALBUTEROL NEB 0.63MG/3	82	85	234	12,390
ALBUTEROL NEB 1.25MG/3	155	178	285	23,250
ALBUTEROL SYP 2MG/5ML	59	60	178	7,580
ALBUTEROL TAB 4MG	2	2	33	129
ALBUTEROL TAB 8MG ER	1	1	30	60
LEVALBUTEROL AER 45/ACT	21	30	148	525
LEVALBUTEROL NEB 0.63MG	8	9	78	1,107
LEVALBUTEROL NEB 1.25MG	7	9	82	1,113
PROAIR HFA AER	252	309	326	2,771
PROAIR RESPI AER	10	10	102	11
PROVENTIL AER HFA	101	126	223	871
VENTOLIN HFA AER	10,398	15,188	615	290,970
XOPENEX HFA AER	4	10	55	150
Total	14,449	19,923	3,004	1,045,660
Grand Total	72,008	95,593	12,407	5,818,587

Short-acting Beta Agonists Utilization – Q4 2017 – Q3 2018

Silversummit Healthplan

Report Date Range	Medication Name	Total Claims	Unique Members	Number of Units	Days Supply
10/01/2017 - 09/30/2018	ALBUTEROL NEB 0.083%	2199	1420	378960	37133
10/01/2017 - 09/30/2018	ALBUTEROL NEB 0.5%	17	15	540	311
10/01/2017 - 09/30/2018	ALBUTEROL NEB 0.63MG/3	142	100	20640	2329
10/01/2017 - 09/30/2018	ALBUTEROL NEB 1.25MG/3	158	129	23467	2687
10/01/2017 - 09/30/2018	ALBUTEROL SYP 2MG/5ML	38	26	4575	384
10/01/2017 - 09/30/2018	ALBUTEROL TAB 2MG	1	1	15	5
10/01/2017 - 09/30/2018	LEVALBUTEROL AER 45/ACT	26	17	405	456
10/01/2017 - 09/30/2018	LEVALBUTEROL NEB 0.31MG	1	1	72	8
10/01/2017 - 09/30/2018	LEVALBUTEROL NEB 0.63MG	16	13	2604	299
10/01/2017 - 09/30/2018	LEVALBUTEROL NEB 1.25MG	12	7	2802	283
10/01/2017 - 09/30/2018	PROAIR HFA AER	667	531	6018.5	14825
10/01/2017 - 09/30/2018	PROAIR RESPI AER	25	20	26	569

Short-acting Beta Agonists Utilization – Q4 2017 – Q3 2018

SilverSummit Healthplan

Report Date Range	Medication Name	Total Claims	Unique Members	Number of Units	Days Supply
10/01/2017 - 09/30/2018	PROVENTIL AER HFA	374	275	2659.9	8253
10/01/2017 - 09/30/2018	VENTOLIN HFA AER	7272	3541	130973.2	156566
10/01/2017 - 09/30/2018	XOPENEX HFA AER	1	1	15	30

The following page contains current
Medicaid Services Manual (MSM) Chapter 1200
Criteria for short-acting beta agonists

U. Xopenex® (Levalbuterol)

Therapeutic Class: Beta Adrenergic Agents
Last Reviewed by the DUR Board: July 26, 2012

Xopenex® is 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. Authorization only for recipients experiencing side effects on one other beta-adrenergic agent of any formulation.

   b. Authorization for patients whose cardiovascular status is considered to be in severe deteriorating condition.

2. Prior Authorization Guidelines

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

Therapeutic Class Overview
Inhaled Beta-Agonists

INTRODUCTION

- Respiratory beta$_2$-agonists are primarily used to treat reversible airway disease. They are Food and Drug Administration (FDA)-approved for the treatment of asthma, chronic obstructive pulmonary disease (COPD), exercise-induced asthma/bronchospasm, and/or reversible bronchospasm.
- Asthma is a chronic lung disease that inflames and narrows the airways, making it difficult to breathe. Asthma causes recurring periods of wheezing, chest tightness, shortness of breath, and coughing. Asthma affects people of all ages, but most often starts during childhood. In the United States, more than 25 million people are known to have asthma, including about 7 million children. The exact cause(s) of asthma are unknown. A combination of factors such as genetics, certain respiratory infections during childhood, and contact with airborne allergens can contribute to its development. Most patients with asthma have allergies (*National Heart, Lung, and Blood Institute [NHLBI] 2014*).
  - Current pharmacologic options for asthma management are categorized as: (1) long-term control medications to achieve and maintain control of persistent asthma, and (2) quick-relief medications used to treat acute symptoms and exacerbations.
  - Long-term control medications for asthma include (*NHLBI 2007*):
    - Corticosteroids (inhaled corticosteroids [ICSs] for long-term control; short courses of oral corticosteroids to gain prompt control of disease, long-term oral corticosteroids for severe persistent asthma)
    - Cromolyn sodium and nedocromil
    - Immunomodulators (ie, omalizumab)
    - Leukotriene modulators
    - Long-acting beta$_2$-agonists (LABAs)
    - Methylxanthines (ie, theophylline)
  - Quick-relief medications for asthma include (*NHLBI 2007*):
    - Anticholinergics (ie, ipratropium bromide), as an alternative bronchodilator for those not tolerating a short-acting beta$_2$-agonist (SABA)
    - SABAs (therapy of choice for relief of acute symptoms and prevention of exercise-induced bronchospasm)
    - Systemic corticosteroids (not short-acting, but used for moderate and severe exacerbations)
  - In recent years, additional medications have been made available for select subsets of patients with asthma, including the interleukin-5 (IL-5) antagonists benralizumab, mepolizumab, and reslizumab for the management of severe asthma with an eosinophilic phenotype (*Prescribing information: Cinqair 2016, Fasenra 2017, Nucala 2017*). Additionally, tiotropium, long used for COPD, has been FDA-approved for the treatment of asthma (*Spiriva Respimat prescribing information 2017*).
  - ICSs are the most effective, most commonly recommended long-term control medications used for the treatment of asthma. The LABAs should not be used as monotherapy for the management of asthma due to increased risk for serious adverse events, including death. However, they are effective adjunctive therapy in patients who are not adequately controlled with an ICS alone. Theophylline and mast-cell stabilizers have weak to low efficacy in asthma. Theophylline has an unfavorable side-effect profile and may be life-threatening at high doses. Mast-cell stabilizers have a more favorable safety profile. Tiotropium is an option for add-on therapy in patients ≥ 12 years old with a history of exacerbations. An IL-5 antagonist or the immunoglobulin E (IgE) antagonist, omalizumab, may be added if patients require a higher level of care. Omalizumab is used in patients with moderate to severe allergic asthma while IL-5 antagonists are used for severe eosinophilic asthma. SABAs are the medication of choice for the relief of bronchospasm during acute exacerbations of asthma (*Fasenra prescribing information 2017, NHLBI 2007, Global Initiative for Asthma [GINA] 2018*).
- COPD is characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities. The abnormalities are usually caused by exposure to noxious particles or gases. Airflow limitation is caused by a combination of small airway disease (eg, obstructive bronchiolitis) and parenchymal destruction (emphysema); the relative contributions of each component vary between patients. The most common symptoms of COPD include dyspnea, cough, and sputum production (*Global Initiative for Chronic Obstructive Lung Disease [GOLD] 2018*).

- COPD affects 6.4% of the United States (U.S.) population and is the major contributor to mortality from chronic lower respiratory diseases, the third leading cause of death in the U.S. (*Centers for Disease Control and Prevention 2017*). Globally, COPD is the fourth leading cause of death and is expected to be the third leading cause of death by 2020; the burden of COPD continues to increase due to continued exposure to risk factors and aging of the population (*GOLD 2018*).
- Cigarette smoking is the main risk factor for COPD; other risk factors include biomass fuel exposure (such as from cooking and heating in poorly ventilated dwellings) and air pollution. Host factors such as genetic abnormalities, abnormal lung development, and accelerated aging can predispose individuals to COPD development (*GOLD 2018*).
- Patients with COPD may experience exacerbations, which are periods of acute worsening of respiratory symptoms (*GOLD 2018*).
- Pharmacologic therapy for COPD can reduce symptoms, reduce the frequency and severity of exacerbations, and improve patients' health status and exercise tolerance. There is no conclusive evidence that COPD medications modify the long-term decline in lung function characteristics of COPD (*GOLD 2018*).
- Pharmacologic options for COPD treatment comprise several classes, including beta$_2$-agonists, anticholinergics, methylxanthines, ICSs, various combination products, and the phosphodiesterase (PDE)-4 inhibitor, roflumilast. Pharmacologic treatments should be individualized based on symptom severity, risk of exacerbations, side effects, comorbidities, drug availability, and cost, as well as the patient's response, preference, and ability to use various drug delivery devices (*GOLD 2018*).
- Inhaled bronchodilators are central to COPD symptom management, and are usually given on a regular basis to prevent or reduce symptoms. Several long-acting inhaled bronchodilators are available, and use of short-acting bronchodilators on a regular basis is not generally recommended (*GOLD 2018*).
- Beta$_2$-agonists differ in their dosing requirements, pharmacokinetic parameters, and potential adverse effects. Several of the SABAs are available generically in at least 1 strength or formulation; however, there are no generic formulations for the LABAs.

- This review includes the single-agent inhaled and oral beta$_2$-agonists. Although several agents are also available in combination inhalers along with an ICS or an anticholinergic, the combination products are not included in this review.
  - Tables in this review are organized by whether the drug product is short- or long-acting. Note that extended-release albuterol is categorized as short-acting for the purposes of this review, along with the other albuterol products.
- Medispan class/subclass: Sympathomimetics/Beta Adrenergics

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Short-acting beta$_2$-agonists (oral and inhaled)	
albuterol inhalation aerosols and powder (ProAir HFA, ProAir RespiClick dry powder inhaler, Proventil HFA, Ventolin HFA)	-
albuterol solution for nebulization	✔
albuterol, oral tablets, extended-release tablets, and syrup	✔
levalbuterol inhalation aerosol (Xopenex HFA and generic)	-*
levalbuterol solution for nebulization (Xopenex and generics)	✔
metaproterenol, oral tablets and syrup	✔
terbutaline, oral tablets and injection	✔
Long-acting beta$_2$-agonists (inhaled)	
Arcapta Neohaler (indacaterol) inhalation powder	-
Brovana (arformoterol) solution for nebulization	-
Perforomist (formoterol) solution for nebulization†	-
Serevent Diskus (salmeterol) inhalation powder	-
Striverdi Respimat (olodaterol) inhalation spray	-

Abbreviations: HFA = hydrofluoroalkane
*No A-rated generics have been approved by the FDA; however, an authorized generic is available.
†Formoterol was previously available as a dry powder inhaler (Foradil Aerolizer); however, this formulation is no longer marketed.
(*Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Generic Name	Treatment and/or prevention of bronchospasm in patients with asthma/reversible obstructive airway disease	Prevention of exercise-induced bronchospasm	Maintenance treatment of bronchoconstriction/ airflow obstruction in patients with COPD	Treatment of reversible bronchospasm occurring in association with emphysema and bronchitis
Short-acting beta$_2$-agonists				
albuterol	✔ *	✔ *†		
levalbuterol	✔ ‡			
metaproterenol	✔			✔
terbutaline	✔ §			✔ §
Long-acting beta$_2$-agonists				
arformoterol			✔	
formoterol			✔	
indacaterol			✔ **	
olodaterol			✔ **	
salmeterol	✔ ‖ ¶	✔ ¶	✔	

Abbreviations: COPD = chronic obstructive pulmonary disease; HFA = hydrofluoroalkane
*Age ≥ 4 years (HFA inhalation aerosols and dry power inhaler); age ≥ 2 (solution for nebulization); age ≥ 2 years (syrup); age ≥ 6 years (tablets and extended-release tablets)
†Inhalation aerosols and dry powder inhaler only
‡Age ≥ 4 years (Xopenex HFA); age ≥ 6 years (Xopenex inhalation solution)
§Age ≥ 12 years
‖Only as a concomitant therapy with a long-term asthma control medication, such as an ICS
¶Age ≥ 4 years
**Indicated for long-term, once daily maintenance treatment
(*Prescribing information: albuterol solution 2014, albuterol syrup 2015, albuterol tablets 2014, albuterol extended-release tablets 2015, Arcapta Neohaler 2013, Brovana 2014, metaproterenol syrup 2014, metaproterenol tablets 2016, Perforomist 2017, ProAir HFA 2016, ProAir RespiClick 2016, Proventil HFA 2017, Serevent Diskus 2016, Striverdi Respimat 2018, terbutaline injection 2011, terbutaline tablets 2016, Ventolin HFA 2018, Xopenex HFA 2017, Xopenex inhalation solution 2017*)

- Information on indications, mechanism of action, pharmacokinetics, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

- Clinical trials have demonstrated the efficacy of SABAs and LABAs in providing relief from asthma exacerbations, COPD exacerbations and exercise-induced asthma (EIA).

SABAs: Asthma and COPD

- In the clinical trials that evaluated SABAs for the treatment of mild asthma, all SABAs have been shown to be efficacious in improving forced expiratory volume in 1 second (FEV_1). In the clinical trials that compared albuterol to levalbuterol, inconsistent results were found (*Carl et al 2003, Gawchik et al 1999, Milgrom et al 2001, Nelson et al 1998, Nowak et al 2004, Nowak et al 2006, Qureshi et al 2005, Schreck et al 2005, Sepracor Trial 1, Sepracor Trial 2, Skoner et al 2001*).
  - In 2 studies (one retrospective, one prospective), levalbuterol resulted in a significantly lower hospitalization rate compared to albuterol (*Carl et al 2003, Schreck et al 2005*).

- In another trial, when the 2 agents were given in the emergency department, there was no significant difference in the time to discharge (*Skoner et al 2001*).
- *Nowak et al* also reported that there was no difference in the time to discharge from the emergency room with albuterol compared to levalbuterol (76 and 78.5 minutes; p = 0.74) (*Nowak et al 2006*).
- Overall, studies have shown no significant differences between the 2 agents in the peak change in FEV_1 and the number and incidence of adverse events experienced (*Carl et al 2003, Gawchik et al 1999, Milgrom et al 2001, Nelson et al 1998, Nowak et al 2004, Nowak et al 2006, Qureshi et al 2005, Schreck et al 2005, Sepracor Trial 1, Sepracor Trial 2, Skoner et al 2001*).
  - In an unpublished study, the difference in peak FEV_1 was statistically significant for albuterol hydrofluoroalkanes (HFA) compared to levalbuterol HFA (p = 0.018) (*Sepracor Trial 2*).

- Albuterol dry powder inhaler was compared to placebo dry powder inhaler in patients with asthma maintained on ICS treatment (*Raphael et al 2014*). Patients treated with albuterol dry powder inhaler had significantly improved FEV_1 area under the curve compared to placebo. In patients with exercise-induced bronchoconstriction undergoing treadmill exercise challenge, placebo-treated patients had a greater decrease in FEV_1 compared with albuterol dry powder inhaler-treated patients (*Ostrom et al 2014*). In a cumulative-dose, crossover study, albuterol dry powder inhaler was compared with albuterol HFA with similar between-group improvements in FEV_1 at 30 minutes (*Miller et al 2014*). Additionally, albuterol dry power inhaler demonstrated favorable FEV_1 improvement in EIA compared to placebo in a crossover study (*Ostrom et al 2015*).

LABAs: Asthma

- The LABAs salmeterol and formoterol have been found to improve FEV_1 in patients with mild to moderate asthma who require persistent use of SABAs. However, the SMART trial found that salmeterol had significant occurrences of combined respiratory-related deaths or respiratory-related life-threatening experiences compared to placebo ($p < 0.05$) (*Nelson et al 2006*). In a meta-analysis, salmeterol and formoterol both demonstrated an increase in severe exacerbations that required hospitalization, life-threatening exacerbations and asthma-related deaths in adults and children alike when compared to placebo (*Salpeter et al 2006*). Due to the results of these studies, all LABAs have a boxed warning stating that these agents may increase the risk of asthma-related death.

LABAs: COPD

- A systematic review concluded that in patients with COPD, there was no difference in the rate of mild exacerbations between patients treated with an ICS or LABA (odd ratio, 1.63; 95% confidence interval [CI], 0.49 to 5.39) or in the rate of moderate or severe COPD exacerbations (rate ratio, 0.96; 95% CI, 0.89 to 1.02) (*Spencer et al 2011*).
- The safety and efficacy of indacaterol were evaluated in randomized controlled trials that compared it to placebo and other agents used in the management of COPD (*Balint et al 2010, Buhl et al 2011, Chapman et al 2011, Dahl et al 2010, Donohue et al 2010, Feldman et al 2010, Korn et al 2011, Kornmann et al 2011, Magnussen et al 2010, Vogelmeier et al 2010*). Notably, most of these trials evaluated indacaterol in doses of 150, 300 and 600 mcg once daily, rather than the FDA-approved dosing of 75 mcg once daily (*Balint et al 2010, Buhl et al 2011, Chapman et al 2011, Dahl et al 2010, Donohue et al 2010, Feldman et al 2010, Korn et al 2011, Kornmann et al 2011, Magnussen et al 2010, Vogelmeier et al 2010*). However, results from placebo-controlled trials of indacaterol 75 mcg have also been published, lending support to the use of the 75 mcg dose (*Gotfried et al 2012, Kerwin et al 2011*).
- Overall, data from published clinical trials demonstrated that treatment with indacaterol consistently results in significantly higher mean trough FEV_1 after 12 weeks of treatment compared to placebo, formoterol, salmeterol and tiotropium. Patients treated with indacaterol also achieved significant improvements in COPD symptoms, as well as health-related quality of life compared to those treated with placebo. Compared to placebo, indacaterol significantly reduces the use of rescue medications, increases the days of no rescue medication use, and improves diary card-derived symptom variables (eg, nights with no awakenings, days with no daytime symptoms, days able to perform usual activities). In general, treatment with indacaterol is favored over other long-acting bronchodilators for these outcomes, but statistical superiority is not consistently achieved (*Balint et al 2010, Buhl et al 2011, Chapman et al 2011, Dahl et al 2010, Donohue et al 2010, Feldman et al 2010, Gotfried et al 2012, Kerwin et al 2011, Korn et al 2011, Kornmann et al 2011, Magnussen et al 2010, Vogelmeier et al 2010*). Recent meta-analyses comparing indacaterol to tiotropium and to twice-daily LABAs (salmeterol or formoterol) demonstrated that patients treated with indacaterol had higher trough FEV_1 and greater improvements in the use of rescue medications and achieving improvements in dyspnea and health status

compared to the alternative treatments. However, the trials included in this meta-analysis used indacaterol doses higher than FDA-approved daily doses of 75 mcg (*Cope et al 2013, Rodrigo et al 2012*).

- Placebo-controlled trials demonstrate that within 5 minutes after administration of indacaterol, significant improvements in bronchodilation are achieved (*Balint et al 2010, Donohue et al 2010, Gotfried et al 2012, Kerwin et al 2011, Magnussen et al 2010, Vogelmeier et al 2010*). These results have also been observed when comparing indacaterol to salmeterol, salmeterol/fluticasone, and tiotropium (*Buhl et al 2011, Korn et al 2011, Vogelmeier et al 2010*).
- In 2 studies, patients diagnosed with COPD were treated with arformoterol, salmeterol, or placebo. These studies found that both arformoterol and salmeterol significantly improved morning trough FEV_1 throughout the 12 weeks of daily treatment compared to placebo ($p < 0.001$ in both trials) (*Baumgartner et al 2007, Sepracor, 2005*). In a head-to-head study against salmeterol, formoterol was associated with a greater change from baseline in FEV_1 at 5 minutes post-dose on day 28 ($p = 0.022$) (*Cote et al 2009*). Currently, there is a lack of head-to-head randomized, double-blind clinical trials to determine a preferential status of one agent over another for the treatment of COPD.
- Two replicate, multicenter, randomized, double-blind, placebo-controlled, parallel-group, Phase 3 studies investigated the long-term efficacy and safety of once-daily olodaterol via Respimat soft-mist inhaler vs placebo and formoterol over 48 weeks in patients with moderate to very severe COPD receiving usual-care background therapy. Patients were randomized to receive once-daily olodaterol 5 or 10 mcg, twice-daily formoterol 12 mcg, or placebo. Co-primary endpoints were FEV_1 area under the curve from 0 to 3 hours (AUC_{0-3}), trough FEV_1, and Mahler transition dyspnea index (TDI) total score after 24 weeks. Overall, in Study 1222.13 (N = 904) and Study 1222.14 (N = 934), patients who received treatment with olodaterol had significantly improved FEV_1 AUC_{0-3} vs placebo in both studies ($p < 0.0001$ for all comparisons) and trough FEV_1 vs placebo ($p < 0.01$). Formoterol also showed statistically significant differences in both Study 1222.13 ($p < 0.01$) and Study 1222.14 ($p < 0.05$) (*Koch et al 2014*).
- Two replicate, randomized, double-blind, placebo-controlled, parallel-group, Phase 3 trials investigated the long-term safety and efficacy of olodaterol in patients with moderate to very severe COPD receiving usual-care background therapy. Patients received olodaterol 5 mcg or 10 mcg or placebo once daily for 48 weeks. Co-primary endpoints were FEV_1 AUC_{0-3} (change from baseline) and trough FEV_1 at 12 weeks. Overall, Study 1222.11 (N = 624) and Study 1222.12 (N = 642) showed that olodaterol 5 mcg and 10 mcg significantly improved the FEV_1 AUC_{0-3} response ($p < 0.0001$) and trough FEV_1 (Study 1222.11, $p < 0.0001$; Study 1222.12, $p < 0.05$, post hoc) at week 12. The incidence of adverse events was comparable with that of placebo (*Ferguson et al 2014*).
- Two replicate, multicenter, randomized, double-blind, double-dummy, placebo-controlled, 4-way cross-over group, Phase 3 studies investigated the long-term efficacy and safety of once-daily olodaterol via Respimat soft-mist inhaler vs placebo and formoterol over 6 weeks in patients with moderate to very severe COPD receiving usual-care background therapy. Patients were randomized to receive once-daily olodaterol 5 or 10 mcg, twice-daily formoterol 12 mcg, or placebo. Co-primary endpoints were FEV_1 area under the curve from 0 to 12 hours (AUC_{0-12}) and FEV_1 area under the curve from 12 to 24 hours (AUC_{12-24}) after 6 weeks. Overall, in Study 1222.24 (N = 99) and Study 1222.25 (N = 100), patients who received treatment with both doses of olodaterol and formoterol had significantly improved FEV_1 profiles (co-primary endpoints of FEV_1 AUC_{0-12} and FEV_1 AUC_{12-24} and the key secondary endpoint [FEV_1 AUC_{0-24}]) vs placebo in both studies (for all comparisons $p < 0.0001$). No statistically significant differences were reported between the 3 active comparators (*Feldman et al 2014*).
- A meta-analysis that compared LABAs (salmeterol, formoterol, and indacaterol) to tiotropium demonstrated that tiotropium was more effective than LABAs as a group in preventing COPD exacerbations and disease-related hospitalizations. However, overall hospitalization rates, mortality, symptom improvement, and changes in lung function were similar among groups (*Chong et al 2012*). Another meta-analysis compared the use of LABAs plus tiotropium to the use of either LABAs alone or tiotropium alone. The analysis demonstrated that there was a significant improvement in FEV_1 with combination therapy compared to tiotropium alone. There was also a small mean improvement in health-related quality of life for patients receiving a LABA plus tiotropium compared to tiotropium alone, but the clinical significance of this small difference is unclear. Hospital admissions and mortality were not significantly different between groups. Data comparing LABA plus tiotropium to LABA alone were somewhat limited, but demonstrated a significant improvement in health-related quality of life, FEV_1 and exacerbations (*Farne et al 2015*).

EIA

- For the treatment of EIA, albuterol, metaproterenol, and formoterol have demonstrated an improvement in FEV_1 compared to placebo (*Berkowitz et al 1986, Bonini et al 2013, Edelman et al 2000, Richter et al 2002, Shapiro et al 2002, Storms et al 2004*).
  - In 1 study, albuterol- and metaproterenol-treated patients had a lower incidence of exercise-induced bronchospasm compared to placebo (*Cote et al 2009*).
  - In another study comparing albuterol, formoterol and placebo for EIA, both active treatment groups provided a statistically significant decrease in mean maximum percent of FEV_1 compared to placebo ($p < 0.01$) (*Shapiro et al 2002*).

CLINICAL GUIDELINES

Asthma

- The National Asthma Education and Prevention Program (NAEPP) guideline from the NHLBI states that the initial treatment of asthma should correspond to the appropriate asthma severity category, and it provides a stepwise approach to asthma management. Long-term control medications such as ICSs, long-acting bronchodilators, leukotriene modifiers, cromolyn, theophylline, and immunomodulators should be taken daily on a long-term basis to achieve and maintain control of persistent asthma. ICSs are the most potent and consistently effective long-term asthma control medication. Quick-relief medications such as SABAs and anticholinergics are used to provide prompt relief of bronchoconstriction and accompanying acute symptoms such as cough, chest tightness, and wheezing. Systemic corticosteroids are important in the treatment of moderate or severe exacerbations because these medications prevent progression of the exacerbation, speed recovery, and prevent relapses (*NHLBI 2007*).
  - LABAs are used in combination with ICSs for long-term control and prevention of symptoms in moderate or severe persistent asthma.
  - Of the adjunctive treatments available, a LABA is the preferred option to combine with an ICS in patients 12 years of age and older. This combination is also an option in selected patients 5 to 12 years of age.
- The Global Initiative for Asthma (GINA) guideline also provides a stepwise approach to asthma management. It recommends an ICS as a preferred controller medication choice, with an increased ICS dose and/or addition of a LABA for increasing symptom severity (higher steps). At the highest step, it is recommended that the patient be referred for add-on treatment (eg, tiotropium, omalizumab, mepolizumab) (*GINA 2018*).

COPD

- The 2018 GOLD guidelines state that the management strategy for stable COPD should be predominantly based on an assessment of the patient's symptoms and future risk of exacerbations. The risk of exacerbations is now based solely on the exacerbation history, whereas in previous versions of the guideline, risk assessment also included consideration of airflow limitation assessed by spirometry. Key recommendations from the GOLD guidelines are as follows (*GOLD 2018*):
  - Inhaled bronchodilators are recommended over oral bronchodilators.
  - LAMAs and LABAs are preferred over short-acting agents except for patients with only occasional dyspnea.
  - Patients may be started on single long-acting bronchodilator therapy or dual long-acting bronchodilator therapy. In patients with persistent dyspnea on 1 bronchodilator, treatment should be escalated to 2.
  - Long-term monotherapy with ICSs is not recommended. Long-term treatment with ICSs may be considered in association with LABAs for patients with a history of exacerbations despite treatment with long-acting bronchodilators.
  - Treatment recommendations are given for patients with COPD based on their GOLD patient group (see Table 3 below).
    - Group A: Patients should be offered bronchodilator treatment (short- or long-acting). This should be continued if symptomatic benefit is documented.
    - Group B: Initial therapy should consist of a long-acting bronchodilator (LAMA or LABA). For patients with persistent breathlessness on monotherapy, use of 2 bronchodilators is recommended (LAMA + LABA). For patients with severe breathlessness, initial therapy with 2 bronchodilators may be considered. If the addition of a second bronchodilator does not improve symptoms, it is suggested that treatment could be stepped down to a single bronchodilator.
    - Group C: Initial therapy should be a LAMA. Patients with persistent exacerbations may benefit from adding a second long-acting bronchodilator (LAMA + LABA, preferred) or using an ICS + LABA.
    - Group D: It is recommended to start therapy with a LAMA + LABA combination. In some patients, initial therapy with an ICS + LABA may be the first choice; these patients may have a history and/or findings suggestive of

asthma-COPD overlap. In patients who develop further exacerbations on LAMA + LABA therapy, alternative pathways include escalation to a LAMA + LABA + ICS (preferred) or a switch to an ICS + LABA. If patients treated with a LAMA + LABA + ICS still have exacerbations, options for selected patients may include addition of roflumilast, addition of a macrolide, or stopping the ICS.

Table 3. Assessment of symptoms and risk of exacerbations to determine GOLD patient group

Exacerbation history	Symptoms	
	mMRC 0 to 1 CAT < 10	mMRC ≥ 2 CAT ≥10
≥ 2 (or ≥ 1 leading to hospital admission)	C	D
0 or 1 (not leading to hospital admission)	A	B

Abbreviations: CAT = COPD assessment test; mMRC = modified British Medical Research Council questionnaire

- Guidelines for the prevention of acute exacerbations of COPD from the American College of Chest Physicians and the Canadian Thoracic Society state that a LAMA is recommended over either a short-acting muscarinic antagonist or a LABA. The guidelines state that certain combination bronchodilators or bronchodilator/ICS combinations may reduce exacerbations, but does not state that any combination is superior to LAMA monotherapy in patients with stable COPD (*Criner et al 2015*).

Exercise-induced bronchoconstriction

- For exercise-induced bronchoconstriction, guidelines from the American Thoracic Society recommend administration of an inhaled SABA 15 minutes prior to exercise. The guidelines also recommend a controller agent added whenever SABA therapy is used at least once daily. Additional guidelines are set forth for patients with symptoms despite using an inhaled SABA before exercise (*Parsons et al 2013*). Joint guidelines from the American Academy of Allergy, Asthma & Immunology, the American College of Allergy, Asthma & Immunology, and the American College of Allergy, Asthma & Immunology state that beta$_2$-agonists (SABAs or LABAs) are most effective at short-term protection against exercise-induced bronchoconstriction and for accelerating recovery from exercise-induced bronchoconstriction. However, daily use of a SABA or LABA will lead to tolerance. Additional or adjunctive options include daily use of leukotriene inhibitors or ICSs, cromolyn sodium before exercise, or ipratropium for patients who have not responded to other agents (*Weiler et al 2016*).

SAFETY SUMMARY

- Contraindications:
  - Serevent Diskus and ProAir RespiClick are contraindicated in patients with a severe hypersensitivity to milk proteins.
  - LABAs should generally not be used as a primary treatment of status asthmaticus or other acute episodes of asthma or COPD that require intensive measures; this is listed as a contraindication for Serevent Diskus.
  - All LABAs are contraindicated for use in patients with asthma without concomitant use of a long-term asthma control medication.
- Key warnings and precautions:
  - All LABAs have a boxed warning describing the increased risk of asthma-related deaths. Because of this risk, use of LABAs for the treatment of asthma without a concomitant long-term asthma control medication, such as an ICS, is contraindicated. LABAs should be used only as additional therapy for patients with asthma who are currently taking but are inadequately controlled on a long-term asthma control medication, such as an ICS.
  - Beta$_2$-agonists may also lead to:
    - paradoxical bronchospasm
    - fatalities with excessive use
    - cardiovascular effects such as increased heart rate, blood pressure, and/or electrocardiogram changes
    - central nervous system effects and/or seizures
  - LABAs should not be used to treat acute symptoms or initiated in the setting of acutely deteriorating asthma or COPD.

- Adverse events
  - Commonly-reported adverse events (≥ 5% for at least 1 medication in the class) include chest pain, palpitations, tachycardia, dizziness, excitement, fatigue, headache, nervousness, shakiness, somnolence, tremor, rash, diarrhea, nausea, vomiting, pain, asthma exacerbation, bronchitis, cough, influenza, nasal congestion, nasopharyngitis/pharyngitis, respiratory disorder, rhinitis, throat irritation, upper respiratory tract infection, viral respiratory infection, accidental injury, fever, and viral infection.
- Albuterol, levalbuterol, metaproterenol, terbutaline, arformoterol, indacaterol, and salmeterol are Pregnancy Category C; formoterol and olodaterol are not currently assigned a Pregnancy Category.

DOSING AND ADMINISTRATION

Table 4. Dosing and Administration

Generic Name	Available Formulations	Route	Usual Recommended Frequency	Comments
Short-acting beta$_2$-agonists				
albuterol	Inhalation: metered dose aerosol inhaler (HFA), metered dose dry powder inhaler, solution for nebulization Oral: extended-release tablets, syrup, tablets	Inhalation, oral	Treatment or prevention of bronchospasm in patients with asthma: • Aerosol/dry powder inhaler: 1 to 2 inhalations every 4 to 6 hours • Solution for nebulization: 3 to 4 times daily • Extended-release tablets: twice daily • Syrup, tablets: 3 to 4 times daily Exercise-induced bronchospasm: • Aerosol/dry powder inhaler: 2 inhalations 15 to 30 minutes before exercise	
levalbuterol	Metered dose aerosol inhaler (HFA), solution for nebulization	Inhalation	Treatment or prevention of bronchospasm in patients with asthma: • Aerosol inhaler: 1 to 2 inhalations every 4 to 6 hours • Solution for nebulization: 3 times daily	
metaproterenol	Syrup, tablets	Oral	3 to 4 times daily	
terbutaline	Injection, tablets	Subcutaneous injection, oral	• Injection: 1 subcutaneous injection, may repeat in 15 to 30 minutes if improvement does not occur; maximum, 0.5 mg in 4 hours • Tablets: 3 times daily, 6 hours apart	Injection: Safety and efficacy in children < 12 years of age have not been established.
Long-acting beta$_2$-agonists				
arformoterol	Solution for nebulization	Inhalation	Twice daily	Safety and efficacy in children have not been established.
formoterol	Solution for nebulization	Inhalation	Twice daily	Safety and efficacy in children have not been established.

Generic Name	Available Formulations	Route	Usual Recommended Frequency	Comments
indacaterol	Capsule for inhalation	Inhalation	Once daily	Safety and efficacy in children have not been established.
olodaterol	Inhalation spray	Inhalation	Once daily	Safety and efficacy in children have not been established.
salmeterol	Dry powder inhaler	Inhalation	Treatment or prevention of bronchospasm in patients with asthma/maintenance treatment of bronchoconstriction in COPD 1 inhalation twice daily Exercise-induced bronchospasm: 1 inhalation at least 30 minutes before exercise	

Abbreviations: COPD = chronic obstructive pulmonary disease; HFA = hydrofluoroalkane

See the current prescribing information for full details

CONCLUSION

- Single-entity respiratory beta$_2$-agonist agents are FDA-approved for the treatment of asthma, COPD, reversible airway obstruction and/or exercise-induced bronchospasm.
  - Beta$_2$-agonists are classified as short- or long-acting based on their onset and duration of action, and are available in various dosage forms, including solution for nebulization, aerosol inhaler, dry powder inhaler, oral solution, immediate- and extended-release tablets, and solution for injection.
  - SABAs are generally dosed multiple times per day for the treatment or prevention of symptoms.
  - LABAs are typically administered twice daily for COPD, with the exception of indacaterol and olodaterol, which are administered once daily.
- Overall, SABAs have demonstrated similar efficacy and safety. Similarly, guidelines do not recommend one LABA over another, and head-to-head clinical trials have not determined the superiority of any one agent.
- All LABAs have a boxed warning stating that these agents may increase the risk of asthma-related death.
  - In the treatment of asthma, LABAs should not be used as monotherapy, but rather added on to another long-acting controller medication such as an ICS if patients are not adequately controlled on the ICS alone.
- GINA and NHLBI guidelines recommend SABAs for symptomatic relief in patients with asthma, which should generally be used on an as-needed or “rescue” basis. For chronic management of asthma, LABAs should be used as add-on therapy in patients not adequately controlled on an ICS as an alternative to maximizing the ICS dose.
  - LABAs may also be used for exercise-induced bronchospasm and provide a longer period of coverage (typically 12 hours or more) compared to the SABAs; however, daily use of a beta$_2$-agonist can lead to tolerance, and daily use of LABA monotherapy is not recommended.
- GOLD guidelines state that inhaled bronchodilators are a key component of COPD treatment, and long-acting agents are generally preferred over short-acting agents for maintenance therapy.
  - Depending on the COPD patient subtype, initial COPD management may include use of a beta$_2$-agonist and/or an anticholinergic agent.
- None of the current asthma or COPD treatment guidelines recommend the use of one specific inhaled beta$_2$-agonist product over another.
  - Administration instructions and inhalation devices vary among products and should be considered in product selection.

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Publication Date: June 01, 2018

Nevada Medicaid
Compounded Drugs
Pharmacy Coverage Guideline

CRITERIA FOR COVERAGE/NONCOVERAGE

Coverage and Limitations

Approval Length: 6 months, unless the provider requests for a shorter length of therapy.

Approval Criteria

All of the following are met:

1. Each active ingredient in the compounded drug is FDA-approved or national compendia* supported for the condition being treated
2. The therapeutic amounts are supported by national compendia* or peer-reviewed literature for the condition being treated in the requested route of delivery
3. If any prescription ingredients require prior authorization and/or step therapy, all drug-specific criteria must be also met
4. The compounded drug must not include any ingredient that has been withdrawn or removed from the market due to safety reasons (refer to Table 1)
5. The patient has tried and failed therapy or had an intolerance to two FDA-approved commercially-available prescription therapeutic alternatives, one of which is the same route of administration as the requested compound, unless **one** of the following criteria are met:
   a. Patient has a contraindication to commercially available products
   b. One or no other therapeutic alternatives are commercially available
   c. Prepared in a strength not commercially available or currently in short supply
   d. Prepared in a different dosage form for a patient who is unable to take the commercially available formulation (mixing or reconstituting commercially available products based on the manufacturer's instructions or the product's approved labeling does NOT meet this criteria).
   e. Patient has an allergy or sensitivity to inactive ingredients (e.g. dyes, preservatives, sugars, etc.) that are found in commercially available products.
6. The compounded drug must not be used for a cosmetic purpose.
7. If the compound is subject to the drug-specific/targeted compound program, the member meets all the applicable drug-specific criteria below for all the targeted ingredient(s) used in the requested compound product.
8. The pharmacy compounding the medication has received the appropriate certification for the dosage form being compounded.
9. Compounding will not be done in a physician’s office.

Nevada Medicaid
Compounded Drugs
Pharmacy Coverage Guideline

*Applies to ALL compounds regardless of final cost

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Compound Medications

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form:

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Compound Medications

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

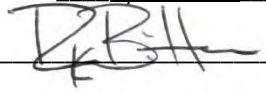
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

HPN maintains a "Compounds & Bulk Powders" clinical protocol (attached) which includes an appendices of lists that give examples of cosmetic ingredients, ingredients on the FDA "Do Not Compound" list, and items that have not been approved for topical use. Lists of ingredients can help reviewers in the clinical review process. HPN is also concerned about the following items: **Requirement 8:** Tracking a pharmacies compounding certification seems to go beyond clinical criteria and is not something HPN is currently doing, aware of how to implement, and unsure of the gains in doing so. **Requirement 9:** If a provider has a dispensary, the approval from the Board of Pharmacy to dispense drugs, and the ability to submit electronic claims, there may not be a reason to exclude them from compounding drugs. **Requirement "*":** HPN feels this statement may require all compounds to undergo prior authorization regardless of cost. While HPN commends the intent of ensuring appropriate and supported use, finding clinical support for items that are inexpensive and the current standard of care may prove difficult and operationally burdensome for providers and all four health plans. **Approval Length:** HPN currently approves compounds for 12 months rather than the proposed six months.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Ryan Bitton

Signature of individual completing this form: 

Clinical Pharmacy Program Guidelines for Compounds and Bulk Powders

Program	Prior Authorization
Medication	Compounds and Bulk Powders
Markets in Scope	Arizona, Hawaii, New Mexico, Florida-CHIP, Maryland, New Jersey, New York, New York EPP, Ohio, Pennsylvania, Rhode Island, California
Issue Date	7/2013
Pharmacy and Therapeutics Approval Date	7/2018
Effective Date	9/2018

1. Background:

Compounded medications can provide a unique route of delivery for certain patient-specific conditions and administration requirements. Compounded medications should be produced for a single individual and not produced on a large scale. A dollar threshold may be used to identify compounds which require Notification and must meet the criteria below in order to be covered. Drugs included in the compound must be a covered product.

2. Coverage Criteria:

A. **Authorization** for compounds and bulk powders will be approved based on **all** of the following criteria:

1. The requested drug component is a covered medication

-AND-

2. **One** of the following:

a. The requested drug component is to be administered for an FDA-approved indication

-OR-

b. The use of this drug is supported by information from the appropriate compendia of current literature*

-AND-

3. If a drug included in the compound requires prior authorization and/or step

therapy, all drug specific clinical criteria must also be met

-AND-

4. If the drug component is no longer available commercially it must not have been withdrawn for safety reasons

-AND-

5. **<u>One</u>** of the following:

   a. A unique vehicle is required for topically administered compounds

   -OR-

   b. A unique dosage form is required for a commercially available product due to patient's age, weight or inability to take a solid dosage form.

   -OR-

   c. A unique formulation is required for a commercially available product due to an allergy or intolerance to an inactive ingredient in the commercially available product

   -AND-

6. Coverage for compounds and bulk powders will **NOT** be approved for any of the following:

   a. For topical compound preparations (e.g. creams, ointments, lotions or gels to be applied to the skin for transdermal, transcutaneous or any other topical route), requested compound contains any FDA approved ingredient that is not FDA approved for TOPICAL use.

   -OR-

   b. Requested compound contains topical fluticasone. Topical fluticasone will NOT be approved unless:

      (1) Topical fluticasone is intended to treat a dermatologic condition. Scar treatments are considered cosmetic and will not be covered

      -AND-

      (2) Patient has a contraindication to all commercially available

topically fluticasone formulations

-OR-

c. Requested compound contains any ingredients when used for cosmetic purposes.

-OR-

d. Requested compound contains any ingredient(s) which are on the FDA's Do Not Compound List.

Authorization will be issued for 12 months

*****Compendia of Current Literature: • American Hospital Formulary Service Drug Information • National Comprehensive Cancer Network Drugs and Biologics Compendium • Thomson Micromedex DrugDex • Clinical Pharmacology • United States Pharmacopoeia-National Formulary (USP-NF) • United States Pharmacopoeia Drug Information (USP DI)

APPENDIX

Example topical compound preparations (e.g. creams, ointments, lotions or gels to be applied to the skin for transdermal, transcutaneous or any other topical route) that contain any FDA approved ingredient that are not FDA approved for TOPICAL use, including but NOT LIMITED TO the following:

(1) Ketamine
(2) Gabapentin
(3) Flurbiprofen (topical ophthalmic use not included)
(4) Ketoprofen
(5) Morphine
(6) Nabumetone
(7) Oxycodone
(8) Cyclobenzaprine
(9) Baclofen
(10) Tramadol
(11) Hydrocodone
(12) Meloxicam
(13) Amitriptyline
(14) Pentoxifylline
(15) Orphenadrine
(16) Piroxicam
(17) Levocetirizine

(18) Amantadine
(19) Oxytocin
(20) Sumatriptan
(21) Chorionic gonadotropin (human)
(22) Clomipramine
(23) Dexamethasone
(24) Hydromorphone
(25) Methadone
(26) Papaverine
(27) Mefenamic acid
(28) Promethazine
(29) Succimer DMSA
(30) Tizanidine
(31) Apomorphine
(32) Carbamazepine
(33) Ketorolac
(34) Dimercaptopropane-sulfonate
(35) Dimercaptosuccinic acid
(36) Duloxetine
(37) Fluoxetine
(38) Bromfenac (topical ophthalmic use not included)
(39) Nepafenac (topical ophthalmic use not included)

Example compounds that contain ingredients for cosmetic purposes:

(1) Hydroquinone
(2) Acetyl hexapeptide-8
(3) Tocopheryl Acid Succinate
(4) PracaSil TM-Plus
(5) Chrysaderm Day Cream
(6) Chrysaderm Night Cream
(7) PCCA Spira-Wash
(8) Lipopen Ultra
(9) Versapro
(10) Fluticasone
(11) Mometasone
(12) Halobetasol
(13) Betamethasone
(14) Clobetasol
(15) Triamcinolone
(16) Minoxidil
(17) Tretinoin
(18) Dexamethasone
(19) Spironolactone
(20) Cycloserine
(21) Tamoxifen

(22) Sermorelin
(23) Mederma Cream
(24) PCCA Cosmetic HRT Base
(25) Sanare Scar Therapy Cream
(26) Scarcin Cream
(27) Apothederm
(28) Stera Cream
(29) Copasil
(30) Collagenase
(31) Arbutin Alpha
(32) Nourisil
(33) Freedom Cepapro
(34) Freedom Silomac Andydrous
(35) Retinaldehyde
(36) Apothederm

Example ingredients on the FDA's Do Not Compound List:

(1) 3,3′,4′,5-tetrachlorosalicylanilide
(2) Adenosine phosphate
(3) Adrenal cortex
(4) Alatrofloxacin mesylate
(5) Aminopyrine
(6) Astemizole
(7) Azaribine
(8) Benoxaprofen
(9) Bithionol
(10) Camphorated oil
(11) Carbetapentane citrate
(12) Casein, iodinated
(13) Cerivastatin sodium
(14) Chlormadinone acetate
(15) Chloroform
(16) Cisapride
(17) Defenfluramine hydrochloride
(18) Diamthazole dihydrochloride
(19) Dibromsalan
(20) Dihydrostreptomycin sulfate
(21) Dipyrone
(22) Encainide hydrochloride
(23) Etretinate
(24) Fenfluramine hydrochloride
(25) Flosequinan
(26) Glycerol, iodinated
(27) Grepafloxacin
(28) Mepazine

(29) Metabromsalan
(30) Methapyrilene
(31) Methopholine
(32) Methoxyflurane
(33) Mibefradil dihydrochloride
(34) Nomifensine maleate
(35) Novobiocin sodium
(36) Oxyphenisatin acetate
(37) Oxyphenisatin
(38) Pemoline
(39) Pergolide mesylate
(40) Phenacetin
(41) Phenformin hydrochloride
(42) Phenylpropanolamine
(43) Pipamazine
(44) Potassium arsenite
(45) Propoxyphene
(46) Rapacuronium bromide
(47) Rofecoxib
(48) Sibutramine hydrochloride
(49) Sparteine sulfate
(50) Sulfadimethoxine
(51) Sweet spirits of nitre
(52) Tegaserod maleate
(53) Temafloxacin hydrochloride
(54) Terfenadine
(55) Ticrynafen
(56) Tribromsalan
(57) Trichloroethane
(58) Troglitazone
(59) Trovafloxacin mesylate:
(60) Urethane
(61) Valdecoxib
(62) Zomepirac sodium

3. **References:**

1. Food and Drug Administration (2014, July 02). Additions and Modifications to the List of Drug Products That Have Been Withdrawn or Removed From the Market for Reasons of Safety and Effectiveness. Retrieved from http://federalregister.gov/a/2014-15371

Program	Prior Authorization - Compounds and Bulk Powders
Change Control	
Date	Change

7/2013	Topical use section updated to include all medications that are not FDA approved for topical use. Reformatted to standard.
10/2013	Added the following to the list of compound ingredients that are not covered: ibuprofen, lipoic acid, beta glucan, ubiquinol, chrysin, glutathione, lactobacillus, vitamin E, ascorbic acid, melatonin, meloxicam, amitriptyline, pentoxifylline, orphenadrine, piroxicam, acetyl hexapeptide-8, tocopheryl acid succinate, PracaSil TM-Plus, Chrysaderm Day Cream, Chrysaderm Night Cream, PCCA Spira-Wash and Lipopen Ultra.
11/2013	Added criteria for topical fluticasone.
2/2014	Added criteria for cholestyramine.
4/2014	Added pyridoxal-5-phosphate (Vitamin B6) and loperamide to list of ingredients that will not be coverage as they are available OTC. Added levocetirizine, amantadine, oxytocin, sumatriptan and chorionic gonadotropin to list of ingredients that will not be covered for topical use. Added Versapro to list of ingredients that will not be covered for cosmetic use.
10/2014	Added Dextromethorphan, Dehydroepiandrosterone, Pregnenolone, Biotin, L-Glutamine, Serotonin, Aloe vera, Sodium butyrate, L-Isoleucine and Vitamin D3 to the list of ingredients that will not be covered as they are available OTC. Added Clomipramine, Dexamethasone, Hydromorphone, Methadone, Papaverine, Mefenamic acid, Promethazine, Succimer DMSA, Tizanidine, Apomorphine, Carbamazepine, Ketorolac, Dimercaptopropane-sulfonate and Dimercaptosuccinic acid to the list of ingredients that will not be covered for topical use. Added Fluticasone, Mometasone, Halobetasol, Betamethasone, Clobetasol, Triamcinolone, Minoxidil, Tretinoin, Dexamethasone, Spironolactone, Cycloserine, Tamoxifen and Sermorelin to the list of ingredients that will not be covered for cosmetic use. Removed criterion that a similar commercially available product is not available.
4/2015	Updated criteria to reflect that if any drug ingredient of the compound requires prior authorization and/or step therapy, that clinical criteria must also be met. Added ginseng, phosphatidylserine and resveratrol to the ingredients that will not be covered as they are available OTC. Added Mederma Cream, PCCA Cosmetic HRT Base, Sanare Scar Therapy Cream, and Scarcin Cream to the ingredients that will not be covered for cosmetic use.
7/2015	Added to the criteria ingredients that should not be compounded as they reside on the FDA's Do Not Compound List. Clarified language around commercially available products.
4/2016	Added criteria to allow for coverage when patient has an allergy

	to the commercially available product. Added methionine and naproxen to ingredients that will not be covered as they are available OTC. Added Apothederm to the list of ingredients that will not be covered for cosmetic use.
10/2016	Removed language that a unique dosage form is required and the commercially available product is excluded. Added carnosine L to the ingredients that will not be covered as they are available OTC. Added duloxetine and fluoxetine to the ingredients that will not be covered for topical use. Added Stera cream, Copasil, collagenase, arbutin alpha, and Nourisil to the list of ingredients that will not be covered for cosmetic use.
12/2016	Moved examples of drugs not approved for topical use, cosmetic use, and FDA's do not compound list to the appendix. Removed statements about leuprolide and cholestyramine since both pertain to off-label use and this would be covered elsewhere in the criteria.
4/2017	Added approval for compendia supported uses in addition to FDA approved indications.
10/2017	Added bromfenac and nepafenac to the ingredients that will not be covered for topical use. Added Freedom Cepapro, Silomac Anhydrous, Retinaldehyde and Apothederm to the list of ingredients that will not be covered for cosmetic use.
7/2018	Removed "refer to criteria "e" below" since there is no longer criteria "e" in the policy

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Compound Medications

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: ___Tom Beranek_____

Signature of individual completing this form: Tom Beranek

Compounded Medication Utilization

Fee for Service Medicaid

October 1, 2017 - September 30, 2018

Count of Claims by Amount Paid by Route of Administration

Route of Admin	Count of Claims
<100	2,616
(blank)	248
EXTERNAL	20
IRRIGATION	78
MOUTH/THROAT	101
OPHTHALMIC	6
ORAL	1,828
RECTAL	1
SUBCUTANEOUS	3
TRANSDERMAL	2
DOES NOT APPLY	329
100-199	108
(blank)	8
EXTERNAL	5
IRRIGATION	5
MOUTH/THROAT	-
ORAL	34
SUBCUTANEOUS	6
TRANSDERMAL	-
DOES NOT APPLY	50
200 - 500	63
(blank)	2
EXTERNAL	2
IRRIGATION	3
ORAL	24
TRANSDERMAL	1
DOES NOT APPLY	31
>500	367
(blank)	11
EXTERNAL	68
ORAL	77
TRANSDERMAL	77
DOES NOT APPLY	134
Grand Total	**3,154**

Compounded Medication Utilization

Fee for Service Medicaid

October 1, 2017 - September 30, 2018

Top 25 Products in Compounds by Paid Amount

Product Name	Count of Claims	Pharmacy Paid
DICLOFENAC GEL 3%	535	$ 1,444,980.31
DOXEPIN HCL CRE 5%	440	$ 1,220,974.58
LIDOCAINE POW HCL	368	$ 1,015,472.48
MENTHOL CRY	175	$ 482,368.75
GABAPENTIN POW	115	$ 198,979.47
ORA-PLUS LIQ	1,043	$ 197,648.72
ORA-SWEET SYP	535	$ 127,009.49
SIMPLE SYP	364	$ 65,924.37
BUPIVACAINE POW HCL	37	$ 57,170.62
CYCLOBENZAPR POW HCL	37	$ 57,170.62
REVATIO TAB 20MG	18	$ 49,958.65
(Blank)	321	$ 48,243.03
CIALIS TAB 10MG	24	$ 45,236.01
CAPSAICIN POW 98.3%	8	$ 26,940.52
LIDOCAINE POW	8	$ 21,809.47
LIDO/PRILOCN CRE 2.5-2.5%	54	$ 12,638.55
KETAMINE HCL POW	4	$ 11,301.40
PCCA-PLUS SUS	266	$ 9,408.45
TOPIRAMATE TAB 200MG	43	$ 9,317.78
GLYCERIN LIQ	484	$ 9,260.91
METHYLPARABE POW	50	$ 8,968.01
PROPYPARABEN POW	50	$ 8,968.01
STERIL WATER SOL IRRIG	315	$ 7,724.38
CHERRY LIQ FLAVOR	156	$ 7,232.62
CHERRY SYP	331	$ 6,999.20

Anthem Compound Utilization

Quarter Serviced **4th Quarter 2017**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
COMPOUND	200	296	4989	41472.995
Grand Total	200	296	4989	41472.995

Quarter Serviced **1st Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
COMPOUND	182	282	3983	50719.5
Grand Total	182	282	3983	50719.5

Quarter Serviced **2nd Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
COMPOUND	198	239	3527	32658
Grand Total	198	239	3527	32658

Quarter Serviced **3rd Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
COMPOUND	200	248	3657	49141
Grand Total	200	248	3657	49141

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
A+D PREVENT OIN	5	6	50	360
ALLERGY REL ELX 12.5/5ML	4	4	22	630
ALLERGY RELF LIQ 12.5/5ML	3	3	15	340
AMIKACIN INJ 500/2ML	2	5	3	13
AMLODIPINE TAB 10MG	1	4	30	900
AMLODIPINE TAB 5MG	1	2	30	45
AMPICILLIN INJ 1GM	2	2	6	23
ANTACID SUS	2	2	3	240
ANTACID LIQ SUS	44	45	151	10,380
ANTACID LIQ SUS FAST REL	3	3	11	480
AQUAPHOR OIN	1	1	5	15
ASCORBIC ACD POW	1	3	30	90
ATENOLOL TAB 100MG	1	1	30	120
ATENOLOL TAB 50MG	4	5	69	192
ATROPINE SUL INJ 0.4MG/ML	10	22	14	205
BANOPHEN LIQ 12.5/5ML	43	47	138	9,918
BENZOCAINE POW	1	1	30	90
CEFEPIME INJ 1GM	2	3	5	13
CEFEPIME INJ 2GM	3	5	3	418
CHERRY SYP	2	2	38	240
CHLD ALLERGY LIQ 12.5/5ML	11	11	52	1,650
CLOMIPHENE POW CITRATE	1	3	28	36
CLONIDINE TAB 0.2MG	1	1	18	20
CVS ALLERGY LIQ 12.5/5ML	2	2	13	210
CVS ANTACID SUS ANTIGAS	1	1	4	276
CVS ANTACID SUS MAX ST	1	1	15	300
CVS ANTACID/ SUS ANTI-GAS	8	8	79	1,512
DERMAZINC SPR	1	1	20	120
DIPHENHIST LIQ 12.5/5ML	4	4	39	640
EMPTY CAPSUL CAP SIZE 1	1	1	30	30
EQ ANTACID SUS	1	1	7	240
EQ ANTACID SUS ANTI-GAS	6	6	41	1,025
ESTRADIOL POW	4	4	30	135
ESTRIOL POW MICRONIZ	2	3	61	130
FLAVOR PLUS LIQ	1	2	30	175
FLECAINIDE TAB 100MG	1	4	14	720
GLYCERIN LIQ	4	9	44	1,260
HYDROCORT TAB 10MG	1	4	30	480

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
HYDROCORT AC POW MICRONIZ	1	1	30	30
HYDROQUINONE POW	1	1	30	60
HYDROXYUREA CAP 500MG	2	6	30	495
IBUPROFEN POW	2	2	44	183
INTRON A INJ 10MU	1	4	14	4
KETAMINE HCL POW	1	2	30	120
LACTIC ACID SOL 85% USP	1	1	30	60
LANSOPRAZOLE POW	1	1	30	180
LIDO/PRILOCN CRE 2.5-2.5%	40	155	36	7,440
LIDOCAINE SOL 2% VISC	138	139	186	27,291
LISINOPRIL POW	1	3	30	180
LISINOPRIL TAB 10MG	1	1	30	300
MEROPENEM INJ 1GM	1	10	1	28
MEROPENEM INJ 500MG	2	5	3	16
METFORMIN POW HCL	1	1	30	120
METRONIDAZOL POW BENZOATE	1	1	10	30
METRONIDAZOL TAB 250MG	1	1	7	130
METRONIDAZOL TAB 500MG	2	2	24	230
MI-ACID SUS	1	1	8	100
MINERAL OIL LIGHT	1	3	30	653
MINTOX SUS	1	1	2	60
NADOLOL TAB 20MG	3	8	30	780
NALTREXONE POW HCL	2	4	30	225
NALTREXONE TAB 50MG	2	4	30	120
NIFEDIPINE POW	1	1	10	30
NITRO-BID OIN 2%	2	2	15	60
NYSTATIN CRE 100000	2	2	30	240
NYSTATIN SUS 100000	8	9	88	3,590
OMEPRAZOLE CAP 20MG	1	1	30	120
OMEPRAZOLE POW	1	1	30	90
ORA-PLUS LIQ	2	2	44	158
PAPAVERINE POW HCL	1	1	14	3
PREDNISOLONE SOL 15MG/5ML	3	3	18	720
PREDNISOLONE SYP 15MG/5ML	5	5	38	2,248
PREVACID 24H CAP 15MG DR	1	2	30	120
PROGESTERONE POW MICRONIZ	25	39	30	1,170
PROPYLENE GL SOL	1	1	30	30

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
Q-DRYL LIQ 12.5/5ML	3	3	20	360
RANITIDINE SYP 75MG/5ML	1	1	2	90
RULOX SUS	23	23	91	3,920
SILADRYL ALR LIQ 12.5/5ML	1	1	10	100
SILDENAFIL TAB 20MG	1	2	30	720
SM ANTACID SUS ADVANCED	1	1	10	100
SM ANTACID SUS ANTI-GAS	1	1	3	240
SOD CHLORIDE INJ 0.9%	1	1	1	4
SOD CHLORIDE TAB 1GM	1	1	30	60
SODIUM POW BICARBON	3	3	60	306
SODIUM CHLOR SOL 0.9% IRR	2	2	29	6,000
SOLU-MEDROL INJ 1000MG	1	5	1	1,040
STERIL WATER INJ	2	6	3	832
SULFASALAZIN TAB 500MG	1	2	30	1,200
TACROLIMUS CAP 0.5MG	1	3	30	360
TACROLIMUS CAP 5MG	4	4	82	127
TESTOSTERONE POW CYPIONAT	1	2	28	10
TETRACYCLINE POW	1	2	10	720
THYROID POW PORCINE	1	3	30	180
TOPIRAMATE CAP 25MG	1	7	14	420
TUTTI FRUTTI LIQ FLAVOR	1	1	10	100
URSODIOL CAP 300MG	3	4	30	1,248
VANCOMYCIN INJ 1000MG	1	1	1	2
VANCOMYCIN INJ 5GM	1	1	1	1
WAL-DRYL LIQ 12.5/5ML	2	3	12	480
Total	506	741	2,938	99,704

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
1/01/18 - 03/31/2018 - Q1				
A+D PREVENT OIN	1	1	30	60
ALLERGY CHLD LIQ 12.5/5ML	3	3	17	390
ALLERGY REL ELX 12.5/5ML	2	2	37	615
ALLERGY RELF LIQ 50/20ML	3	3	35	1,000
AMIODARONE TAB 200MG	1	1	30	120
AMLODIPINE TAB 10MG	4	7	30	1,385
AMPICILLIN INJ 1GM	2	2	5	19
AMPICILLIN INJ 2GM	1	1	2	606
ANTACID SUS	3	3	32	480
ANTACID & SUS ANTIGAS	2	2	8	240
ANTACID LIQ SUS	44	46	120	10,250
ANTACID LIQ SUS FAST REL	5	5	39	420
AQUAPHOR OIN	2	2	24	135
ASCORBIC ACD POW	2	4	30	150
ATENOLOL TAB 50MG	2	3	55	134
ATROPINE SUL INJ 0.4MG/ML	10	22	14	170
ATROPINE SUL SOL 1% OP	3	3	53	30
BANOPHEN CAP 25MG	1	1	3	120
BANOPHEN LIQ 12.5/5ML	42	44	154	7,840
BENZOCAINE POW	1	1	30	90
BUDESONIDE POW	1	1	15	3,000
CARAFATE SUS 1GM/10ML	2	2	15	260
CEFEPIME INJ 1GM	2	5	5	26
CEFTAZIDIME INJ 1GM	1	1	2	606
CHLD ALLERGY LIQ 12.5/5ML	6	6	8	680
CHLORAL CRY HYDRATE	2	2	31	23
CIPROFLOXACN TAB 250MG	2	2	15	75
CLOMIPHENE POW CITRATE	2	3	58	36
COLISTIMETH INJ 150MG	1	1	2	3
COMFORT GEL SUS ANTACID	1	1	5	300
CVS ALLERGY LIQ 12.5/5ML	1	1	14	30
CVS ALLERGY LIQ 25/10ML	1	1	5	150
CVS ANTACID SUS MAX ST	1	1	7	120
CVS ANTACID/ SUS ANTI-GAS	4	4	39	460
DERMAZINC SPR	1	1	10	120
DIPHENHIST LIQ 12.5/5ML	6	6	40	810
DIPHENHYDRAM ELX 12.5/5ML	2	2	45	210

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
1/01/18 - 03/31/2018 - Q1				
DONNATAL ELX	1	1	16	500
DOXYCYCL HYC CAP 100MG	1	1	14	244
EMPTY CAPSUL CAP SIZE 1	1	2	30	60
EQ ANTACID SUS	1	1	5	15
EQ ANTACID SUS ANTI-GAS	1	1	6	120
EQ ANTACID SUS MAX ST	2	2	12	90
ESTRADIOL POW	2	3	30	90
ESTRIOL POW MICRONIZ	1	3	30	120
FLAVOR PLUS LIQ	2	4	30	495
FLECAINIDE TAB 100MG	1	4	14	560
GLYCERIN LIQ	4	7	44	861
HYDROCORT POW	1	1	30	30
HYDROCORT TAB 10MG	1	2	30	240
HYDROCORT AC POW MICRONIZ	1	1	30	30
HYDROXOCOBAL POW	1	1	30	10
HYDROXYUREA CAP 500MG	3	7	30	675
HYDROXYUREA POW	2	2	55	310
HYOSCYAMINE ELX 0.125/5	1	1	8	500
LACTIC ACID SOL 85% USP	1	1	30	60
LANOLIN ANHY OIN	1	2	30	120
LANSOPRAZOLE CAP 30MG DR	3	3	72	125
LANSOPRAZOLE POW	1	1	30	180
LEVETIRACETM INJ 500/5ML	1	1	2	420
LIDO/PRILOCN CRE 2.5-2.5%	123	709	6	34,032
LIDOCAINE SOL 2% VISC	137	143	228	28,269
LISINOPRIL TAB 20MG	1	3	30	180
MEROPENEM INJ 1GM	1	1	1	3
METFORMIN POW HCL	2	2	30	240
METRONIDAZOL POW	1	1	7	60
METRONIDAZOL TAB 250MG	2	2	11	70
METRONIDAZOL TAB 500MG	2	2	21	200
MI-ACID SUS	1	1	6	120
MUPIROCIN OIN 2%	1	1	30	30
NADOLOL TAB 20MG	3	7	30	750
NALTREXONE POW HCL	1	3	30	90
NALTREXONE TAB 50MG	2	3	30	90
NIFEDIPINE POW	1	1	15	30

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
1/01/18 - 03/31/2018 - Q1				
NITRO-BID OIN 2%	3	4	45	120
NYSTATIN SUS 100000	9	9	91	2,240
OMEPRAZOLE CAP 20MG	4	6	44	1,180
OMEPRAZOLE POW	2	4	30	1,890
ORA-PLUS LIQ	2	2	30	660
OSELTAMIVIR CAP 75MG	5	5	19	375
PREDNISOLONE SOL 15MG/5ML	1	1	14	80
PREDNISOLONE SYP 15MG/5ML	5	5	34	1,140
PROGESTERONE POW MICRONIZ	21	29	30	870
PROGESTERONE POW WETTABLE	1	2	30	60
PROPYLENE GL SOL	2	2	30	60
RULOX SUS	26	28	79	5,510
SILDENAFIL TAB 20MG	1	3	30	1,080
SOD CHLORIDE INJ 0.9%	1	1	14	15
SODIUM POW BICARBON	3	3	60	150
STERIL WATER INJ	2	5	15	1,359
SUPREME CRE	1	1	30	30
TACROLIMUS CAP 0.5MG	1	3	30	360
TACROLIMUS CAP 1MG	1	1	30	60
TESTOSTERONE POW	2	2	30	60
TESTOSTERONE POW CYPIONAT	1	1	28	5
THYROID POW PORCINE	1	3	30	180
TOBRAMYCIN INJ 40MG/ML	1	4	1	430
TOPIRAMATE CAP 25MG	2	4	29	240
URSODIOL CAP 300MG	1	1	24	90
VANCOMYCIN INJ 1000MG	3	7	6	24
VANCOMYCIN INJ 10GM	1	1	7	70
WAL-DRYL LIQ 12.5/5ML	2	2	24	420
Total	587	1,266	3,011	119,940

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
4/01/18 - 06/30/2018 - Q2				
A+D PREVENT OIN	3	5	45	480
ALLERGY CHLD LIQ 12.5/5ML	3	3	17	260
ALLERGY REL ELX 12.5/5ML	1	1	5	275
ALLERGY RELF LIQ 50/20ML	1	1	4	100
ALMACONE SUS	1	1	10	200
AMIODARONE TAB 200MG	2	5	30	500
AMLODIPINE TAB 10MG	4	7	54	1,230
ANTACID SUS	3	3	10	200
ANTACID & SUS ANTIGAS	1	1	5	100
ANTACID LIQ SUS	62	66	137	15,471
ANTACID LIQ SUS FAST REL	4	4	13	390
AQUAPHOR OIN	5	5	56	150
ASCORBIC ACD POW	2	3	30	150
ATENOLOL TAB 100MG	2	3	30	216
ATENOLOL TAB 50MG	1	1	14	21
ATROPINE SUL SOL 1% OP	17	19	55	190
BACLOFEN POW	1	1	14	14
BACLOFEN TAB 10MG	1	1	30	90
BANOPHEN LIQ 12.5/5ML	46	49	83	7,133
BENADRYL ALL LIQ 12.5/5ML	1	1	6	120
BORIC ACID POW	1	1	30	25
CARAFATE SUS 1GM/10ML	1	2	12	960
CHERRY SYP	3	6	58	1,060
CHLD ALLERGY LIQ 12.5/5ML	4	4	34	610
CLOMIPHENE POW CITRATE	1	3	30	36
COMFORT GEL SUS ANTACID	1	1	6	240
COMFORT GEL SUS ANTI-GAS	1	1	9	237
CVS ALLERGY LIQ 12.5/5ML	1	1	30	90
CVS ANTACID SUS MAX ST	1	1	3	120
CVS ANTACID SUS SUPREME	1	1	3	240
CVS ANTACID/ SUS ANTI-GAS	8	8	86	1,760
DERMAZINC SPR	1	1	30	120
DESITIN PST 40%	2	2	30	330
DEXAMETHASON ELX 0.5/5ML	1	1	6	270
DIPHENHIST LIQ 12.5/5ML	2	2	10	450
DIPHENHYDRAM ELX 12.5/5ML	1	1	12	240
DONNATAL ELX MINT	1	1	2	100

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
4/01/18 - 06/30/2018 - Q2				
EMPTY CAPSUL CAP SIZE 1	1	3	30	90
EQ ANTACID SUS	1	1	18	180
EQ ANTACID SUS ANTI-GAS	1	1	5	100
ESTRADIOL POW	3	5	58	132
ESTRIOL POW MICRONIZ	1	2	30	90
ETHOXY LIQ DIGLYCOL	1	1	30	30
FLAVOR PLUS LIQ	2	4	30	495
FLECAINIDE TAB 100MG	2	7	29	780
GLYCERIN LIQ	1	3	30	630
GLYCOPYRROL TAB 1MG	1	2	30	900
GLYCOPYRROL TAB 2MG	1	1	30	180
HUMALOG INJ 100/ML	1	2	10	20
HYDROCORT TAB 10MG	2	4	45	375
HYDROCORT AC POW MICRONIZ	1	2	30	120
HYDROQUINONE POW	1	1	30	60
HYDROXYUREA CAP 500MG	3	3	14	133
HYDROXYUREA POW	5	10	29	608
HYOSCYAMINE ELX 0.125/5	1	1	8	500
HYOSYNE ELX 0.125/5	1	3	8	1,500
LANOLIN ANHY OIN	1	2	30	120
LANSOPRAZOLE CAP 30MG DR	6	6	58	340
LIDO/PRILOCN CRE 2.5-2.5%	175	1,203	22	57,744
LIDOCAINE SOL 2% VISC	97	101	206	20,363
LISINOPRIL TAB 20MG	1	3	30	180
MAALOX SUS ADVANCED	1	1	6	120
MAG-AL PLUS LIQ	1	1	3	237
METFORMIN POW HCL	2	2	30	176
METRONIDAZOL TAB 250MG	2	2	16	146
METRONIDAZOL TAB 500MG	2	2	13	100
NADOLOL TAB 20MG	3	9	30	900
NALTREXONE TAB 50MG	1	1	30	30
NAPROXEN POW	1	1	14	140
NITRO-BID OIN 2%	3	3	45	90
NYSTATIN SUS 100000	10	14	118	6,540
OMEPRAZOLE CAP 20MG	1	1	30	80
OMEPRAZOLE POW	1	3	14	595
ORA-PLUS LIQ	3	3	30	940

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
4/01/18 - 06/30/2018 - Q2				
PREDNISOLONE SYP 15MG/5ML	1	1	11	320
PREDNISONE SOL 5MG/5ML	1	1	6	120
PROGESTERONE POW MICRONIZ	24	39	30	1,170
PROPRANOLOL TAB 20MG	1	1	30	84
Q-DRYL LIQ 12.5/5ML	2	2	13	180
RANITIDINE SYP 75MG/5ML	1	1	5	90
RULOX SUS	47	48	124	8,532
SILDENAFIL TAB 20MG	2	3	30	840
SIMPLE SYP	1	1	30	24
SM ANTACID SUS ADVANCED	1	1	4	120
SOD CHLORIDE GRA	1	1	14	25
SOD CHLORIDE INJ 0.9%	2	4	5	22
SOD CHLORIDE TAB 1GM	1	3	12	360
SODIUM POW BICARBON	3	5	75	402
SODIUM POW CHLORIDE	1	2	14	40
SUPREME CRE	1	1	30	30
TACROLIMUS CAP 0.5MG	2	3	35	360
TACROLIMUS CAP 5MG	1	2	30	60
THYROID POW PORCINE	2	5	30	240
TIZANIDINE POW HCL	1	3	14	1,260
URSODIOL CAP 300MG	2	4	30	306
VANCOMYCIN INJ 1 GM	1	1	5	50
VANCOMYCIN INJ 1000MG	2	2	12	204
VANCOMYCIN INJ 10GM	1	1	5	50
ZONISAMIDE CAP 100MG	1	2	30	1,320
Total	636	1,768	2,882	146,151

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/01/18 - 09/30/2018 - Q3				
A+D PREVENT OIN	1	1	30	60
ALLERGY CHLD LIQ 12.5/5ML	3	3	13	690
ALLERGY REL ELX 12.5/5ML	3	3	5	360
ALLERGY RELF LIQ 12.5/5ML	3	3	30	570
ALLERGY RELF LIQ 50/20ML	4	4	24	460
AMIODARONE TAB 200MG	4	8	44	1,015
AMLODIPINE TAB 10MG	5	11	30	2,162
AMLODIPINE TAB 5MG	2	2	30	240
ANTACID SUS	6	6	25	745
ANTACID LIQ SUS	33	36	159	8,924
ANTACID LIQ SUS FAST REL	2	2	10	170
AQUAPHOR OIN	4	4	60	120
AQUAPHOR OIN ADVANCED	1	1	10	30
ATENOLOL TAB 100MG	1	2	30	150
ATENOLOL TAB 50MG	2	6	14	179
ATROPINE SUL SOL 1% OP	7	10	40	100
BACLOFEN POW	1	5	14	70
BACLOFEN TAB 10MG	2	4	44	580
BANOPHEN LIQ 12.5/5ML	47	48	170	7,653
BORIC ACID POW	1	2	14	28
CARAFATE SUS 1GM/10ML	1	1	5	150
CARVEDILOL TAB 25MG	1	1	30	15
CHERRY SYP	2	4	30	798
CHLD ALLERGY LIQ 12.5/5ML	2	2	50	840
CIPROFLOXACN TAB 250MG	1	1	5	20
CLOMIPHENE POW CITRATE	1	1	30	12
COMFORT GEL SUS ANTACID	1	1	2	45
COMFORT GEL SUS ANTI-GAS	1	1	8	240
CVS ALLERGY LIQ 25/10ML	1	1	30	600
CVS ANTACID/ SUS ANTI-GAS	8	8	71	1,080
DESITIN PST 40%	1	1	20	55
DEXAMETHASON ELX 0.5/5ML	1	1	6	240
DIPHENHIST LIQ 12.5/5ML	5	5	37	500
DIPHENHYDRAM ELX 12.5/5ML	2	2	9	230
EMPTY CAPSUL CAP SIZE 1	1	2	30	60
ENALAPRIL TAB 2.5MG	1	1	30	180
ENALAPRIL TAB 20MG	1	2	30	300

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/01/18 - 09/30/2018 - Q3				
EQ ANTACID SUS ANTI-GAS	1	1	2	120
EQ ANTACID SUS MAX ST	1	1	25	200
ESTRADIOL POW	1	2	30	60
ESTRIOL POW MICRONIZ	1	3	30	180
ETOPOSIDE INJ 20MG/ML	1	1	11	26
FLAVOR PLUS LIQ	1	2	30	180
FLECAINIDE TAB 100MG	1	7	15	840
GENTAMICIN INJ 40MG/ML	1	1	30	2,000
GERI-LANTA SUS	1	1	14	90
GLYCERIN LIQ	5	7	30	1,050
GLYCOPYRROL TAB 2MG	2	6	30	828
HUMALOG INJ 100/ML	1	2	10	20
HYDROCORT TAB 10MG	1	3	30	505
HYDROXYUREA CAP 500MG	1	1	14	56
HYDROXYUREA POW	5	16	14	812
KAOPECTATE SUS 262/15ML	1	3	24	1,440
LACTIC ACID SOL 85% USP	2	2	30	120
LANSOPRAZOLE CAP 30MG DR	5	6	55	810
LIDO/PRILOCN CRE 2.5-2.5%	143	936	18	44,928
LIDOCAINE POW HCL	1	1	14	90
LIDOCAINE SOL 2% VISC	92	96	191	19,117
MEROPENEM INJ 1GM	1	1	2	5
METRONIDAZOL TAB 250MG	1	1	10	15
METRONIDAZOL TAB 500MG	3	3	49	430
NADOLOL TAB 20MG	3	11	44	960
NITRO-BID OIN 2%	3	3	59	90
NYSTATIN SUS 100000	11	14	82	4,140
OMEPRAZOLE CAP 20MG	2	3	30	510
OMEPRAZOLE POW	2	6	44	250
ORA-PLUS LIQ	3	5	30	557
PREDNISOLONE SOL 15MG/5ML	1	1	5	320
PREDNISOLONE SYP 15MG/5ML	1	1	5	200
PROGESTERONE POW MICRONIZ	25	37	30	1,110
PROGESTERONE POW WETTABLE	1	1	30	30
PROPRANOLOL TAB 20MG	1	3	30	378
RULOX SUS	46	46	141	6,765
SILDENAFIL TAB 100MG	2	3	23	175

Compounded Medication HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/01/18 - 09/30/2018 - Q3				
SILDENAFIL TAB 20MG	1	1	31	450
SOD CHLORIDE TAB 1GM	1	8	12	960
SODIUM POW BICARBON	1	1	15	60
SODIUM POW CHLORIDE	1	1	14	20
SPIRONOLACT TAB 25MG	1	1	30	40
TACROLIMUS CAP 0.5MG	1	3	30	360
TACROLIMUS CAP 5MG	3	5	57	318
TETRACYCLINE POW	1	1	4	240
THYROID POW PORCINE	3	6	52	262
TIZANIDINE POW HCL	1	7	14	2,940
URSODIOL CAP 300MG	2	2	36	140
VALACYCLOVIR TAB 500MG	1	1	30	150
WAL-DRYL LIQ 12.5/5ML	3	3	8	280
ZONISAMIDE CAP 100MG	1	2	30	1,320
Total	558	1,475	2,843	126,618
Grand Total	2,287	5,250	11,674	492,413

Compounded Medication Utilization – Q4 2017 – Q3 2018

SilverSummit Healthplan

Report Date Range	Total Claims	Unique Members	Number of Units	Days Supply
10/01/2017 -09/30/2018	295	178	60762	3106

Prior Authorization Guideline

Guideline Name Xofluza (baloxavir marboxil)

1 . Indications

Influenza, treatment: Treatment of acute uncomplicated influenza in patients ≥12 years who have been symptomatic for no more than 48 hours.

2 . Criteria

1. Coverage and Limitations

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

   a. The recipient has a diagnosis of Influenza.

      And

   b. The recipient has experienced flu symptoms for less than 48 hours.

      And

   c. The recipient is 12 years of age or older;

      And

   d. The requested dose is appropriate to weight of recipient.

2. Prior Authorization Guidelines:

   a. Prior Authorization approval will be for one single dose.

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Xofluza®

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

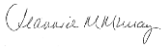
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Unable to approve or disapprove sincedrug has not been reviewed by Anthem P&T Committee as of yet. Does Xofluza show clinical effectiveness greater than Tamiflu? Will there be the ability to allow for preferred drug in this class over Xofluza?

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Xofluza®

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

HPN hasn't reviewed for formulary inclusion at the time of this document's creation. Initial plan is to have non-formulary coverage and have oseltamivir as the formulary covered product for the treatment of acute uncomplicated influenza.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Ryan Bitton

Signature of individual completing this form: _____

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Xofluza®

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Recommend more specific dosage regimen based on weight:

Dose does not exceed one of the following (a or b):

a. Weight 40 kg to < 80 kg: 40 mg (1 tablet) once;
b. Weight ≥ 80 kg: 80 mg (1 tablet) once.

Recommend adding:

Approval duration: 4 weeks(one dose only)

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: ____Tom Beranek_____

Signature of individual completing this form: Tom Beranek _____

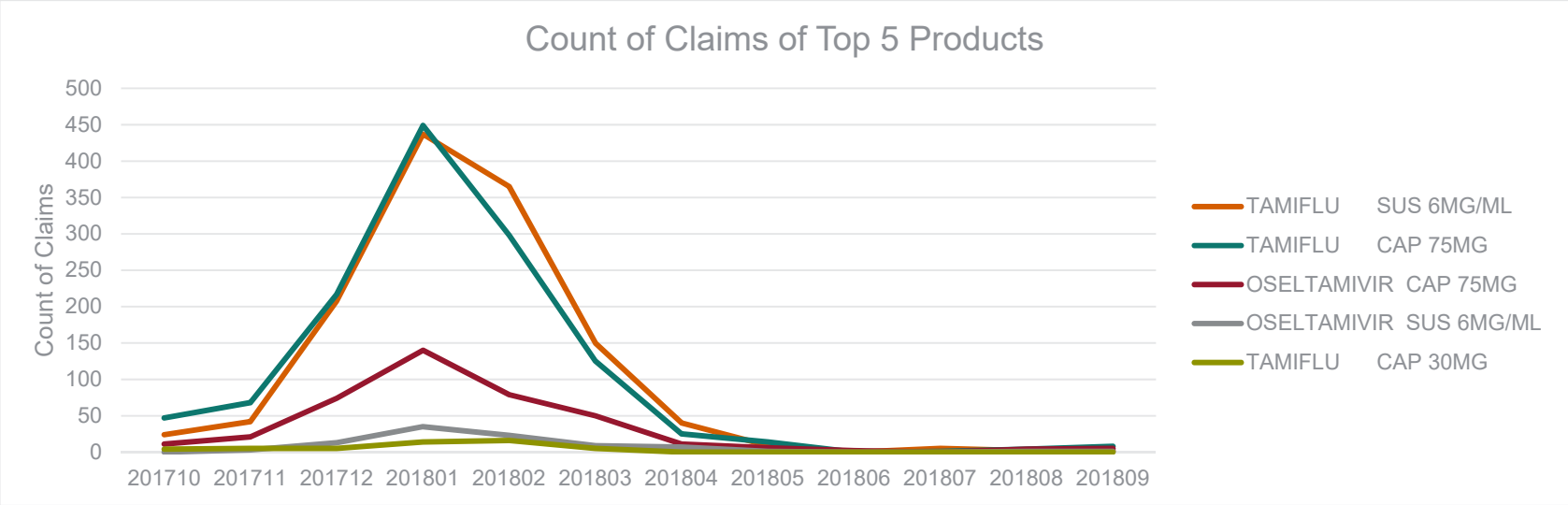
Influenza Antiviral Agents

Summary of Utilization

October 1, 2017 - September 30, 2018

Fee for Service Medicaid

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
TAMIFLU SUS 6MG/ML	1,259	1,284	7,474	118,218	$ 297,934.25
TAMIFLU CAP 75MG	1,214	1,256	6,645	12,400	$ 181,957.85
OSELTAMIVIR CAP 75MG	380	403	1,722	3,201	$ 6,320.23
OSELTAMIVIR SUS 6MG/ML	93	93	414	6,800	$ 5,498.27
TAMIFLU CAP 30MG	42	49	176	551	$ 7,594.99
TAMIFLU CAP 45MG	38	38	202	377	$ 5,313.58
OSELTAMIVIR CAP 30MG	25	27	92	183	$ 689.12
RELENZA MIS DISKHALE	9	9	124	180	$ 619.91
RIMANTADINE TAB 100MG	6	6	132	264	$ 652.96
OSELTAMIVIR CAP 45MG	4	4	18	41	$ 121.53
Grand Total	**3,070**	**3,169**	**16,999**	**142,216**	**$ 506,702.69**



Anthem Flu Utilization

Quarter Serviced	**4th Quarter 2017**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
OSELTAMIVIR 6 MG/ML SUSPENSION	737	737	4385	68580
OSELTAMIVIR PHOS 30 MG CAPSULE	27	27	142	405
OSELTAMIVIR PHOS 45 MG CAPSULE	25	25	125	250
OSELTAMIVIR PHOS 75 MG CAPSULE	805	809	4161	8017
RELENZA 5 MG DISKHALER	4	4	40	80
TAMIFLU 6 MG/ML SUSPENSION	204	204	1181	17040
Grand Total	**1800**	**1806**	**10034**	**94372**

Quarter Serviced	**1st Quarter 2018**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
OSELTAMIVIR 6 MG/ML SUSPENSION	1889	1911	11262	178342
OSELTAMIVIR PHOS 30 MG CAPSULE	33	33	174	484
OSELTAMIVIR PHOS 45 MG CAPSULE	23	23	115	230
OSELTAMIVIR PHOS 75 MG CAPSULE	1314	1329	6924	13211
RELENZA 5 MG DISKHALER	1	1	5	20
TAMIFLU 45 MG CAPSULE	1	1	5	10
TAMIFLU 6 MG/ML SUSPENSION	63	63	388	6245
TAMIFLU 75 MG CAPSULE	3	3	15	30
Grand Total	**3323**	**3364**	**18888**	**198572**

Quarter Serviced	**2nd Quarter 2018**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
OSELTAMIVIR 6 MG/ML SUSPENSION	183	184	1117	16495
OSELTAMIVIR PHOS 30 MG CAPSULE	5	5	25	70
OSELTAMIVIR PHOS 45 MG CAPSULE	2	2	10	20
OSELTAMIVIR PHOS 75 MG CAPSULE	132	133	700	1317
TAMIFLU 6 MG/ML SUSPENSION	5	5	28	420
Grand Total	**327**	**329**	**1880**	**18322**

Quarter Serviced	**3rd Quarter 2018**			
Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
OSELTAMIVIR 6 MG/ML SUSPENSION	26	26	158	2220
OSELTAMIVIR PHOS 30 MG CAPSULE	1	1	5	10
OSELTAMIVIR PHOS 75 MG CAPSULE	42	42	217	410
Grand Total	**69**	**69**	**380**	**2640**

Influenza Treatment HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
OSELTAMIVIR CAP 30MG	63	64	21	903
OSELTAMIVIR CAP 45MG	44	44	15	430
OSELTAMIVIR CAP 75MG	1,326	1,335	71	13,242
OSELTAMIVIR SUS 6MG/ML	1,056	1,062	139	96,740
RELENZA MIS DISKHALE	1	1	30	20
RIMANTADINE TAB 100MG	2	2	15	30
TAMIFLU CAP 45MG	1	1	5	10
TAMIFLU CAP 75MG	2	2	5	20
TAMIFLU SUS 6MG/ML	75	75	63	6,600
Total	2,570	2,586	364	117,995
01/01/18 - 03/31/18 - Q1				
OSELTAMIVIR CAP 30MG	107	107	45	1,521
OSELTAMIVIR CAP 45MG	56	56	15	555
OSELTAMIVIR CAP 75MG	2,247	2,273	94	22,896
OSELTAMIVIR SUS 6MG/ML	2,551	2,582	244	241,425
RELENZA MIS DISKHALE	2	2	40	40
RIMANTADINE TAB 100MG	2	2	7	21
TAMIFLU CAP 30MG	2	2	5	20
TAMIFLU CAP 45MG	1	1	5	10
TAMIFLU CAP 75MG	17	17	5	170
TAMIFLU SUS 6MG/ML	69	70	66	6,660
Total	5,054	5,112	526	273,318
04/01/18 - 06/30/18 - Q2				
OSELTAMIVIR CAP 30MG	13	13	17	190
OSELTAMIVIR CAP 45MG	2	2	5	20
OSELTAMIVIR CAP 75MG	208	210	57	2,080
OSELTAMIVIR SUS 6MG/ML	200	202	96	19,255
TAMIFLU CAP 75MG	1	1	5	10
TAMIFLU SUS 6MG/ML	3	3	7	240
Total	427	431	187	21,795

Influenza Treatment HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/01/18 - 09/30/18 - Q3				
OSELTAMIVIR CAP 30MG	5	5	5	60
OSELTAMIVIR CAP 45MG	1	1	5	10
OSELTAMIVIR CAP 75MG	51	51	22	507
OSELTAMIVIR SUS 6MG/ML	41	41	35	3,480
Total	98	98	67	4,057
Grand Total	8,149	8,227	1,144	417,165

Xofluza Utilization – Q4 2017 – Q3 2018

Silversummit Healthplan

Report Date Range	Medication Name	Total Claims	Unique Members	Number of Units	Days Supply
10/01/2017 - 09/30/2018	OSELTAMIVIR CAP 30MG	15	15	222	71
10/01/2017 - 09/30/2018	OSELTAMIVIR CAP 45MG	7	7	70	35
10/01/2017 - 09/30/2018	OSELTAMIVIR CAP 75MG	428	415	4239	2232
10/01/2017 - 09/30/2018	OSELTAMIVIR SUS 6MG/ML	316	309	28625	1793
10/01/2017 - 09/30/2018	TAMIFLU CAP 75MG (Brand)	10	10	92	57
10/01/2017 - 09/30/2018	TAMIFLU SUS 6MG/ML (Brand)	22	22	2030	118

SilverSummit Healthplan

Therapeutic Class Overview
Antivirals, Influenza

INTRODUCTION

- Influenza is an infectious respiratory illness caused by the influenza A and influenza B viruses. Influenza epidemics occur annually in the United States, typically from late fall to early spring. Although the majority of infected individuals recover without complications, some cases of influenza result in severe illness or death *(Grohskopf et al 2018)*.
- The virus is primarily transmitted through direct contact large-particle respiratory droplets from an infected individual's coughs and sneezes. It is also spread through contact with surfaces contaminated by infected respiratory droplets. Adults begin to shed virus 1 day prior to symptom onset, and they remain contagious for 5 to 7 days after falling ill *(Centers for Disease Control and Prevention [CDC] 2016)*.
- Signs and symptoms of uncomplicated influenza illness include fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis. Complications of influenza infection include sinusitis, otitis media, pneumonia, sepsis, and exacerbation of chronic medical conditions. Elderly adults, young children, pregnant women, and patients with chronic medical conditions have a higher risk of developing complications from influenza *(CDC 2018[a])*.
- Annual influenza vaccination is the most effective method for preventing seasonal influenza virus infection and its complications. Antiviral prescription medications are also available for influenza prophylaxis and treatment; however, antiviral chemoprophylaxis is not a substitute for annual influenza vaccination *(Grohskopf et al 2018)*.
- Initiation of antiviral therapy to treat influenza is recommended as early as possible for patients with confirmed or suspected influenza who are hospitalized, have severe, complicated, or progressive illness, or are at higher risk for influenza complications *(Fiore et al 2011)*. Additionally, due to the increased influenza activity and a lower vaccine effectiveness for the 2017-2018 influenza season, a December 2017 CDC advisory recommended that all hospitalized patients and all high-risk patients (hospitalized or outpatient) with suspected influenza should be treated as soon as possible with a neuraminidase inhibitor. Although initiation within 2 days of symptom onset is ideal, the CDC stated that benefit may still be seen even when treatment is initiated later *(CDC 2017)*.
- Three classes of antiviral medications are available and included in this review. The adamantanes include amantadine and Flumadine (rimantadine). The neuraminidase inhibitors include Rapivab (peramivir), Relenza (zanamivir), and Tamiflu (oseltamivir). Currently, the only endonuclease inhibitor on the market is Xofluza (baloxavir marboxil), which was approved by the Food and Drug Administration (FDA) in late October 2018.
- Although the adamantanes are active against influenza A virus, resistance is high amongs currently circulating virus strains. The adamantanes lack activity against influenza B virus. Therefore, amantadine and rimantadine are not recommended for treatment or chemoprophylaxis during the current influenza season *(CDC 2018[b])*.
- The neuraminidase inhibitors are active against both influenza A and influenza B viruses. Rapivab (peramivir), Relenza (zanamivir), and oseltamivir are the only antivirals recommended for the current influenza season in the United States *(CDC 2018[b])*.
- Since Xofluza (baloxavir) was recently approved, it has not been incorporated into existing guidelines. The CDC plans to revise their 2018-2019 recommendations to incorporate baloxavir into their recommendations (*CDC 2018[b]*).
- Circulating influenza viruses are constantly evolving, and drug-resistant influenza virus strains have been reported. Prescribers should refer to influenza drug susceptibility patterns and treatment effects when selecting an antiviral agent *(CDC 2018[b])*.
- Medispan class: Antiparkinson, Dopaminergic and Influenza Agents. The only agent from the Antiparkinson, Dopaminergic category that will be included in this review is amantadine for the influenza indication.

Table 1. Medications Included Within Class Review

Drug	Generic Availability
amantadine	✔
Flumadine (rimantadine)	✔
Rapivab (peramivir)	-
Relenza (zanamivir)	-
Tamiflu (oseltamivir)	✔
Xofluza (baloxavir marboxil)	-

(*Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018)*

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication[1]	amantadine[2]	Flumadine (rimantadine)	Rapivab[3] (peramivir)	Relenza[4] (zanamivir)	Tamiflu[5] (oseltamivir)	Xofluza (baloxavir marboxil)
Prophylaxis and treatment of signs and symptoms of infection caused by various strains of influenza A virus	✔					
Prophylaxis and treatment of illness caused by various strains of influenza A virus in adults (17 years and older)		✔				
Prophylaxis against influenza A virus in children (1 to 16 years of age)		✔				
Treatment of acute uncomplicated influenza in patients 2 years and older who have been symptomatic for no more than 2 days			✔			
Prophylaxis of influenza in adults and pediatric patients aged 5 years and older				✔		
Treatment of uncomplicated acute illness due to influenza A and B virus in adults and pediatric patients aged 7 years and older who have been symptomatic for no more than 2 days				✔		
Prophylaxis of influenza A and B in patients 1 year and older					✔	
Treatment of acute, uncomplicated illness due to influenza A and B infection in patients 2 weeks of age and older who have been symptomatic for no more than 48 hours					✔	

Indication[1]	amantadine[2]	Flumadine (rimantadine)	Rapivab[3] (peramivir)	Relenza[4] (zanamivir)	Tamiflu[5] (oseltamivir)	Xofluza (baloxavir marboxil)
Treatment of acute uncomplicated influenza in patients 12 years and older who have been symptomatic for no more than 48 hours						✔

[1] The changing of viruses over time is a limitation of use for antivirals. The emergence of resistance mutations could decrease drug effectiveness. Other factors, such as changes in viral virulence, may also diminish the clinical benefit of antivirals. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when selecting an antiviral.
[2] Amantadine is also indicated in the treatment of parkinsonism and drug-induced extrapyramidal reactions.
[3] Limitations of use for Rapivab (peramivir):
- Efficacy is based on clinical trials of naturally occurring influenza in which the predominant influenza infections were influenza A virus; a limited number of subjects infected with influenza B virus were enrolled.
- Efficacy could not be established in patients with serious influenza requiring hospitalization.

[4] Limitations of use for Relenza (zanamivir):
- Not recommended for treatment or prophylaxis of influenza in individuals with underlying airways disease (such as asthma or chronic obstructive pulmonary disease) due to the risk of serious bronchospasm.
- Has not been proven effective for treatment of influenza in individuals with underlying airways disease.
- Has not been proven effective for prophylaxis of influenza in the nursing home setting.

[5] Limitations of use for Tamiflu (oseltamivir):
- Not recommended for patients with end-stage renal disease not undergoing dialysis.

(Prescribing information: amantadine capsules 2017, amantadine oral solution 2016, amantadine tablets 2017, Flumadine 2010, Rapivab 2018, Relenza 2018, Tamiflu 2018, Xofluza 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

Adamantanes

- Clinical trials have demonstrated that the adamantanes are effective in both the prophylaxis and treatment of influenza A virus *(Bryson et al 1980, Crawford et al 1988, Dolin et al 1982, Hall et al 1987, Hayden et al 1989, Jackson et al 2011, Jefferson et al 2006[a], Jefferson et al 2006[b], Monto et al 1995, Reuman et al 1989)*.
- One systematic review assessed the efficacy and safety of adamantanes in healthy adults by analyzing 20 prophylaxis and 13 treatment randomized trials comparing amantadine or rimantadine with placebo. For prophylaxis, amantadine was 61% better than placebo at reducing influenza risk (P<0.001). Although rimantadine was 72% better than placebo at preventing influenza, statistical significance was not achieved. There was significant heterogeneity between the prophylaxis trials, and only a small sample size was available for rimantadine compared to amantadine. For treatment, amantadine and rimantadine both reduced the duration of fever by 1 day. Both agents caused gastrointestinal side effects, but amantadine caused significantly more adverse effects in the central nervous system than rimantadine *(Jefferson et al 2006[a])*.
- Influenza A virus resistance to amantadine and rimantadine has developed over the years. During the 2009 to 2010 influenza season, 100% of the 18 influenza H3N2 viruses tested in the United States were resistant to adamantanes. Similarly, 99.8% of the pandemic H1N1 viruses tested were resistant to adamantanes. Due to influenza A virus resistance and lack of activity against influenza B virus, the adamantanes are not recommended for the current influenza season *(CDC 2010[b], CDC 2018[b])*.

Neuraminidase inhibitors

- The neuraminidase inhibitors have demonstrated efficacy for their respective indications. Relenza (zanamivir) inhalation and oral oseltamivir are effective in both the prophylaxis and treatment of influenza A and B. Clinical trials have demonstrated a reduction in laboratory-confirmed influenza, illness, fever duration, secondary complications, and

household contacts with influenza infection *(Aoki et al 2003, Chik et al 2004, Cooper et al 2003, Fry et al 2014, Halloran et al 2007, Hayden et al 1997, Hayden et al 1999, Hayden et al 2000, Hayden et al 2004, Hedrick et al 2000, Hiba et al 2011, Kaiser et al 2003, Kawai et al 2005, Kawai et al 2006, Lin et al 2006, MIST Study Group 1998, Monto et al 1999[a], Monto et al 1999[b], Monto et al 2002, Nicholson et al 2000, Peters et al 2001, Reuman et al 1989, Singh et al 2003, Treanor et al 2000, Turner et al 2003, Wang et al 2012, Welliver et al 2001, Whitley et al 2001)*.

- One systematic review analyzed 20 oseltamivir and 26 Relenza (zanamivir) randomized, placebo-controlled trials in order to better define their efficacy and safety. In prophylaxis trials, the risk of symptomatic influenza was reduced by 3.05% in patients treated with oseltamivir compared to placebo and 1.98% in patients treated with Relenza (zanamivir) compared to placebo. In adults, the time to first alleviation of symptoms was reduced by 0.7 days (P<0.0001) in patients receiving oseltamivir compared to placebo and 0.6 days (P<0.00001) in patients receiving Relenza (zanamivir) compared to placebo. Oseltamivir significantly reduced the time to alleviation of symptoms in non-asthmatic children and decreased the incidence of self-reported pneumonia. Relenza (zanamivir) significantly reduced the risk of bronchitis in adults with influenza. Neither treatment was a significant improvement over placebo in time to symptom alleviation in asthmatic children or risk of hospitalizations, otitis media, or sinusitis. Many studies included were at a high risk of selection bias due to inadequate reporting and a high risk of attrition bias due to selective reporting. All trials were sponsored by the manufacturers *(Jefferson et al 2014)*.
- In a systematic review of other published systematic reviews and meta-analyses, treatment of influenza with neuraminidase inhibitors (oseltamivir or zanamivir) was found to be likely effective in reducing mortality amongst hospitalized patients; the odds of mortality appeared especially lower when therapy was started early (≤ 48 hours of symptom onset). When used for treatment in the general population, these agents appear to reduce the duration of symptoms by approximately 0.5 to 1 day. Both oseltamivir and zanamivir were found likely to be effective at reducing secondary symptomatic influenza transmission when used prophylactically (*Doll et al 2017*).
- Rapivab (peramivir) intravenous (IV) infusion is approved for the treatment of influenza A and B in adults. The primary endpoint for the main clinical trial supporting FDA approval of Rapivab (peramivir) was time to alleviation of symptoms. The trial evaluated 296 previously healthy adults presenting with the onset of influenza-like illness within the previous 48 hours and a positive influenza rapid antigen test. In this multicenter, double-blind, placebo-controlled clinical trial, patients were randomized to Rapivab (peramivir) 300 mg, 600 mg, or placebo as a single IV dose. Acetaminophen use was permitted. Patients self-reported body temperature, symptoms, and resumption of activities over 14 days. The primary endpoint, the median time to alleviation of symptoms, was significantly earlier with Rapivab (peramivir) 300 mg (59.1 hours) and 600 mg (59.9 hours) compared to placebo (81.8 hours; both P=0.0092). There was no significant difference in the incidence of all adverse events in patients receiving Rapivab (peramivir) compared to placebo. Diarrhea was the most common adverse event, occurring in 14.1%, 15.2% and 17% of the Rapivab (peramivir) 300 mg, 600 mg, and placebo groups, respectively *(Kohno et al 2010)*.
- Although studies have evaluated Rapivab (peramivir) in hospitalized patients and in children, both of these populations are not included in the FDA-approved labeling *(De Jong et al 2014, Ison et al 2014, Ison et al 2013, Sugaya et al 2012)*. The Phase 3 clinical trial of Rapivab (peramivir) in hospitalized influenza patients failed to meet its primary endpoint of reducing the time to clinical resolution compared to placebo. There are no clinical endpoints that have been validated for clinical trials of neuraminidase inhibitors treating hospitalized patients with influenza *(FDA 2014)*. In 2009, the United States issued an Emergency Use Authorization (EUA) program allowing Rapivab (peramivir) for the treatment of suspected or confirmed 2009 H1N1 influenza A virus infection in hospitalized patients *(Birnkrant 2009)*. Patients eligible for treatment were hospitalized, unable to tolerate or unresponsive to other available antivirals, or lacked a dependable oral or inhalation drug delivery route. The Public Health Emergency determination for the 2009 H1N1 influenza pandemic expired on June 23, 2010 *(CDC 2010[a])*.
- Numerous placebo-controlled trials have demonstrated the efficacy of neuraminidase inhibitors individually, but head-to-head trials directly comparing the agents are limited. One randomized, double-blind, placebo-controlled safety trial compared the use of oseltamivir, Relenza (zanamivir), and placebo in 390 healthy adults for influenza chemoprophylaxis over 16 weeks. The study showed that both treatments were well tolerated compared to placebo, and there were no discontinuations due to adverse events *(Anekthananon et al 2013)*.
- A Phase 3 multinational, multicenter, double-blind, randomized, noninferiority trial compared a single dose of 300 or 600 mg IV Rapivab (peramivir) to 5 days of oral oseltamivir in 1,091 patients with seasonal influenza. The primary endpoint, time to alleviation of influenza symptoms, had a median of 78.0 hours in patients receiving 300 mg of Rapivab (peramivir), 81.0 hours in patients receiving 600 mg of Rapivab (peramivir), and 81.8 hours in patients receiving oseltamivir. Both strengths of Rapivab (peramivir) were noninferior to oseltamivir with a noninferiority margin of 0.170.

There was no significant difference between treatments in the incidence of complications of influenza infection *(Kohno et al 2011)*.

- A meta-analysis including 2 controlled clinical trials and 5 observational trials (N = 1676) examined the comparative efficacy of IV Rapivab (peramivir) and oral oseltamivir in the treatment of seasonal influenza. No significant differences between treatments were noted for the following outcomes: mortality, hospital length of stay, virus titer 48 hours after admission, and incidence of adverse events. However, the time to resolution of influenza symptoms or fever was shorter with Rapivab (peramivir) versus oseltamivir treatment (mean difference, -7.17 hours; $p < 0.01$) (*Lee et al 2017*).
- Observational studies comparing the clinical efficacy of Rapivab (peramivir), Relenza (zanamivir), and oseltamivir in treating influenza have demonstrated within-class variation in the time to alleviation of influenza symptoms. The lack of robust data from randomized, head-to-head trials prevents the recommendation of one neuraminidase inhibitor over another. Local and seasonal susceptibility trends, route of administration, and patient-specific factors such as age and compliance should be taken into account when selecting an agent for antiviral drug therapy *(Kawai et al 2008, Takemoto et al 2013)*.
- While influenza virus strains resistant to specific neuraminidase inhibitors have emerged, overall resistance remains low. According to surveillance data on seasonal influenza virus strains, the rate of resistance to oseltamivir is 1 to 3% and resistance to Relenza (zanamivir) is less than 1% *(Li et al 2015)*.

Endonuclease inhibitor

- In a Phase 3, double-blind, randomized, placebo- and oseltamivir-controlled trial (CAPSTONE-1), 1436 patients 12 to 64 years of age with influenza-like illness were randomized in a 2:2:1 ratio to receive a single, weight-based oral dose of baloxavir, treatment-dose oseltamivir for 5 days, or matching placebo. The primary endpoint, time to alleviation of influenza symptoms, was 53.7 hours (95% confidence interval [CI], 49.5 to 58.5) with baloxavir compared with 80.2 hours (95% CI, 72.6 to 87.1) with placebo ($p < 0.001$). The median time to alleviation of symptoms was similar between baloxavir and oseltamivir (53.5 hours and 53.8 hours, respectively). Treatment-related adverse events were more common with oseltamivir (8.4%) than baloxavir (4.4%; $p = 0.009$), or placebo (3.9%) (*Hayden et al 2018*).

CLINICAL GUIDELINES

- Annual influenza vaccination is the most effective method for preventing seasonal influenza virus infection and its complications. All individuals 6 months of age and older should receive an influenza vaccination each year, unless contraindicated. The prophylactic antiviral administration is not a substitute for early influenza vaccination *(Grohskopf et al 2018)*.
- Amantadine and rimantadine are not recommended for antiviral treatment or prophylaxis of influenza A virus strains in the United States due to high rates of resistance *(American Academy of Pediatrics [AAP] 2018, Fiore et al 2011, CDC 2018[b])*.
- The antivirals recommended by the CDC for the current influenza season include oseltamivir, Relenza (zanamivir) and Rapivab (peramivir). Routine or widespread use of antivirals for chemoprophylaxis is not recommended due to concerns for viral resistance. Oseltamivir and Relenza (zanamivir) are recommended for post-exposure prophylaxis in patients who are severely immunosuppressed and in patients at a high risk for influenza complications who are either not a candidate for vaccination or received their annual vaccination less than 2 weeks prior to exposure *(CDC 2018[b])*.
- Treatment of influenza with antiviral therapy is recommended as early as possible for patients with confirmed or suspected influenza who are hospitalized, have severe, complicated, or progressive illness, or are at a high risk for complications *(CDC 2018[b])*.
- Populations at a high risk for influenza complications and recommended to receive antiviral treatment include children younger than 2 years old, adults age 65 and above, pregnant or postpartum women, American Indians, Alaska Natives, obese patients with a body mass index (BMI) of 40 kg/m^2 and above, patients younger than 19 years old receiving long-term treatment with aspirin, residents of nursing homes, and patients with immunosuppression, chronic disorders (eg, pulmonary, cardiovascular, renal, hepatic, hematological and metabolic), or neurologic conditions *(CDC 2018[b])*. Additionally, due to the increased influenza activity and a lower vaccine effectiveness for the 2017-2018 influenza season, a December 2017 CDC advisory recommends that all hospitalized patients and all high-risk patients (hospitalized or outpatient) with suspected influenza should be treated as soon as possible with a neuraminidase inhibitor. Although initiation within 2 days of symptom onset is ideal, the CDC is stating that benefit may still be seen even when treatment is initiated later *(CDC 2017)*.

- Antiviral therapy works best when administered within 48 hours of symptom onset. Treatment initiation should not be delayed for the results of diagnostic testing. Early administration of antivirals may shorten the duration of fever, reduce the risk of influenza-related complications such as otitis media and pneumonia, reduce death in hospitalized patients, and decrease the duration of hospitalization in hospitalized children *(CDC 2018[b])*.

SAFETY SUMMARY

- Common adverse events with adamantanes include nausea, dizziness, insomnia, headache, anorexia, dry mouth, and agitation.
- Amantadine and rimantadine should be used with caution in patients with epilepsy due to an increased risk for seizures.
- Amantadine has anticholinergic effects and is contraindicated in patients with untreated angle closure glaucoma. There have also been reports of death from overdose and suicide attempts with amantadine.
- Common adverse events with neuraminidase inhibitors include nausea, vomiting, and headache. The most common adverse effect with Rapivab (peramivir) is diarrhea.
- All 3 neuraminidase inhibitors have labeled warnings for neuropsychiatric events such as hallucinations and delirium. Patients should be monitored for signs of abnormal behavior.
- Oseltamivir and Rapivab (peramivir) have warnings for serious skin and hypersensitivity reactions, including Stevens-Johnson Syndrome.
- Relenza (zanamivir) has a warning for bronchospasm and should not be used in patients with asthma or chronic obstructive pulmonary disease. It is also contraindicated in patients with milk protein allergies.
- Common adverse events with Xofluza (baloxavir marboxil) include diarrhea, headache, bronchitis, nausea, and nasopharyngitis.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration*

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
amantadine	Capsules, oral solution, tablets	Oral	Once daily or twice daily Adults: 200 mg once daily or 100 mg twice daily Pediatric patients: 1 to 9 years: 4.4 to 8.8 mg/kg/day not to exceed 150 mg per day 9 to 12 years: 100 mg twice daily The safety and efficacy of amantadine in newborn infants and infants below the age of 1 year have not been established.	Should be taken for 10 days following a known exposure. If using in conjunction with vaccine until antibody response, then take for 2 to 4 weeks. Treatment of illness should be started within 24 to 48 hours of symptom onset and continued for 24 to 48 hours after symptoms disappear. For adult patients intolerant to 200 mg daily dose because of central nervous system or other toxicities: 100 mg daily dose Because amantadine is primarily excreted in the urine, it accumulates in the plasma and in the body when renal function declines. Thus, the dose of amantadine should be reduced in patients with renal impairment and in individuals who are 65 years of age or older according to the following: For CrCl = 30 to 50 mL/min:

				200 mg 1st day, then 100 mg daily For CrCl = 15 to 29 mL/min: 200 mg 1st day, then 100 mg on alternate days For CrCl < 15 mL/min and HD: 200 mg every 7 days For patients ≥ 65 years: 100 mg once daily The dose of amantadine may need reduction in patients with congestive heart failure, peripheral edema, or orthostatic hypotension.
Flumadine (rimantadine)	Tablets	Oral	Twice daily **Adults (17 years and older)** Treatment: 100 mg twice daily for 7 days Prophylaxis: 100 mg twice daily **Pediatric patients** Prophylaxis in patients 1 to 9 years: 5 mg/kg/day, not to exceed 150 mg per day 10 to 16 years: Refer to the adult dose The safety and efficacy of rimantadine in pediatric patients below the age of 1 year have not been established.	Treatment of illness should be started within 48 hours of symptoms. A suspension can be made from the tablets and is stable for 14 days. Dose adjustment in patients ≥ 65 years: 100 mg once daily Dose adjustment in patients with CrCl < 29 mL/min: 100 mg daily Dose adjustment in patients with severe hepatic dysfunction: 100 mg daily
Rapivab (peramivir)	Injection	IV	Patients ≥ 13 years: 600 mg as a single dose Patients < 13 years: 2 to 12 years: 12 mg/kg (maximum dose 600 mg) as a single dose Safety and effectiveness in pediatric patients < 2 years of age have not been established.	One time dose should be provided within 2 days of onset of influenza symptoms A single dose administered by IV infusion for a minimum of 15 minutes. Rapivab must be diluted prior to administration. Dose adjustment in adults and adolescents 13 years of age or older with CrCl = 30 to 49 mL/min: 200 mg Dose adjustment in pediatric patients 2 to 12 years of age with CrCl = 30 to 49

				mL/min: 4 mg/kg Dose adjustment in adults and adolescents 13 years of age or older with CrCl = 10 to 29 mL/min: 100 mg Dose adjustment in pediatric patients 2 to 12 years of age with CrCl = 10 to 29 mL/min: 2 mg/kg HD: Administer after dialysis
Relenza (zanamivir)	Inhalation powder (in blisters)	Oral inhalation via Diskhaler device	Once daily or twice daily, depending on the indication Treatment (≥ 7 years): 10 mg twice daily for 5 days Prophylaxis in household setting (≥ 5 years): 10 mg once daily for 10 days Prophylaxis in community outbreak (adults and adolescents): 10 mg once daily for 28 days	The 10-mg dose is provided by 2 inhalations (one 5-mg blister per inhalation). Patients scheduled to use an inhaled bronchodilator at the same time as Relenza should use their bronchodilator before taking Relenza. If Relenza is prescribed for children, it should be used only under adult supervision and instruction, and the supervising adult should first be instructed by a healthcare professional. Due to the low systemic bioavailability of Relenza following oral inhalation, no dosage adjustments are necessary for patients with renal Impairment; however, the potential for drug accumulation should be considered.
Tamiflu (oseltamivir)	Capsules, powder for oral suspension	Oral	Once daily or twice daily, depending on the indication **Patients ≥ 13 years** Treatment: 75 mg twice daily for 5 days Prophylaxis: 75 mg once daily for at least 10 days following close contact with an infected individual and up to 6 weeks during a community outbreak. In immunocompromised patients, may be continued for up to 12 weeks. **Patients < 13 years** Treatment:	Start treatment within 48 hours of symptom onset or close contact with the infected individual. Taking with food may enhance tolerability. In an emergency, a suspension can be made from capsules. Dosage adjustment is recommended for patients with a CrCl between 10 and 60 mL/minute and for patients with ESRD undergoing routine HD or CAPD. Not recommended for patients with ESRD not undergoing dialysis. No dosage adjustment for mild to moderate hepatic impairment.

			• 2 weeks to < 1 year: 3 mg/kg twice daily for 5 days • 1 to 12 years: 30 to 75 mg twice daily for 5 days; specific weight-based dosing recommendations as follows: ○ ≤ 15 kg: 30 mg twice daily ○ 15.1 kg to 23 kg: 45 mg twice daily ○ 23.1 kg to 40 kg: 60 mg twice daily ○ ≥ 40.1 kg: 75 mg twice daily <u>Prophylaxis</u>: • 1 to 12 years: 30 to 75 mg once daily for 10 days; specific weight-based dosing recommendations as follows: ○ ≤ 15 kg: 30 mg once daily ○ 15.1 kg to 23 kg: 45 mg once daily ○ 23.1 kg to 40 kg: 60 mg once daily ○ ≥ 40.1 kg: 75 mg once daily • During a community outbreak, can continue for up to 6 weeks (or up to 12 weeks in immuno-compromised patients).	Safety not evaluated in patients with severe hepatic impairment.
Xofluza (baloxavir marboxil)	Tablets	Oral	Single, weight-based dose <u>Patients 40 kg to < 80 kg:</u> • Single dose of 40 mg <u>Patients ≥ 80 kg:</u> • Single dose of 80 mg Safety and effectiveness in pediatric patients < 12 years of age have not been established.	Initiate treatment within 48 hours of symptom onset. Take orally as a single dose with or without food; however, coadministration with dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives, antacids, or oral supplements should be avoided. No dosage adjustment is recommended for CrCl ≥ 50 mL/min or mild to moderate hepatic impairment; safety has not been evaluated in severe renal or hepatic impairment.

CAPD=continuous ambulatory peritoneal dialysis; CrCl =creatinine clearance; ESRD=end stage renal disease; HD=hemodialysis
*See the current prescribing information for full details

CONCLUSION

- The first line of protection against influenza is vaccination. All individuals 6 months of age and older without contraindications should receive yearly influenza vaccination *(AAP 2018, Fiore et al 2011, Grohskopf et al 2018)*.

- Antivirals are available for the prevention and treatment of influenza. Overall, the adamantanes and neuraminidase inhibitors have demonstrated safety and efficacy for their respective indications. However, amantadine and rimantadine are not currently recommended due to high rates of resistance in circulating influenza virus strains *(CDC 2018[b])*.
- Relenza (zanamivir) and oseltamivir are both effective in preventing influenza but are not substitutes for annual vaccination. They are recommended as post-exposure chemoprophylaxis in patients with a high risk for influenza complications who are not sufficiently protected by vaccination *(Fiore et al 2011, CDC 2018[b], Harper et al 2009, Panel on Opportunistic Infections 2018)*. Rapivab (peramivir) is not approved or recommended for influenza prophylaxis *(CDC 2018[b])*.
- Rapivab (peramivir), Relenza (zanamivir), and oseltamivir effectively treat influenza by reducing the duration of fever and illness. Initiation of treatment is recommended as soon as possible for patients with suspected influenza who are hospitalized, severely ill, or at high risk for influenza complications *(AAP 2018, CDC 2017, CDC 2018[b], Fiore et al 2011, Harper et al 2009, Panel on Opportunistic Infections 2018)*.
- Xofluza (baloxavir marboxil) is a recently approved antiviral agent with a novel mechanism of action (inhibition of polymerase acidic (PA) endonuclease). It has not yet been incorporated into existing guidelines.
- Limited within-class comparisons prevent the recommendation of one neuraminidase inhibitor over another. Factors to consider when selecting an antiviral agent include the route of administration, seasonal and geographical susceptibility trends, and patient-specific factors such as age and compliance *(Takemoto et al 2013)*.
- The most common adverse events with amantadine and rimantadine are nausea, insomnia, dizziness, headache, anorexia, dry mouth, and agitation. The adamantanes are associated with an increased risk for seizures.
- The most common adverse events with Relenza (zanamivir) and oseltamivir are headache, nausea, and vomiting. Diarrhea is the most common adverse event with Rapivab (peramivir). The neuraminidase inhibitors have a labeled warning for neuropsychiatric events such as delirium and abnormal behavior leading to injury.
- The most common adverse events with Xofluza (baloxavir) are diarrhea, headache, bronchitis, nausea, and nasopharyngitis.

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Publication Date: November 12, 2018

Prior Authorization Guideline

Guideline Name Entresto (sacubitril/valsartan)

1 . Indications

Heart failure: Reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction; usually administered in conjunction with other heart failure therapies, in place of an angiotensin-converting enzyme (ACE) inhibitor or other angiotensin II receptor blocker (ARB)

Proposed removal of prior authorization criteria.

2 . Criteria

~~1. Coverage and Limitations~~

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

~~a. The recipient has a diagnosis of chronic heart failure NYHA Class II to IV; and~~
~~b. The recipient has reduced left ventricular ejection fraction (LVEF); and~~
~~c. The recipient is 18 years of age or older; and~~
~~d. The prescriber is a cardiologist or there is documentation in the recipient's medical record that a cardiologist has been consulted; and~~
~~e. The recipient has had a trial of an ACE or an ARB for at least four weeks prior to the initiation of therapy; and~~
~~f. The recipient will not concurrently receive an ACE inhibitor; and~~
~~g. The recipient is on an individualized dose of a beta blocker or the recipient has a contraindication to beta blocker use; and~~
~~h. Entresto® will be given twice daily with a maximum dose of 97/103 mg.~~

~~2. Prior Authorization Guidelines:~~
~~a. Prior Authorization approval will be for one year.~~

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Entresto®

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

I. Individual is using for the treatment of New York Heart Association (NYHA) class II, III, or IV heart failure symptoms; AND II. Individual has a left ventricular ejection fraction less than or equal to 35%.

May wish to call out when it should not be approved for any of the following: I. Individual is pregnant or wishing to become pregnant; OR II. Individual is breastfeeding; OR III. Individual will be utilizing an angiotensin-converting enzyme (ACE) inhibitor OR angiotensin receptor blocker (ARB) in combination with Entresto (sacubitril/valsartan); OR IV. Individual will be utilizing in combination with Tekturna (aliskiren)/Tekturna HCT (aliskiren/hydrochlorothiazide) and has a diagnosis of: A. Diabetes; OR B. Renal impairment (eGFR) < 60 mL/min/1.73 m2; OR V. Individual has a history of hereditary angioedema or angioedema related to previous ACE inhibitor or ARB therapy; OR VI. Individual has severe hepatic impairment (Child-Pugh C); (Note: Entresto (sacubitril/valsartan) has a black box warning for use in pregnancy as it can cause injury and death to a developing fetus. When pregnancy is detected, Entresto should be discontinued and alternative treatments considered. If Entresto is considered lifesaving for the mother, she should be advised of the potential risk to the fetus.)

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting. If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: Jeannine M Murray

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Entresto

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

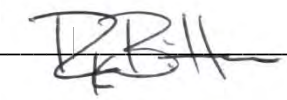
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

HPN has a protocol for Entresto and feels the criteria ensures use in appropriate population. HPN does not advocate PA removal at this time. HPN criteria is attached for completeness. It includes appropriate diagnosis, appropriate ejection fraction, beta-blocker use or contraindication, specialist requirement, and other safety considerations.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Ryan Bitton

Signature of individual completing this form: 

Clinical Pharmacy Program Guidelines for Entresto

Program	Prior Authorization
Medication	Entresto (valsartan-sacubitril)
Markets in Scope	Nevada
Issue Date	5/2015
Pharmacy and Therapeutics Approval Date	2/2018
Effective Date	4/2018

1. Background:

Entresto (valsartan-sacubitril) is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure patients with chronic heart failure and reduced ejection fraction.

2. Coverage Criteria:

A. **Initial Therapy**

1. **Entresto** will be approved based on **one** of the following criteria:

a. As continuation of therapy initiated during an inpatient stay

-OR-

b. **Entresto** will be approved based on **all** of the following

(1) Diagnosis of heart failure (with or without hypertension)

-AND-

(2) Ejection fraction is less than or equal to 40 percent

-AND-

(3) Heart failure is classified as one of the following:
(a) New York Heart Association Class II
(b) New York Heart Association Class III
(c) New York Heart Association Class IV

-AND-

(4) **<u>One</u>** of the following:

(a) Patient is on a stabilized dose and receiving concomitant therapy with one of the following beta-blockers:
i. bisoprolol
ii. carvedilol
iii. metoprolol

-OR-

(b) Patient has a contraindication or intolerance to beta-blocker therapy

-AND-

5) Patient does not have a history of angioedema

-AND-

(6) Patient will discontinue any use of concomitant ACE Inhibitor or ARB before initiating treatment with Entresto. ACE inhibitors must be discontinued at least 36 hours prior to initiation of Entresto

-AND-

(7) Patient is not concomitantly on aliskiren therapy.

-AND-

(8) Entresto is prescribed by, or in consultation with, a cardiologist.

Authorization will be issued for 12 months.

B. **<u>Reauthorization</u>**

1. **Entresto** will be approved based on **<u>both</u>** of the following criteria:

a. The Entresto dose has been titrated to a dose of 97 mg/103 mg twice daily, or to a maximum dose as tolerated by the patient

-AND-

b. Documentation of positive clinical response to therapy

Authorization will be issued for 12 months.

3. References:

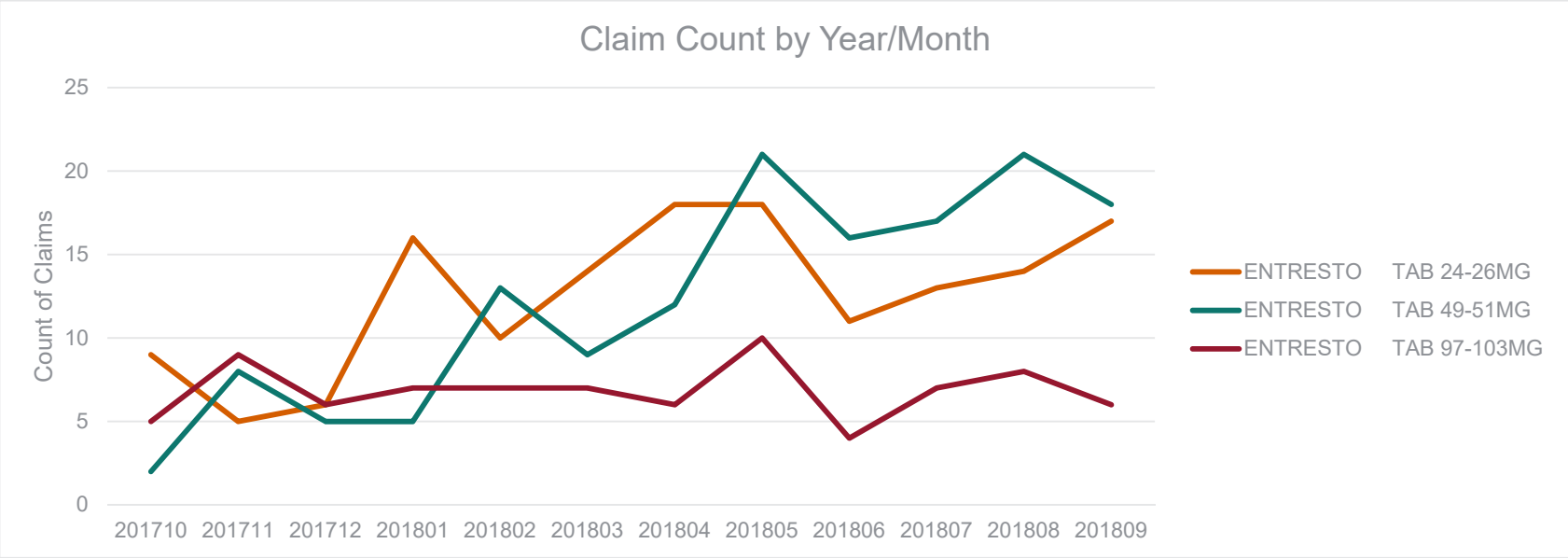
1. Entresto Prescribing Infation. Novartis Pharmaceuticals Corporation. East Hanover, NJ. November 2017.
2. McMurray JJ, Desai AS, Gong J. Dual angiotensin receptor and neprilysin inhibition as an alternative to angiotensin-converting enzyme inhibition in patients with chronic systolic heart failure: rationale for and design of the prospective comparison of ARNI with ACEI to determine impact on global mortality and morbidity in heart failure trial (PARADIGM-HF). European Journal of Heart Failure 2013; 15: 1062–1073
3. McMurray JJ, Packer M, Desai AS, et al. Angio-tensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014;371:993-1004.
4. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure. Circulation 2013; 128:e240-e327.
5. Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFS A Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. *Circulation*. 2016; 134:e282-e293.

Program	Prior Authorization - Entresto (valsartan-sacubitril)
Change Control	
5/2015	New program.
6/2016	Additional criteria added to align with Employer & Individual Medical Necessity program. Updated policy template.
2/2017	Removed requirement that angioedema must be associated with an ACE inhibitor or ARB, based on the 2016 ACC/AHA/HFSA recommendation that Entresto should not be administered to patients with a history of angioedema. Updated references and policy template.
9/2017	Removed BNP requirement.
2/2018	Updated metoprolol to remove specification of metoprolol succinate. Revised ejection fraction from 35% to 40%.

Entresto (Sacubitril/Valsartan)

Summary of Utilization
October 1, 2017 - September 30, 2018
Fee for Service Medicaid

Product Name		Count of Members	Count of Claims	Sum of Days	Sum of Qty		Sum of Amt Paid
ENTRESTO	TAB 24-26MG	136	151	4,354	8,517	$	38,037.92
ENTRESTO	TAB 49-51MG	135	147	4,656	9,366	$	40,073.17
ENTRESTO	TAB 97-103MG	76	82	2,731	5,461	$	26,802.55
Grand Total		**347**	**380**	**11,741**	**23,344**	**$**	**104,913.64**



Entresto (sacubitril/valsartan) HPN Utilization

October 1, 2017 - September 30, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
ENTRESTO	22	46	95	2,650
Total	22	46	95	2,650
01/01/18 - 03/31/18 - Q1				
ENTRESTO	26	53	90	3,120
Total	26	53	90	3,120
04/01/18 - 06/30/18 - Q2				
ENTRESTO	37	73	90	4,380
Total	37	73	90	4,380
07/01/18 - 09/30/18 - Q3				
ENTRESTO	38	76	119	4,468
Total	38	76	119	4,468
Grand Total	123	248	394	14,618

Entresto® (sacubitril/valsartan) Utilization – Q4 2017 – Q3 2018

SilverSummit Healthplan

Report Type	Report Date Range	Total Claims	Unique Members	Number of Units	Days Supply
ENTRESTO TAB 24-26MG	10/01/2017 -09/30/2018	16	5	960	480
ENTRESTO TAB 49-51MG	10/01/2017 -09/30/2018	4	2	210	120
ENTRESTO TAB 97-103MG	10/01/2017 -09/30/2018	12	3	720	360
TOTAL ENTRESTO UTILIZATION	10/01/2017 -09/30/2018	32	10	1890	960

The following page contains current Medicaid Services Manual Chapter 1200, Appendix A coverage criteria for Entresto® (sacuitril/valsartan).

JJJ. Entresto® (sacubitril/valsartan)

Therapeutic Class: Angiotension II Receptor Blocker
Last Reviewed by the DUR Board: November 5, 2015

Entresto® (sacubitril/valsartan) is subject to prior authorization 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. The recipient has a diagnosis of chronic heart failure NYHA Class II to IV; and

   b. The recipient has reduced left ventricular ejection fraction (LVEF); and

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

   d. The prescriber is a cardiologist or there is documentation in the recipient's medical record that a cardiologist has been consulted; and

   e. The recipient has had a trial of an ACE or an ARB for at least four weeks prior to the initiation of therapy; and

   f. The recipient will not concurrently receive an ACE inhibitor; and

   g. The recipient is on an individualized dose of a beta blocker or the recipient has a contraindication to beta blocker use; and

   h. Entresto® will be given twice daily with a maximum dose of 97/103 mg.

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

Therapeutic Class Overview
Angiotensin II Receptor Blockers (ARBs)

INTRODUCTION

- Approximately 92.1 million American adults are living with some form of cardiovascular (CV) disease or the after-effects of stroke according to the American Heart Association (AHA) Heart Disease and Stroke Statistics 2018 update *(Benjamin et al 2018).* Cardiovascular disease accounts for an estimated 836,546 deaths in the US annually; about 1 of every 3 deaths.
- The estimated prevalence of heart failure (HF) is 6.5 million for Americans aged ≥ 20 years. Projections show that the prevalence of HF will increase 46% from 2012 to 2030, resulting in > 8 million people ≥ 18 years of age with HF (*Benjamin et al 2018*).
- Hypertension (HTN) is an independent risk factor for CV disease and increases the mortality risks of CV disease and other diseases *(Benjamin et al 2018).* The 2017 American College of Cardiology (ACC)/AHA clinical practice guideline defines HTN as blood pressure (BP) ≥ 130/80 mm Hg (*Whelton et al 2017).* Nearly half of American adults (46%) have HTN based on this definition.
- Lowering of BP has been shown to reduce the risk of fatal and nonfatal CV events including stroke and myocardial infarctions (MIs). Lipid control, diabetes mellitus (DM) management, smoking cessation, exercise, weight management, and limiting sodium intake may also reduce CV risk *(Benjamin et al 2018).*
- Numerous classes of antihypertensives are available to reduce BP. Some examples of antihypertensives include diuretics, angiotensin converting enzyme inhibitors (ACE-Is), angiotensin II receptor blockers (ARBs), beta blockers, and calcium channel blockers (CCBs). Selection of antihypertensive therapy for a specific patient is determined by patient characteristics such as ethnic group, and the presence of compelling indications such as HF, DM, chronic kidney disease (CKD), history of stroke or MI, and risk factors for coronary heart disease (CHD). Some patients require 2 or more antihypertensives from different pharmacological classes to achieve BP control *(Go et al 2014, Weber et al 2014, Whelton et al 2017).*
- In general, guideline-recommended BP goals in hypertensive adults range from < 130/80 mm Hg to < 140/90 mm Hg *(de Boer et al 2017, Whelton et al 2017).*
  - Blood pressure goals for older patients have long been a point of debate. The SPRINT trial followed patients ≥ 50 years with high BP and increased CV risks under intense hypertensive treatment (with a systolic blood pressure [SBP] goal of < 120 mm Hg) compared to standard HTN treatment (with an SBP goal of < 140 mm Hg) over a period of 3.2 years. The trial ended early; however, results demonstrated a reduced primary composite outcome of MI, acute coronary syndrome (ACS), stroke, HF, or CV death driven mainly by reduced HF events and CV death with intense treatment compared to standard treatment. The SPRINT trial pointed to potential clinical benefits associated with more intensive treatment in certain patients, although early termination of the trial and variations in the BP-measurement technique employed have called into question the generalizability of the results *(SPRINT Research Group 2015).*
  - A recent guideline from the American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) on treatment of HTN in adults aged ≥ 60 years recommends standard and intense SBP treatment goals of < 150 mm Hg and < 140 mm Hg, respectively, with more intense BP reduction reserved for patients with a history of stroke or transient ischemic attack *(Qaseem et al 2017).*
- The cardinal symptoms of HF are dyspnea and fatigue. HF leads to exercise intolerance, fluid retention, pulmonary congestion, and peripheral edema, often resulting in hospitalization (*Yancy* et al, *2013*).
- There are 2 forms of HF:
  - Heart failure with reduced ejection fraction (HFrEF) or systolic HF: ejection fraction (EF) ≤ 40%
  - Heart failure with preserved ejection fraction (HFpEF) or diastolic HF: EF ≥ 50%
- Recent guideline updates from the ACC/AHA/Heart Failure Society of America (HFSA) state that in patients with chronic symptomatic HFrEF New York Heart Association (NYHA) Class II or III who tolerate an ACE-I or ARB, replacement by an angiotensin receptor and neprilysin inhibitor (ARNI), such as sacubitril/valsartan, is recommended to further reduce morbidity and mortality (*Yancy et al 2016, Yancy et al 2017*).

- Sacubitril/valsartan is usually administered in place of an ACE-I or other ARB; although, the role for the management of HF is not as well established as ACE-Is or other ARBs. Based on study data, there is minimal evidence of benefits and harms in the following populations: very elderly patients, African Americans, NYHA Class I or IV, patients with low BP or co-morbid HTN refractory to treatment, and patients with HFpEF. Further studies are warranted in these groups.
- This review includes the ARBs, the ARB combination products, and the only approved ARNI (sacubitril/valsartan). ARBs work primarily through reduction of systemic vascular resistance as a result of selective antagonism of angiotensin II at the angiotensin II AT1 receptor. Angiotensin II is the primary vasoactive hormone.
  - The ARBs are Food and Drug Administration (FDA)-approved to treat HTN. Some ARBs have additional indications for HF, diabetic nephropathy, or CV risk reduction in certain high-risk populations.
  - The ARB combinations are products that combine an ARB with a diuretic (ie, chlorthalidone, hydrochlorothiazide [HCTZ]), a beta blocker (ie, nebivolol), and/or a CCB (ie, amlodipine) in a fixed-dose formulation. By combining agents from different classes, these combination products are meant to increase the effectiveness of antihypertensive therapy through complementary mechanisms of action while minimizing the potential for dose-related adverse effects. All ARB combination products are FDA-approved for the treatment of HTN. Losartan/HCTZ is also indicated to reduce the risk of stroke in patients with HTN and left ventricular (LV) hypertrophy.
  - Sacubitril/valsartan is indicated to reduce the risk of CV death and hospitalization for HF in patients with chronic HFrEF.
- Medispan classes: Angiotensin II Receptor Antagonists; Antihypertensive Combinations - ARB/CCB combinations, beta blocker/ARB combination, ARB/thiazide and thiazide-like combinations, and ARB/CCB/thiazide combinations; Cardiovascular Agents, ARNI – Angiotensin II receptor antagonist/neprilysin inhibitor combination

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Single-Entity ARBs	
Atacand (candesartan)	✔
Avapro (irbesartan)	✔
Benicar (olmesartan)	✔
Cozaar (losartan)	✔
Diovan, Prexxartan (valsartan)	✔ *
Edarbi (azilsartan)	-
eprosartan	✔ †
Micardis (telmisartan)	✔
ARB/Diuretic Combinations	
Atacand HCT (candesartan/hydrochlorothiazide)	✔
Avalide (irbesartan/hydrochlorothiazide)	✔
Benicar HCT (olmesartan/hydrochlorothiazide)	✔
Diovan HCT (valsartan/hydrochlorothiazide)	✔
Edarbyclor (azilsartan/chlorthalidone)	-
Hyzaar (losartan/hydrochlorothiazide)	✔
Micardis HCT (telmisartan/hydrochlorothiazide)	✔
ARB/Beta Blocker Combinations	
Byvalson (valsartan/nebivolol)	-
ARB/CCB Combinations	
Azor (olmesartan/amlodipine)	✔
Exforge (valsartan/amlodipine)	✔
Twynsta (telmisartan/amlodipine)	✔
ARB/CCB/Diuretic Combinations	
Exforge HCT (valsartan/amlodipine/hydrochlorothiazide)	✔
Tribenzor (olmesartan/amlodipine/hydrochlorothiazide)	✔
ARB/Neprilysin inhibitor Combination	

Drug	Generic Availability
Entresto (sacubitril/valsartan)	-

Abbreviations: ARB = angiotensin II receptor blocker; CCB = calcium channel blocker
*Prexxartan (valsartan) oral solution was FDA-approved in December 2017; however, it has not launched. There is no generic valsartan oral solution available.
†Branded Teveten (eprosartan) is no longer marketed.
(Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018)

INDICATIONS

Table 2. FDA-approved indications for single-entity ARBs

Indication	Atacand (candesartan)	Avapro (irbesartan)	Benicar (olmesartan)	Cozaar (losartan)	Diovan/ Prexxartan (valsartan)	Edarbi (azilsartan)	eprosartan	Micardis (telmisartan)
Hypertension in adults	✔	✔	✔	✔	✔	✔	✔	✔
Hypertension in children ages 1 to < 17 years	✔							
Hypertension in children ages 6 to 16 years			✔	✔	✔			
Treatment of diabetic nephropathy in hypertensive patients with type 2 DM, an elevated serum creatinine, and proteinuria		✔		✔				
Heart failure (NYHA Class II to IV) in adults	✔				✔			
Reduction in the risk of stroke in patients with hypertension and LV hypertrophy				✔				
Post-MI: Reduction of cardiovascular mortality in clinically stable patients with LV failure or LV dysfunction					✔			
Cardiovascular risk reduction in patients 55 years of age or older at high risk of developing major cardiovascular events who are unable to take ACE-Is								✔

Abbreviations: ACE-I = angiotensin converting enzyme inhibitor; LV = left ventricular; MI = myocardial infarction; NYHA = New York Heart Association
(Prescribing information: Atacand 2018, Avapro 2016, Benicar 2018, Cozaar 2015, Diovan 2017, Edarbi 2016, eprosartan 2014, Micardis 2018, Prexxartan 2018)

Table 3. FDA-approved indications for combination products containing ARBs

Drug	Hypertension	Reduction in the Risk of CV Death and HF Hospitalization in Patients with Chronic HF and Reduced EF	Reduction in the Risk of Stroke in Patients with Hypertension and Left Ventricular Hypertrophy
ARB/Diuretic Combinations			
Atacand HCT (candesartan/hydrochlorothiazide)	✔ *	-	-
Avalide (irbesartan/hydrochlorothiazide)	✔ †	-	-
Benicar HCT (olmesartan/hydrochlorothiazide)	✔ *	-	-
Diovan HCT (valsartan/hydrochlorothiazide)	✔ †	-	-

Drug	Hypertension	Reduction in the Risk of CV Death and HF Hospitalization in Patients with Chronic HF and Reduced EF	Reduction in the Risk of Stroke in Patients with Hypertension and Left Ventricular Hypertrophy
Edarbyclor (azilsartan/chlorthalidone)	✔ †	-	-
Hyzaar (losartan/hydrochlorothiazide)	✔ ‡	-	✔ §
Micardis HCT (telmisartan/hydrochlorothiazide)	✔ *	-	-
ARB/Beta Blocker Combination			
Byvalson (valsartan/nebivolol)	✔ †	-	-
ARB/CCB Combinations			
Azor (olmesartan/amlodipine)	✔ †	-	-
Exforge (valsartan/amlodipine)	✔ †	-	-
Twynsta (telmisartan/amlodipine)	✔ †	-	-
ARB/CCB/Diuretic Combinations			
Exforge HCT (valsartan/amlodipine/hydrochlorothiazide)	✔ *	-	-
Tribenzor (olmesartan/amlodipine/hydrochlorothiazide)	✔ *	-	-
ARB/Neprilysin inhibitor Combination			
Entresto (sacubitril/valsartan)		✔ ‖	

Abbreviations: ARB = angiotensin II receptor blocker; CCB = calcium channel blocker; CV = cardiovascular; EF = ejection fraction; HF = heart failure

*This fixed-dose combination is not indicated for initial therapy.

†Indicated to treat HTN in patients not adequately controlled on monotherapy or as initial therapy in patients who are likely to need multiple drugs to achieve their BP goals.

‡The fixed-dose combination is not indicated for initial therapy, except when the HTN is severe enough that the value of achieving prompt BP control exceeds the risks of initiating combination therapy in these patients.

§There is evidence that this benefit does not extend to African American patients.

‖NYHA Class II to IV

(Prescribing information: Atacand HCT 2016, Avalide 2017, Azor 2017, Benicar HCT 2017, Byvalson 2016, Diovan HCT 2015, Edarbyclor 2016, Entresto 2017, Exforge 2015, Exforge HCT 2015, Hyzaar 2015, Micardis HCT 2018, Tribenzor 2017, Twynsta 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

Single-Entity ARBs

- ARBs have demonstrated efficacy for the treatment of HTN in adults. A Cochrane systematic review of 46 randomized, placebo-controlled trials evaluated the BP lowering ability of 9 different ARBs (N = 13,451) in patients with a baseline BP of 156/101 mm Hg. On average, SBP was lowered by 8 mm Hg and diastolic blood pressure (DBP) by 5 mm Hg with maximum recommended doses of ARBs. No clinically meaningful differences within the ARB class were observed in the reduction of BP *(Heran et al 2008).*
  - Meta-analyses have shown that ACE-Is and ARBs have similar long-term effects on BP *(Sanders et al 2011, Savarese et al 2013).* Additionally, a Cochrane review involving 11,007 subjects with primary HTN found no evidence of a difference in total mortality or CV outcomes for ACE-Is in comparison to ARBs (*Li 2014*).
- Telmisartan is indicated to reduce CV risk in patients unable to take ACE-Is. The ONTARGET trial compared telmisartan and ramipril monotherapy and in combination with each other and demonstrated no significant difference between any groups in death from CV causes, MI, stroke, or hospitalization for HF *(ONTARGET Investigators 2008).* In the

TRANSCEND trial, no significant difference was observed between telmisartan and placebo in death from CV causes, MI, stroke, or HF hospitalizations. The composite endpoint of death from CV causes, MI, and stroke occurred in significantly fewer patients in the telmisartan group, but this significance was lost after adjustment for multiplicity of comparisons and overlap with the primary outcome *(Foulquier et al 2014, TRANSCEND Investigators 2008)*.

- Losartan is indicated to reduce the risk of stroke in patients with HTN and LV hypertrophy. The efficacy of losartan was demonstrated in the LIFE trial and its corresponding sub-analyses. Losartan was compared to therapy with atenolol. Results demonstrated a 24.9% relative risk reduction for stroke in patients treated with losartan-based regimens compared to atenolol-based regimens *(Dahlöf et al 2002)*. However, a post-hoc analysis in African American patients showed an increase in the composite of CV death, MI, and stroke with losartan compared to atenolol *(Julius et al 2004)*.
- Candesartan and valsartan are indicated to treat HF. Trials demonstrated the efficacy of candesartan alone and in combination with ACE-I therapy compared to placebo in reducing the risk of all-cause mortality, CV death, and/or HF hospitalization *(McMurray et al 2003, Pfeffer et al 2003b, Yusuf et al 2003)*. When compared to enalapril in the RESOLVD trial, candesartan was not significantly better in improving 6-minute walking distance, NYHA functional class, or quality of life *(McKelvie et al 1999)*. Losartan was compared to captopril in patients with HF, and no significant difference was observed in renal function or all-cause mortality *(Pitt et al 1997, Pitt et al 2000)*. However, there was a significantly lower risk of sudden death and resuscitated cardiac arrest with losartan *(Pitt et al 2000)*. The Val-HeFT trial showed no significant difference in all-cause mortality between valsartan and placebo. However, the valsartan group demonstrated a significant improvement in NYHA functional class, HF hospitalizations, morbidity, and mortality *(Cohn et al 2001)*.
- Valsartan is indicated to reduce CV mortality in patients with post-MI LV failure or dysfunction. The VALIANT trial compared valsartan with captopril and combination therapy with valsartan plus captopril. No significant differences in all-cause mortality, CV death, reinfarction, or HF hospitalization were observed between monotherapy groups or combination therapy compared to captopril monotherapy *(Pfeffer et al 2003a)*. Losartan has also been evaluated in patients post-MI compared to and in combination with captopril. Results were similar to those of the VALIANT trial *(Dickstein et al 2002)*.
- Irbesartan and losartan are indicated for the treatment of diabetic nephropathy in patients with type 2 DM and HTN. However, clinical benefit in diabetic nephropathy has been shown with other ARBs, including candesartan, losartan, telmisartan, and valsartan *(Barnett et al 2004, Galle et al 2008, Hou et al 2007, Mogensen et al 2000, Viberti et al 2002)*.
- The ORIENT and ROADMAP studies followed patients with DM and compared the effects of olmesartan versus placebo. Outcomes demonstrated a higher rate of death from CV causes in both trials compared to placebo. This finding contradicts outcomes of other studies that include ARBs and/or olmesartan. A number of factors may have contributed to these outcomes including concomitant medications, patients with higher CV risks, and other potential confounders. Further studies in diabetic patients are needed to validate findings *(Haller et al 2011, Imai et al 2011)*.
- Studies have demonstrated that the combination of 2 inhibitors of the renin angiotensin-aldosterone system (RAAS), including an ACE-I with an ARB, provides no renal or CV benefits, with an increase in significant adverse events, particularly in patients with DM and/or renal insufficiency. Most notably, patients receiving combination therapy had increased rates of hyperkalemia, hypotension, and renal dysfunction. All agents in the class have safety warnings against combined use *(Fried et al 2013, ONTARGET Investigators 2008, Parving et al 2012, Pfeffer et al 2003a, Sakata et al 2015)*.

Combination Products Containing ARBs

- Clinical trials assessing the combination ARBs in the treatment of HTN have demonstrated that, in general, dual therapy combinations of ARBs plus a diuretic (either HCTZ or chlorthalidone) or amlodipine achieve greater reductions in BP and higher BP control rates compared to monotherapy regimens of ARBs, amlodipine, or diuretics *(Chrysant et al 2004, Chrysant et al 2008, Derosa et al 2014, Destro et al 2008, Flack et al 2009, Littlejohn et al 2009, Neutel et al 2006, Neutel et al 2008, Neutel et al 2012, Philipp et al 2007, Sachse et al 2002, Salerno et al 2004, Sharma et al 2007a, Sharma et al 2012, Waeber et al 2001, Zhu et al 2012)*. A meta-analysis by Conlin et al found that combination therapy with ARBs and HCTZ resulted in substantially greater reductions in SBP and DBP compared to ARB monotherapy *(Conlin et al 2000)*.
- Trials assessing triple therapy regimens with an ARB, amlodipine, and HCTZ demonstrate significantly greater BP reductions with triple therapy compared to combination and monotherapy *(Calhoun et al 2009a, Calhoun et al 2009b, Destro et al 2010, Ohma et al 2000, Wright et al 2011)*.

- The safety and efficacy of nebivolol/valsartan 5/80 mg was based on a double-blind, placebo-controlled, parallel-group, dose-escalating, Phase 3, randomized controlled trial in 4,159 patients with Stage 1 or 2 HTN. Patients were randomized to 1 of 4 treatment arms (with a total of 7 dose groups plus placebo): (1) nebivolol/valsartan (5/80 mg, 5/160 mg, or 10/160 mg); (2) nebivolol monotherapy (5 mg or 20 mg); (3) valsartan monotherapy (160 mg or 320 mg); or (4) placebo. All treatment was administered in fixed doses once per day for 4 weeks; doses were then doubled for weeks 5 to 8 of treatment. Compared to placebo, nebivolol/valsartan 5/80 mg significantly lowered SBP by 8.3 mmHg and DBP by 7.2 mmHg, monotherapy with nebivolol 5 mg lowered SBP by 4.7 mmHg and DBP by 4.4 mmHg, and monotherapy with valsartan 80 mg lowered SBP by 5.4 mmHg and DBP by 3.9 mmHg after 4 weeks of treatment. Higher doses of the combination did not lead to further clinically meaningful reductions in BP. No adverse events were observed more frequently with nebivolol/valsartan compared to placebo. As anticipated with beta blocker and ARB therapy, serious adverse reactions such as hypotension or hyperkalemia may occur *(Giles et al 2014)*.
- Head-to-head trials have not consistently demonstrated superiority of one ARB combination product over another *(Ambrosioni et al 2010, Bobrie et al 2005, Cushman et al 2012, Derosa et al 2014, Fogari et al 2006, Lacourcière et al 2003, Ohma et al 2000, Sharma et al 2007b, Toh et al 2016, White et al 2008, Wright et al 2011)*.
- The efficacy and safety of sacubitril/valsartan were evaluated in the PARADIGM-HF trial. (*McMurray et al 2014*). A total of 8,442 patients were randomized head-to-head to enalapril 10 mg twice daily or sacubitril/valsartan 97/103 mg twice daily.
- In the PARADIGM-HF trial, the following results were demonstrated after 2.25 years of treatment:
  - CV mortality: The absolute risk was 3.1% less for sacubitril/valsartan-treated patients than those treated with enalapril (risk reduction [RR], 20%; hazard ratio [HR], 0.8; 95% confidence interval [CI], 0.71 to 0.89; P < 0.001; number needed to treat [NNT], 32; 95% CI, 22 to 62).
  - HF hospitalization: The absolute risk was 2.8% less for sacubitril/valsartan-treated patients than those treated with enalapril (RR, 21%; HR, 0.79; 95% CI, 0.71 to 0.89; P < 0.001; NNT, 36; 95% CI, 21 to 77).
  - Combined measure of CV mortality or HF hospitalization (primary endpoint): The absolute risk was 4.7% less for sacubitril/valsartan-treated patients than those treated with enalapril (RR, 20%; HR, 0.8; 95% CI, 0.73 to 0.87; P < 0.001; NNT, 22; 95% CI, 15 to 35).
  - Symptomatic relief: Kansas City Cardiomyopathy Questionnaire (KCCQ) scores were utilized to measure a patient's physical functioning, symptoms, and quality of life (range, 0 to 100 points) with higher scores indicating better health status. At 8 months, scores significantly improved by 1.64 points favoring sacubitril/valsartan over enalapril (P = 0.001). There are different approaches to determining clinical significant KCCQ scores. Based on the varied approaches, clinically significant changes in KCCQ scores have ranged from a difference of 5-point to 10-point declines. In trials, changes of 4 points have been noted in stable HF patients; therefore, the 1.6-point difference in KCCQ for sacubitril/valsartan may not have resulted in an enhanced quality of life when compared to those treated with enalapril regardless of statistical significance (*Green et al 2000, Cardiovascular Outcomes 2008*).
- *Packer et al* published a follow-up analysis of the PARADIGM-HF trial, which outlined the incremental effects of sacubitril/valsartan over enalapril for those with non-fatal progression of HF in surviving patients.
  - Data demonstrated that sacubitril/valsartan-treated patients had slower progression of clinical deterioration compared to enalapril-treated patients in many endpoints that are markers for HF progression (ie, intensified outpatient therapy, emergency department visits, number of hospitalizations, etc.). However, sacubitril/valsartan was not significantly different from enalapril in the number of hospitalized days per admission per patient or in patients requiring cardiac resynchronization therapy, ventricular assist device implants, or a heart transplant (*Packer et al 2015*).
- A separate analysis of the PARADIGM-HF trial reported results for additional composite endpoint rates:
  - CV mortality, HF hospitalization, MI, stroke, and resuscitated sudden death: 24.3% with sacubitril/valsartan vs 28.4% with enalapril (HR, 0.83; 95% CI, 0.76 to 0.90; P < 0.001).
  - CV mortality, non-fatal MI, unstable or other hospitalized angina, or percutaneous or surgical coronary revascularization: 17.1% with sacubitril/valsartan vs 20.3% with enalapril (HR, 0.83; 95% CI, 0.75 to 0.92; P < 0.001) (*Mogensen et al 2017*).
- *Lewis et al* published an analysis focused specifically on the health-related quality of life outcomes in PARADIGM-HF. Consistent with the main publication, small but statistically significant improvements in KCCQ scores were reported. At 8 months, the sacubitril/valsartan group noted improvements versus the enalapril group in both KCCQ clinical summary score (CSS) (+0.64 vs -0.29; P = 0.008) and KCCQ overall summary score (OSS) (+1.13 vs -0.14; P < 0.001). Additionally, at 8 months, the proportion of patients with a clinically significant improvement (≥ 5-point increase) in KCCQ score was slightly greater with sacubitril/valsartan vs enalapril (34.5% vs 33.4% for OSS and 32.8% vs 32.6% for

CSS) and the proportion with deterioration (≥ 5-point decrease) was less with sacubitril/valsartan versus enalapril (27.2% vs 30.5% for OSS and 27.2% vs 31.2% for CSS). Trends were similar through the 36-month time period but were not statistically significant at some later time points; the ability to draw conclusions is limited by the low completion rate of 29% at 36 months (*Lewis et al 2017*).

- *Chandra et al* examined the effects of sacubitril/valsartan on physical and social activity limitations in patients with HF in a secondary analysis of the PARADIGM-HF trial. Patients receiving this therapy had significantly better adjusted change scores in most physical and social activities at 8 months and during 36 months as compared to patients given enalapril. The largest improvements were in household chores (adjusted change score difference, 2.35; 95% CI: 1.19 to 3.50; P < 0.001) and sexual relationships (adjusted change score difference, 2.71; 95% CI, 0.97 to 4.46; P = 0.002) (*Chandra et al 2018*).
- Based on a cohort analysis of data from the run-in period of PARADIGM-HF, a total of 2,079 patients (19.8%) discontinued treatment with sacubitril/valsartan and were identified as not tolerating treatment. A total of 55% of patients who withdrew from therapy discontinued due to adverse effects (53.7% during phase 1 of the run-in period with enalapril and 56.1% during phase 2 of the run-in period with sacubitril/valsartan).
  - According to the analysis, an increased risk of discontinuation of either drug during run-in was associated with patients with a low estimated glomerular filtration rate (adjusted odds ratio [OR], 1.49; 95% CI, 1.35 to 1.65), HF due to ischemic cause (adjusted OR, 1.25; 95% CI, 1.13 to 1.39), higher N-terminal pro-B-type natriuretic peptide (adjusted OR, 1.2 per log increment; 95% CI, 1.14 to 1.26), and lower systolic BP (adjusted OR, 1.11 per 10 mmHg decrease; 95% CI, 1.07 to 1.14).
  - In patients tolerant to enalapril, an increased risk of sacubitril/valsartan discontinuation was associated with lower DBP (adjusted OR, 1.19 per 10 mm Hg decrease; 95% CI, 1.11 to 1.27).
  - The most common adverse effects for enalapril and sacubitril/valsartan were hypotension (24.7% vs 29.8%, respectively), hyperkalemia (29.4% vs 22.5%, respectively), and worsening renal function (30.6% vs 31.6%, respectively). Of note, angioedema occurred in 0.2% of patients entering the run-in period; however, taking into account the baseline group, this may be lower than observed in a real world setting (*Desai et al 2016*).
- As part of the post-marketing requirements for sacubitril/valsartan, a clinical trial evaluating cognitive effects was required. This trial is not anticipated to be completed until October 2021 (*FDA approval letter 2015*). However, an analysis of cognitive-related events in HFrEF trials was conducted. Based on a search of adverse event reports, dementia-related adverse effects were similar for enalapril and sacubitril/valsartan for both the narrow (0.36% vs 0.29%, respectively; HR, 0.73; 95% CI, 0.33 to 1.59) and broad search terms (2.3% vs 2.48%, respectively; HR, 1.01; 95% CI, 0.75 to 1.37). PARADIGM-HF patients were followed for a median of 2.25 years (upper range to 4.3 years); however, longer term follow-up may be warranted in order to detect any potential impacts on cognition (*Cannon et al 2016*).

CLINICAL GUIDELINES

- The 2017 ACC/AHA guideline for the prevention, detection, evaluation, and management of high BP in adults *(Whelton et al 2017)* offers updated classifications of HTN and goals of treatment (see Table 4).

Table 4. Classification of BP measurements

BP Category	BP	Treatment or follow-up
Normal	SBP < 120 mm Hg *and* DBP < 80 mm Hg	▪ Evaluate yearly; lifestyle changes are recommended
Elevated	SBP 120 - 129 mm Hg *and* DBP < 80 mm Hg	▪ Evaluate in 3 to 6 months; lifestyle changes are recommended
HTN stage 1	SBP 130 - 139 mm Hg *or* DBP 80 - 89 mm Hg	▪ Assess the 10-year risk for heart disease and stroke using the ASCVD risk calculator. ▪ If ASCVD risk is < 10%, lifestyle changes are recommended. A BP target of < 130/80 mm Hg may be reasonable. ▪ If ASCVD risk is > 10%, or the patient has known CVD, DM, or CKD, lifestyle changes and 1 BP-lowering medication are recommended. A target BP of < 130/80 mm Hg is recommended.

HTN stage 2	SBP ≥ 140 mm Hg *or* DBP ≥ 90 mm Hg	▪ Lifestyle changes and BP-lowering medication from 2 different classes are recommended.

Abbreviations: ASCVD = atherosclerotic cardiovascular disease, BP = blood pressure, CKD = chronic kidney disease, CVD = cardiovascular disease, DBP = diastolic blood pressure, DM = diabetes mellitus, HTN = hypertension, SBP = systolic blood pressure

- In patients with stage 1 HTN, it is reasonable to initiate therapy with a single antihypertensive agent. In patients with stage 2 HTN and BP more than 20/10 mm Hg higher than their target, 2 first-line agents of different classes should be initiated.
  - First-line antihypertensive agents include: thiazide diuretics, CCBs, and ACE-Is or ARBs.
  - Diuretics, ACE-Is, ARBs, CCBs, and beta blockers have been shown to prevent CVD compared with placebo.
    - ARBs were notably less effective in preventing HF and stroke compared with CCBs in black patients. Thiazide diuretics (especially chlorthalidone) or CCBs are the best initial choice for single-drug therapy in this population.
  - ARBs are preferred for treatment of HTN for those with CKD stage 3, or for stage 1 or 2 with albuminuria.
- The American Diabetes Association position statement on DM and HTN *(de Boer et al 2017)* recommends that most patients with DM and HTN be treated to a goal BP of < 140/90 mm Hg. Lower BP targets such as < 130/80 mm Hg may be appropriate for individuals at high risk of CVD.
  - Treatment for HTN should include drug classes demonstrated to reduce CV events in patients with DM: ACE-Is, ARBs, thiazide diuretics, or dihydropyridine CCBs.
  - Patients with BP ≥ 160/100 mm Hg should have prompt initiation of 2 drugs or a single-pill combination of drugs demonstrated to reduce CV events in patients with DM.
  - An ACE-I or ARB, at the maximum tolerated dose indicated for BP treatment, is the recommended first-line treatment for HTN in patients with DM and urine albumin-to-creatinine ratio ≥ 30 mg/g creatinine.
- The American Academy of Pediatrics clinical practice guideline for high BP in children and adolescents *(Flynn et al 2017)* recommends that the treatment goal with nonpharmacologic and pharmacologic therapy should be a reduction in SBP and DBP to < 90th percentile and < 130/80 mm Hg in adolescents ≥ 13 years old.
  - In hypertensive children and adolescents who have failed lifestyle modifications, clinicians should initiate pharmacologic treatment with an ACE-I, ARB, long-acting CCB, or thiazide diuretic.
  - Children and adolescents with CKD, HTN, and proteinuria should be treated with an ACE-I or ARB.
- Various other guidelines and position statements place ARBs as first-line therapy in patients with DM and microalbuminuria; with stable CAD and HTN; and after an MI. ARBs have demonstrated clinical benefit and reductions in morbidity and mortality in these populations *(Amsterdam et al 2014, Go et al 2014, Rosendorff et al 2015, Weber et al 2014).*
  - Due to differences in the activity of the RAAS, ARBs are often less effective as HTN monotherapy in black patients (African or Caribbean descent). Alternative first-line options for these patients include CCBs and thiazide diuretics *(Weber et al 2014).*
- HF guidelines recommend evidence-based maximally tolerated doses of ACE-Is or ARBs, and beta blockers and/or diuretics, as needed, for first-line treatment in patients with HFrEF (NYHA Class I to IV; Stage C) (*Ponikowski et al 2016, Yancy et al 2013, Yancy et al 2016, Yancy et al 2017).*
- Key recommendations from the 2016 and 2017 Focused Update of the ACC/AHA/HFSA HF guidelines related to ACE-Is, ARBs, and ARNI in Stage C HFrEF include the following (*Yancy et al 2016, Yancy et al 2017):*
  - The clinical strategy of inhibition of the RAAS with ACE-Is or ARBs or ARNI in conjunction with evidence-based beta blockers, and aldosterone antagonists in selected patients, is recommended for patients with chronic HFrEF to reduce morbidity and mortality. (Sacubitril/valsartan is recommended with a lower level of evidence than ACE-Is and ARBs.)
  - The use of ACE-Is is beneficial for patients with prior or current symptoms of HFrEF to reduce morbidity and mortality.
  - The use of ARBs to reduce morbidity and mortality is recommended in patients with prior or current symptoms of chronic HFrEF who are intolerant to ACE-Is because of cough or angioedema.
  - In patients with chronic symptomatic HFrEF NYHA Class II or III who tolerate an ACE-I or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.
  - ARNI therapy should not be administered concomitantly with ACE-Is or within 36 hours of the last dose of an ACE-I.
  - ARNI therapy should not be administered to patients with a history of angioedema.

SAFETY SUMMARY

Boxed Warnings

- Use during pregnancy should be avoided. When pregnancy is detected, ARBs should be discontinued as soon as possible. Drugs that act directly on the RAAS can cause injury and death to the developing fetus.

Contraindications

- ARBs are contraindicated in patients with DM who are also receiving Tekturna (aliskiren) therapy.
- ARB combinations containing diuretics (ie, HCTZ, chlorthalidone) are contraindicated in patients with anuria.
- Nebivolol/valsartan is additionally contraindicated in patients with severe bradycardia, heart block greater than first degree, cardiogenic shock, decompensated cardiac failure, sick sinus syndrome (unless a permanent pacemaker is in place), and severe hepatic impairment.
- Sacubitril/valsartan is contraindicated in patients with a history of angioedema related to previous ACE-I or ARB therapy concomitant use with aliskiren in patients with diabetes or ACE-Is in all patients. Sacubitril/valsartan should not be administered within 36 hours of switching from or to an ACE-I.

Warnings and Precautions

- In general, ARBs have warnings for fetal toxicity, hypotension (especially in volume- or salt-depleted patients), impaired renal function, and hyperkalemia/electrolyte imbalances. Treatment should be discontinued when pregnancy is detected.
  - Candesartan and olmesartan have warnings for morbidity in infants < 1 year of age.
  - Olmesartan has a unique warning for sprue-like enteropathy, which is manifested by severe, chronic diarrhea with substantial weight loss.
  - Telmisartan has a unique warning for use in patients with impaired hepatic function, as it is eliminated mostly by biliary excretion.
- Diuretics (ie, HCTZ, chlorthalidone) may alter glucose tolerance and raise levels of cholesterol, triglycerides, and serum uric acid levels (which may precipitate gout). Diuretics may cause elevations of serum calcium and monitoring is recommended in patients with hypercalcemia.
  - HCTZ may also cause an idiosyncratic reaction resulting in acute transient myopia and acute angle-closure glaucoma.
  - Thiazide diuretics have been reported to cause exacerbation or activation of systemic lupus erythematosus.
- Nebivolol has warnings for abrupt cessation of therapy, cardiac failure, bronchospastic diseases, thyrotoxicosis, and peripheral vascular disease.
- Amlodipine has warnings for increased angina and hepatic impairment.
- Sacubitril/valsartan has additional warnings for angioedema, hypotension, a risk of decreased or impaired renal function in susceptible patients, and hyperkalemia.

Adverse Effects

- Common adverse effects with ARBs include hypotension, dizziness, back pain, and headache.
  - The most common adverse reaction with azilsartan is diarrhea.
- The CCB amlodipine may cause peripheral edema.
- The most common adverse effects reported (incidence ≥ 5%) with sacubitril/valsartan include hypotension, hyperkalemia, cough, dizziness, and renal failure. With regard to hypotension, a recent Institute for Safe Medication Practices (ISMP) Quarter Watch reported that many patients initiating therapy on sacubitril/valsartan experienced significant complications ranging from dizziness to blackouts and other consequences serious enough to require hospitalization (*ISMP Quarter Watch 2017*).
- The FDA has required post-marketing studies for sacubitril/valsartan in order to assess the incidence of angioedema in patients of African or Caribbean descent (Black patients) and the risk of cognitive dysfunction in HF patients with HFpEF (*FDA approval letter 2015*). Postmarketing reports include hypersensitivity, including rash, pruritus, and anaphylactic reactions.
- Experts have raised questions regarding the potential for impact on cognitive dysfunction due to the mechanism of action of sacubitril/valsartan, particularly in patients with Alzheimer's disease. The concern is specifically around the sacubitril component and issues with the neprilysin inhibition in the brain. Theoretically, neprilysin inhibition could lead to amyloid deposits, which has been linked to dementia.

- According to pharmacodynamic studies, sacubitril/valsartan 400 mg (2 x 97/103 mg tablets) once daily increased cerebrospinal fluid amyloid-β ($A\beta_{1-38}$) concentrations after 2 weeks in healthy patients. Also, the active metabolite (LBQ657) does minimally cross the blood brain barrier. The clinical relevance of increased concentrations is unknown (*Vodovar et al 2015*).

Important Drug Interactions

- Dual blockade of the RAAS with ACE-Is, ARBs, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure).
  - Most patients receiving the combination of 2 RAAS inhibitors do not obtain any additional benefit compared to monotherapy.
- In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, concomitant use of non-steroidal anti-inflammatory agents (NSAIDs) with ARBs may result in deterioration of renal function, including acute renal failure. The antihypertensive effect of ARBs may be attenuated by NSAIDs.
- Concomitant use of ARBs and potassium-sparing diuretics (eg, spironolactone, amiloride, triamterene) can increase the risk of hyperkalemia.
- ARBs may increase serum lithium concentration; lithium levels should be monitored.
- Concurrent administration of the bile acid sequestering agent, colesevelam hydrochloride, reduces the systemic exposure and peak plasma concentration of olmesartan.
- Concomitant use of telmisartan and ramipril is not recommended due to increased exposure to ramipril and ramiprilat.
- HCTZ absorption is impaired in the presence of anionic exchange resins (ie, cholestyramine and colestipol resins).
- Concomitant use of HCTZ with carbamazepine has been associated with an increased risk for symptomatic hyponatremia.
- Nebivolol should not be used with cytochrome P450 (CYP) 2D6 inhibitors.
- Amlodipine should not be coadministered with doses higher than 20 mg of simvastatin per day.
- Exposure to amlodipine is increased with CYP3A4 inhibitors.

DOSING AND ADMINISTRATION

- In general, the safety and efficacy of ARBs have not been established in severe hepatic impairment.
- ARB combination products containing diuretics are not recommended in patients with severe renal impairment.
- Some ARB combination products are not recommended as initial therapy in patients with hepatic impairment because the recommended ARB starting dose is not available in the fixed-dose combination product.
- ARB combination products containing amlodipine are not recommended as initial therapy in elderly patients or patients with severe hepatic impairment because the recommended amlodipine starting dose of 2.5 mg is not available in the fixed-dose combination product.

Table 5. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Single-Entity ARBs				
Atacand (candesartan)	Tablets	Oral	HTN: Once or twice daily HF: Once daily	Initiate with 8 mg once daily in moderate hepatic impairment.
Avapro (irbesartan)	Tablets	Oral	Once daily	
Benicar (olmesartan)	Tablets	Oral	Once daily	
Cozaar (losartan)	Tablets	Oral	Once daily	Initiate with 25 mg once daily in mild to moderate hepatic impairment.
Diovan, Prexxartan (valsartan)	Tablets, oral solution	Oral	HTN: Once daily HF/post-MI: Twice daily	Safety and efficacy not established in severe renal impairment

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			Oral solution: Twice daily	
Edarbi (azilsartan)	Tablets	Oral	Once daily	
eprosartan	Tablets	Oral	Once or twice daily	Max 600 mg per day in moderate or severe renal impairment
Micardis (telmisartan)	Tablets	Oral	Once daily	
ARB/Diuretic Combinations				
Atacand HCT (candesartan/hydrochlorothiazide)	Tablets	Oral	Once daily	
Avalide (irbesartan/hydrochlorothiazide)	Tablets	Oral	Once daily	
Benicar HCT (olmesartan/hydrochlorothiazide)	Tablets	Oral	Once daily	
Diovan HCT (valsartan/hydrochlorothiazide)	Tablets	Oral	Once daily	
Edarbyclor (azilsartan/chlorthalidone)	Tablets	Oral	Once daily	
Hyzaar (losartan/hydrochlorothiazide)	Tablets	Oral	Once daily	
Micardis HCT (telmisartan/hydrochlorothiazide)	Tablets	Oral	Once daily	
ARB/Beta Blocker Combinations				
Byvalson (valsartan/nebivolol)	Tablets	Oral	Once daily	Not recommended in moderate to severe hepatic impairment or severe renal impairment.
ARB/CCB Combinations				
Azor (olmesartan/amlodipine)	Tablets	Oral	Once daily	
Exforge (valsartan/amlodipine)	Tablets	Oral	Once daily	
Twynsta (telmisartan/amlodipine)	Tablets	Oral	Once daily	
ARB/CCB/Diuretic Combinations				
Exforge HCT (valsartan/ amlodipine/hydrochlorothiazide)	Tablets	Oral	Once daily	
Tribenzor (olmesartan/ amlodipine/hydrochlorothiazide)	Tablets	Oral	Once daily	
ARB/Neprilysin inhibitor Combination				
Entresto (sacubitril/valsartan)	Tablets	Oral	Twice daily	Reduce initial dose for: • ACE-I/ARB naïve • Prior low dose of ACE-I/ ARB before initiating sacubitril/valsartan • Severe renal or moderate hepatic impairment

Abbreviations: ACE-I = angiotensin converting enzyme-inhibitor; ARB = angiotensin II receptor blocker; CCB = calcium channel blocker; HF = heart failure; HTN = hypertension; MI = myocardial infarction

See the current prescribing information for full details

CONCLUSION

- The single-entity and combination ARB products are FDA-approved for the treatment of HTN, and most are generically available. Some ARBs have additional indications for HF, diabetic nephropathy, or CV risk reduction in certain high-risk populations.
- Evidence-based guidelines recognize the important role ARBs play in the treatment of HTN and other CV and renal diseases. The current ACC/AHA guidelines recommend a BP goal of < 130/80 mm Hg for most patients *(Whelton et al 2017)*.
- ARBs have demonstrated efficacy in lowering SBP and DBP in patients with HTN.
  - Head-to-head trials have not consistently demonstrated superiority of one ARB compared to another.
  - Clinical trials assessing the ARB combination products in the treatment of HTN have demonstrated that, in general, dual therapy combinations of ARBs plus either HCTZ, nebivolol, or amlodipine achieve greater reductions in BP and higher BP control rates compared to monotherapy regimens. Head-to-head trials have not consistently demonstrated superiority of one combination product over another.
  - ARBs have generally demonstrated comparable efficacy to ACE-Is across indications.
- Studies have demonstrated that the combination of 2 inhibitors of the RAAS, including an ACE-I with an ARB, provides no renal or CV benefits and increased risk of adverse events, including hyperkalemia, hypotension, and renal dysfunction. All agents in this class have safety warnings against combined use.
- All ARBs have a boxed warning for use in pregnancy and are contraindicated in patients with DM who are also receiving aliskiren therapy. Other warnings include hypotension, renal failure, and hyperkalemia.
- Common adverse effects of ARBs include hypotension, dizziness, back pain, and headache.
- Current guidelines recommend ARBs as a first-line therapy for patients with HTN, DM with microalbuminuria, stable CAD with HTN, and post-MI *(Amsterdam et al 2014, de Boer et al 2017, Go et al 2014, Rosendorff et al 2015, Weber et al 2014, Whelton et al 2017).*
  - Due to differences in the activity of the RAAS, ARBs are often less effective as HTN monotherapy in black patients; CCBs and thiazide diuretics should be used as first-line options in these patients.
- Recent guideline updates from the ACC/AHA/HFSA state that in patients with chronic symptomatic HFrEF NYHA Class II or III who tolerate an ACE-I or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality (*Yancy et al 2016, Yancy et al 2017*).

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Publication Date: July 3, 2018

Prior Authorization Guideline

Guideline Name Epidiolex (Cannabidiol)

1 . Indications

Drug Name: Epidiolex (Cannabidiol)

Indications

Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) Indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age or older.

2 . Criteria

Product Name: Epidiolex

Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	PA Criteria

Approval Criteria

1 Member has a diagnosis of Lennox-Gastaut syndrome or Dravet syndrome.

AND

2 Member is two years of age or older.

AND

3 A recent serum transaminase (ALT and AST) and total bilirubin level has been obtained and is within normal limits.

AND

4 Prescribed by or in consultation with a neurologist.

AND

5 The total dose will not exceed 20 mg/kg/day (10mg/kg twice daily)

AND

6 The medication will be used as adjunctive therapy (Patient has been taking one or more antiepileptic drugs and has chart notes confirming presence of at least 4 convulsive seizures per month)

Product Name: Epidiolex

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	PA Criteria

Approval Criteria

1 Member is responding positively to therapy (decrease in frequency of seizures).

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Epidiolex®

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Anthem will maintain own criteria as it is not more restrictive than proposed. Anthem requires diagnosis and age requirement only.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: Jeannine M Murray

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Epidiolex®

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

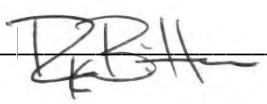
HPN has the following suggestions:

- Remove the specialist requirement and AST/ALT/Bilirubin requirement
- Remove the requirement for four seizures in the past month
- Remove the initial authorization of three months and move to twelve months
- For Lennox-Gastaut Syndrome, require failure of two of the following : Divalproex, Lamotrigine, Topiramate, Valproic Acid.
- For Lennox-Gastaut Syndrome, document that one of the following has occurred for the failures of previous drugs: (1) Both of the following: (a) Documented history of persisting seizures after titration to the highest tolerated dose with each medication trial AND (b) Lack of compliance as a reason for treatment failure has been ruled out; OR (2) Both of the following: (a) Documentation of failure due to intolerable side effects. (b) Reasonable efforts were made to minimize the side effect (e.g. change timing of dosing, divide dose out for more frequent but smaller doses, etc.)

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Ryan Bitton

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Epidiolex®

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☒ I approve the criteria as presented by OptumRx

☐ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: ____Tom Beranek_____

Signature of individual completing this form: Tom Beranek _____

Epidiolex

Summary of Utilization

October 1, 2017 - September 30, 2018

Fee for Service Medicaid

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
EPIDIOLEX SOL 100MG/ML	-	-	-	-	$ -
Grand Total	**-**	**-**	**-**	**-**	**$ -**

Epidiolex (Cannabidiol) HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
EPIDIOLEX	0	0	0	0
Total	0	0	0	0
01/01/18 - 03/31/18 - Q1				
EPIDIOLEX	0	0	0	0
Total	0	0	0	0
04/01/18 - 06/30/18 - Q2				
EPIDIOLEX	0	0	0	0
Total	0	0	0	0
07/01/18 - 09/30/18 - Q3				
EPIDIOLEX	0	0	0	0
Total	0	0	0	0
Grand Total	0	0	0	0

INTRODUCTION

- Epilepsy is a disease of the brain defined by any of the following (*Fisher et al 2014*):
  - At least 2 unprovoked (or reflex) seizures occurring > 24 hours apart;
  - 1 unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after 2 unprovoked seizures, occurring over the next 10 years;
  - Diagnosis of an epilepsy syndrome.
- Types of seizures include generalized seizures, focal (partial) seizures, and status epilepticus (*Centers for Disease Control and Prevention [CDC] 2018, Epilepsy Foundation 2016*).
  - Generalized seizures affect both sides of the brain and include:
    - Tonic-clonic (grand mal): begin with stiffening of the limbs, followed by jerking of the limbs and face
    - Myoclonic: characterized by rapid, brief contractions of body muscles, usually on both sides of the body at the same time
    - Atonic: characterized by abrupt loss of muscle tone; they are also called drop attacks or akinetic seizures and can result in injury due to falls
    - Absence (petit mal): characterized by brief lapses of awareness, sometimes with staring, that begin and end abruptly; they are more common in children than adults and may be accompanied by brief myoclonic jerking of the eyelids or facial muscles, a loss of muscle tone, or automatisms.
  - Focal seizures are located in just 1 area of the brain and include:
    - Simple: affect a small part of the brain; can affect movement, sensations, and emotion, without a loss of consciousness
    - Complex: affect a larger area of the brain than simple focal seizures and the patient loses awareness; episodes typically begin with a blank stare, followed by chewing movements, picking at or fumbling with clothing, mumbling, and performing repeated unorganized movements or wandering; they may also be called “temporal lobe epilepsy” or “psychomotor epilepsy”
    - Secondarily generalized seizures: begin in 1 part of the brain and spread to both sides
  - Status epilepticus is characterized by prolonged, uninterrupted seizure activity.
- Seizure classifications from the International League against Epilepsy (ILAE) were updated in 2017. The ILAE classification of seizure types is based on whether the seizure has a focal, generalized, or unknown onset; has a motor or non-motor onset; and whether the patient is aware or has impaired awareness during the event (for focal seizures). Additional classification details may also be used (*Fisher et al 2017A, Fisher et al 2017B*).
  - There is variation between the ILAE classifications and many of the Food and Drug Administration (FDA)-approved indications for antiepileptic drugs (AEDs). For example, a “focal aware” seizure corresponds to the prior term “simple partial seizure,” and a “focal impaired awareness” seizure corresponds to the prior term “complex partial seizure.”
- A number of epilepsy syndromes have also been described; these are defined by groups of features that tend to occur together such as having a similar seizure type, age of onset, part of the brain involved, and electroencephalogram (EEG) pattern (*Epilepsy Foundation 2013*). An example is a childhood epilepsy syndrome called Lennox-Gastaut syndrome (LGS), which is characterized by several seizure types including tonic (stiffening) and atonic (drop) seizures. In LGS, there is a classic EEG pattern seen and intellectual development is usually impaired (*Epilepsy Foundation 2014*).
- Epilepsy management is focused on the goals of 1) controlling seizures, 2) avoiding treatment-related adverse effects (AEs), and 3) maintaining or restoring quality of life. Management options vary based on the seizure type. It is usually appropriate to refer patients to a neurologist to establish the epilepsy diagnosis and formulate the management strategy (*Schachter 2018*).
  - A correct diagnosis is essential to proper treatment selection. For example, absence seizures are commonly confused with complex partial seizures. However, drugs that reduce absence seizures are generally ineffective for complex partial seizures, and the most effective drugs for complex partial seizures may be ineffective against or even increase the frequency of absence seizures (*Epilepsy Foundation 2016*).

- When possible, monotherapy with a single AED is the preferred treatment approach. Combination therapy may be associated with decreased patient adherence to therapy and an increased incidence of AEs and drug interactions. When combination therapy is needed, it is recommended to select products with different mechanisms of action and AE profiles. There is little comparative clinical data to support the use of specific combinations (*Schachter et al 2018*).
- Several broad classes of AEDs are available, including barbiturates, benzodiazepines, hydantoins, and miscellaneous agents (see Table 1). Of these agents, mephobarbital and ezogabine are not currently marketed as either brand or generic formulations, but are included in this review for informational and historical purposes.
- Cannibidiol (Epidiolex) was FDA-approved in June 2018 for use in pediatric patients 2 years of age and older with LGS or Dravet syndrome (*FDA news release 2018*). It is the first FDA-approved drug for treatment of patients with Dravet syndrome and is the first approved drug that contains a purified substance, cannabidiol, derived from marijuana. It is pending a Drug Enforcement Administration (DEA) scheduling designation (*GW Pharmaceuticals News Release).*
- Stiripentol (Diacomit) capsules and powder for oral suspension were FDA-approved in August 2018 for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam.
- Everolimus tablets for oral suspension (Afinitor Disperz) received an expanded indication in April 2018 for use in partial-onset seizures associated with tuberous sclerosis complex (TSC). This product is a kinase inhibitor that also has several oncology indications.
- Several of the AEDs are used for additional indications beyond the management of epilepsy, including (but not limited to) bipolar disorder, migraine prophylaxis, and several types of neuropathic pain. These additional indications are listed in Table 2; however, this review primarily focuses on the use of AEDs for the management of epilepsy. Additionally, brands and formulations FDA-approved and marketed only for non-epilepsy indications are not included within this review; these include gabapentin tablets (Gralise), FDA-approved only for the management of postherpetic neuralgia, gabapentin enacarbil extended-release tablets (Horizant), FDA-approved only for management of postherpetic neuralgia and treatment of moderate-to-severe restless leg syndrome, and pregabalin extended-release tablets (Lyrica CR), FDA-approved only for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia.
- Medispan class: Antianxiety agents, benzodiazepines; Anticonvulsants, AMPA glutamate receptor antagonists; Anticonvulsants, anticonvulsants – misc; Anticonvulsants, carbamates; Anticonvulsants, GABA modulators; Anticonvulsants, hydantoins; Anticonvulsants, succinimides; Anticonvulsants, valproic acid; Hypnotics/Sedatives/Sleep Disorder Agents, barbiturate hypnotics

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Barbiturates	
Mephobarbital* (Mebaral)‡	-‡
Pentobarbital (Nembutal†)	✔
Phenobarbital* (Luminal†, Solfoton†)	✔
Primidone (Mysoline)	✔
Benzodiazepines	
Clobazam (Onfi)	-
Clonazepam (Klonopin§)	✔
Clorazepate (Tranxene T-Tab§)	✔
Diazepam (Diastat¶, Valium§)	✔ ‖
Hydantoins	
Ethotoin (Peganone)	-
Fosphenytoin (Cerebyx)	✔
Phenytoin (Dilantin§, Phenytek)	✔ ‖
Miscellaneous	
Brivaracetam (Briviact)	-
Cannabidiol (Epidiolex)***	-
Carbamazepine (Carbatrol, Epitol**, Equetro, Tegretol§, Tegretol-XR)	✔
Divalproex sodium (Depakote, Depakote ER, Depakote Sprinkle)	✔
Eslicarbazepine (Aptiom)	-

Drug	Generic Availability
Ethosuximide (Zarontin)	✔
Everolimus (Afinitor Disperz)	-
Ezogabine (Potiga)‡	-
Felbamate (Felbatol)	✔
Gabapentin (Neurontin)	✔
Lacosamide (Vimpat)	-#
Lamotrigine (Lamictal, Lamictal ODT, Lamictal XR)	✔
Levetiracetam (Keppra, Keppra XR, Roweepra**, Roweepra XR**, Spritam)	✔‖
Methsuximide (Celontin)	-
Oxcarbazepine (Oxtellar XR, Trileptal)	✔‖
Perampanel (Fycompa)	-
Pregabalin (Lyrica)	-
Rufinamide (Banzel)	-#
Stiripentol (Diacomit)	-
Tiagabine (Gabitril)	✔‖
Topiramate (Topamax, Topamax Sprinkle, Topiragen††, Trokendi XR, Qudexy XR¶)	✔‖
Valproic acid (Depacon, Depakene, Stavzor DR‡)	✔‖
Vigabatrin (Sabril, Vigadrone**)	✔‖
Zonisamide (Zonegran§)	✔

* Not FDA approved
† Brand product not currently marketed; generic is available
‡ No brand or generic currently marketed
§ Brand marketing status may vary by strength and/or formulation
‖ Generic availability may vary by strength and/or formulation
¶ Authorized generic available; no A-rated generics approved via abbreviated new drug application
# Generic is FDA-approved for at least 1 strength or formulation, but not currently marketed
** Branded generic
†† Branded generic; not currently marketed
*** Cannabidiol is not yet available as DEA schedule designation is pending (anticipated by Fall 2018) (*GW Pharmaceuticals News Release 2018*)

(*Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018*)

INDICATIONS

- Tables 2A and 2B provide an overview of anticonvulsant indications. Except where noted, only FDA-approved products and indications are included. For items marked with an asterisk, there is additional information about the indication provided in the box following the tables.
- Acute-care indications that are not related to convulsive disorders (for example, pre-procedural use of benzodiazepines in hospital settings) are not included.

Table 2A. Indications for anticonvulsants (Part 1 of 2)

Indications	Brivaracetam	Cannabidiol	Carbamazepine	Clobazam	Clonazepam	Clorazepate	Diazepam	Divalproex Sodium	Eslicarbazepine	Ethosuximide	Ethotoin	Everolimus	Ezogabine	Felbamate	Fosphenytoin	Gabapentin	Lacosamide	Lamotrigine	Levetiracetam
Partial seizures (simple partial, complex partial and/or secondarily generalized)	✔ *		✔ *			A		✔, A*	✔, A*		✔ *		A*	✔, A*		A*	✔ *	✔, A*	A*
Primary generalized tonic-clonic seizure (grand mal)			✔								✔				✔ *			A*	A*
Absence seizure (petit mal)					✔ *			✔, A*		✔									
Multiple seizure types that include absence seizures								A											
Seizures of Lennox-Gastaut syndrome (LGS)		✔ *		A*	✔, A									A*				A*	
Seizures of Dravet syndrome		✔ *																	
Juvenile myoclonic epilepsy (JME)																			A*
Emergency/acute/short-term use for seizure control (see notes)							✔ *								✔ *				
Akinetic and myoclonic seizures					✔, A														
Convulsive disorders (see notes)							A*												
Certain mixed seizure patterns or other partial or generalized seizures			✔ *																
Migraine prophylaxis								✔ *											
Trigeminal neuralgia			✔ *																
Postherpetic neuralgia																✔ *			
Bipolar disorder			✔ *					✔ *										✔ *	
Panic disorder, with or without agoraphobia					✔														
Anxiety disorder; short-term relief of anxiety symptoms						✔	✔												
Symptomatic relief of acute alcohol withdrawal						✔	✔												

Indications	Brivaracetam	Cannabidiol	Carbamazepine	Clobazam	Clonazepam	Clorazepate	Diazepam	Divalproex Sodium	Eslicarbazepine	Ethosuximide	Ethotoin	Everolimus	Ezogabine	Felbamate	Fosphenytoin	Gabapentin	Lacosamide	Lamotrigine	Levetiracetam
Relief of skeletal muscle spasm, spasticity, athetosis, and stiff-man syndrome							A												
Partial-onset seizures associated with tuberous sclerosis complex (TSC)												A*							

✓ = monotherapy (or not specified); A = adjunctive therapy

Table 2B. Indications for Anticonvulsants (Part 2 of 2)

Indications	Mephobarbital†	Methsuximide	Oxcarbazepine	Pentobarbital	Perampanel	Phenobarbital†	Phenytoin	Pregabalin	Primidone	Rufinamide	Stiripentol	Tiagabine	Topiramate	Valproic acid	Vigabatrin	Zonisamide
Partial seizures (simple partial, complex partial and/or secondarily generalized)			✓, A*		✓*		✓*	A*	✓, A*			A*	✓, A*	✓, A*	A*	A*
Primary generalized tonic-clonic seizure (grand mal)	✓				A*		✓*		✓, A*				✓, A*			
Absence seizure (petit mal)	✓	✓*												✓, A*		
Multiple seizure types which include absence seizures														A*		
Seizures of LGS										A*			A*			
Seizures of Dravet syndrome											A*					
Emergency/acute/short-term use for seizure control (see notes)				✓*			✓*									
Infantile spasms															✓*	
Convulsive disorders (see notes)						✓*										
Migraine prophylaxis													✓*	✓*		

Indications	Mephobarbital†	Methsuximide	Oxcarbazepine	Pentobarbital	Perampanel	Phenobarbital†	Phenytoin	Pregabalin	Primidone	Rufinamide	Stiripentol	Tiagabine	Topiramate	Valproic acid	Vigabatrin	Zonisamide
Postherpetic neuralgia								✔								
Bipolar disorder														✔ *		
Sedative for anxiety, tension, and apprehension	✔															
Neuropathic pain associated with diabetic peripheral neuropathy								✔								
Neuropathic pain associated with spinal cord injury								✔								
Fibromyalgia								✔								

✓ = monotherapy (or not specified); A = adjunctive therapy
†Mephobarbital and phenobarbital are not approved by the FDA.

***Notes: Additional Detail on Selected Anticonvulsant Indications**

- **Brivaracetam**:
  - Treatment of partial-onset seizures in patients ≥ 4 years of age (oral formulations); ≥ 16 years of age (IV formulation)
- **Cannabidiol**
  - Treatment of seizures associated with LGS or Dravet syndrome in patients ≥ 2 years of age
- **Carbamazepine**:
  - Partial seizures with complex symptomatology (psychomotor, temporal lobe); patients with these seizures appear to show greater improvement than those with other types; generalized tonic-clonic seizures (grand mal); mixed seizure patterns which include the above, or other partial or generalized seizures
  - Absence seizures do not appear to be controlled; carbamazepine has been associated with increased frequency of generalized convulsions in these patients
  - Treatment of pain associated with true trigeminal neuralgia; beneficial results also reported in glossopharyngeal neuralgia
  - Bipolar indication is for an extended-release capsule formulation (Equetro) only: treatment of patients with acute manic or mixed episodes associated with bipolar I disorder
- **Clobazam**:
  - Seizures associated with LGS in patients aged ≥ 2 years
- **Clonazepam**:
  - In patients with absence seizures who have failed to respond to succinimides, clonazepam may be useful
- **Diazepam**:
  - Oral diazepam may be used adjunctively in convulsive disorders
  - Rectal diazepam is indicated in the management of selected, refractory patients with epilepsy on stable regimens of AEDs who require intermittent use of diazepam to control bouts of increased seizure activity
  - Injectable diazepam is a useful adjunct in status epilepticus and severe recurrent convulsive seizures
- **Divalproex sodium**:
  - Monotherapy and adjunctive therapy in the treatment of patients with complex partial seizures that occur either in isolation or in association with other types of seizures (age ≥ 10 years for all formulations)

- Monotherapy and adjunctive therapy in the treatment of simple and complex absence seizures (age ≥ 10 years for extended-release tablets; age not specified for tablets/sprinkle capsules)
- The tablets and extended-release tablets have indications in bipolar disorder and migraine prophylaxis; the sprinkle capsule formulation does not. For bipolar disorder, safety and effectiveness for long-term use (> 3 weeks) has not been demonstrated in controlled clinical trials. Bipolar disorder indications are as follows:
  - Treatment of the manic episodes associated with bipolar disorder (tablets)
  - Treatment of acute manic or mixed episodes associated with bipolar disorder, with or without psychotic features (extended-release tablets)

- **Eslicarbazepine:**
  - Treatment of partial-onset seizures in patients ≥ 4 years of age
- **Ethotoin**:
  - Complex partial (psychomotor) seizures
- **Everolimus**
  - Adjunctive treatment of adult and pediatric patients ≥ 2 years of age with TSC-associated partial-onset seizures (tablets for oral suspension only)
- **Ezogabine**:
  - Adjunctive treatment of partial-onset seizures in patients ≥18 years of age who have responded inadequately to several alternative treatments and for whom the benefits outweigh the risk of retinal abnormalities and potential decline in visual acuity
- **Felbamate**:
  - Not first-line; recommended only in patients who respond inadequately to alternative treatments and whose epilepsy is so severe that a substantial risk of aplastic anemia and/or renal failure is deemed acceptable
  - Monotherapy or adjunctive therapy in the treatment of partial seizures, with and without generalization, in adults with epilepsy
  - Adjunctive therapy of partial and generalized seizures associated with LGS in children (age not specified)
- **Fosphenytoin**:
  - Treatment of generalized tonic-clonic status epilepticus
  - Prevention and treatment of seizures occurring during neurosurgery
  - Can be substituted short-term for oral phenytoin when oral phenytoin administration is not possible
- **Gabapentin**:
  - Adjunctive therapy in the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients ≥ 3 years of age with epilepsy.
  - Management of postherpetic neuralgia in adults
- **Lacosamide**:
  - Treatment of partial-onset seizures in patients ≥ 4 years of age (tablet and oral solution)
  - Treatment of partial-onset seizures in patients ≥ 17 years of age (injection)
- **Lamotrigine immediate-release formulations**:
  - Age ≥ 2 years for adjunctive therapy for partial-onset seizures, primary generalized tonic-clonic seizures, and generalized seizures of LGS
  - Age ≥ 16 years for conversion to monotherapy in patients with partial-onset seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single AED
  - Maintenance treatment of bipolar disorder to delay the time to occurrence of mood episodes in patients treated for acute mood episodes with standard therapy (treatment of acute manic or mixed episodes is not recommended)
- **Lamotrigine extended-release tablets**:
  - Age ≥ 13 years for adjunctive therapy for primary generalized tonic-clonic seizures and partial onset seizures with or without secondary generalization, and age ≥13 years for conversion to monotherapy in patients with partial-onset seizures who are receiving treatment with a single AED
  - The extended-release formulation is not FDA-approved for bipolar disorder
- **Levetiracetam**:
  - Adjunctive therapy in the treatment of partial onset seizures in adults and children ≥ 1 month of age with epilepsy (age ≥ 4 years and weighing > 20 kg for the tablets for oral suspension [Spritam])
  - Adjunctive therapy in the treatment of myoclonic seizures in adults and adolescents ≥ 12 years with JME

- Adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in adults and children ≥ 6 years of age with idiopathic generalized epilepsy
- The extended-release tablets are only indicated for adjunctive therapy in the treatment of partial-onset seizures in patients ≥ 12 years of age with epilepsy

- **Methsuximide**:
  - Control of absence (petit mal) seizures that are refractory to other drugs
- **Oxcarbazepine immediate-release formulations**:
  - Monotherapy in the treatment of partial seizures in adults and children 4 to 16 years of age
  - Adjunctive therapy in the treatment of partial seizures in adults and children 2 to 16 years of age
- **Oxcarbazepine extended-release tablets**:
  - Adjunctive therapy in the treatment of partial seizures in adults and children 6 to 17 years of age
- **Pentobarbital**:
  - In anesthetic doses in the emergency control of certain acute convulsive episodes, eg, those associated with status epilepticus, cholera, eclampsia, meningitis, tetanus, and toxic reactions to strychnine or local anesthetics
- **Perampanel**:
  - Treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy ≥ 12 years of age
  - Adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients with epilepsy ≥ 12 years of age
- **Phenobarbital (not FDA-approved)**:
  - Phenobarbital tablets are indicated for use as an anticonvulsant; the elixir is indicated for the treatment of generalized and partial seizures; the injection is indicated as an anticonvulsant for the treatment of generalized tonic-clonic and cortical focal seizures, in the emergency control of certain acute convulsive episodes, and in pediatric patients as an anticonvulsant
- **Phenytoin oral formulations**:
  - Treatment of tonic-clonic (grand mal) and complex partial (psychomotor, temporal lobe) seizures and prevention and treatment of seizures occurring during or following neurosurgery (the oral suspension does not have the neurosurgery indication)
- **Phenytoin injection**:
  - Treatment of generalized tonic-clonic status epilepticus and prevention and treatment of seizures occurring during neurosurgery
  - Can be substituted as short-term use for oral phenytoin when oral phenytoin administration is not possible
- **Pregabalin**:
  - Adjunctive therapy for treatment of partial onset seizures in patients ≥ 4 years of age
- **Primidone**:
  - Control of grand mal, psychomotor, and focal epileptic seizures; may control grand mal seizures refractory to other anticonvulsant therapy
- **Rufinamide**:
  - Adults and pediatric patients ≥ 1 year of age
- **Stiripentol**
  - Treatment of seizures associated with Dravet syndrome in patients ≥ 2 years of age taking clobazam; no clinical data to support its use as monotherapy
- **Tiagabine**:
  - Adjunctive therapy in adults and children ≥ 12 years of age in the treatment of partial seizures
- **Topiramate**:
  - Initial monotherapy in patients with partial onset or primary generalized tonic-clonic seizures (age ≥ 2 years for tablets, immediate-release sprinkle capsules, and Qudexy XR extended-release capsules; age ≥ 6 years for Trokendi XR extended-release capsules)
  - Adjunctive therapy for adults and pediatric patients with partial onset seizures or primary generalized tonic-clonic seizures and in patients with seizures associated with LGS (age ≥ 2 years for tablets, immediate-release sprinkle capsules, and Qudexy XR extended-release capsules; age ≥ 6 years for Trokendi XR extended-release capsules)
  - Prophylaxis of migraine headache in patients ≥ 12 years of age
- **Valproic acid**:

- Monotherapy and adjunctive therapy in the treatment of patients with complex partial seizures (in adults and pediatric patients down 10 years) that occur either in isolation or in association with other types of seizures; sole and adjunctive therapy in the treatment of simple and complex absence seizures, and adjunctively in patients with multiple seizure types which include absence seizures
- Migraine prophylaxis and bipolar disorder indications are for the delayed-release capsule formulation only (Stavzor, which is not currently marketed). For bipolar disorder:
  - Acute treatment of manic or mixed episodes associated with bipolar disorder, with or without psychotic features; safety and effectiveness for long-term use (> 3 weeks) has not been demonstrated in controlled clinical trials

- **Vigabatrin**:
  - Refractory complex partial seizures as adjunctive therapy in patients ≥ 10 years of age who have responded inadequately to several alternative treatments; not indicated as a first-line agent
  - Infantile spasms as monotherapy in infants 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss
- **Zonisamide**:
  - Adjunctive therapy in the treatment of partial seizures in adults with epilepsy

- 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

- Overall, the anticonvulsants have demonstrated efficacy for their FDA-approved uses. Clinical trial data demonstrating efficacy of the anticonvulsants for the treatment of epilepsy is described in the prescribing information for the individual products, particularly for anticonvulsants more recently approved by the FDA. However, the prescribing information for some older, conventional products (eg, benzodiazepines, carbamazepine, ethotoin, ethosuximide, methsuximide, phenytoin, and primidone) and non-FDA approved products (eg, mephobarbital, phenobarbital) do not contain efficacy data in their prescribing information.
- No single AED is clearly the most effective. Comparative efficacy data for the management of epilepsy are limited, and trials have generally not shown significant differences among drugs in terms of efficacy. However, the quality of the data is limited and generally derived from short-term trials (*Karceski 2017*).
- When possible, monotherapy with a single AED is the preferred treatment approach. Combination therapy may be associated with decreased patient adherence to therapy and an increased incidence of AEs and drug interactions. (*Schachter et al 2018*). Most patients with epilepsy are treated with anticonvulsant monotherapy (*Nevitt et al 2017*).
- An evidence review summarized AED efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes (*Glauser et al 2013*). This publication provides conclusions based on a review of 64 randomized trials and 11 meta-analyses. Conclusions include the following:
  - As initial monotherapy for adults with newly diagnosed or untreated partial-onset seizures:
    - Carbamazepine, levetiracetam, phenytoin, and zonisamide are established as efficacious/effective.
    - Valproate is probably efficacious/effective.
    - Gabapentin, lamotrigine, oxcarbazepine, phenobarbital, topiramate, and vigabatrin are possibly efficacious/effective.
    - Clonazepam and primidone are potentially efficacious/effective.
  - As initial monotherapy for children with newly diagnosed or untreated partial-onset seizures:
    - Oxcarbazepine is established as efficacious/effective.
    - Carbamazepine, phenobarbital, phenytoin, topiramate, valproate, and vigabatrin are possibly efficacious/effective.
    - Clobazam, carbamazepine, lamotrigine, and zonisamide are potentially efficacious/effective.
  - As initial monotherapy for elderly adults with newly diagnosed or untreated partial-onset seizures:
    - Gabapentin and lamotrigine are established as efficacious/effective.
    - Carbamazepine is possibly efficacious/effective.
    - Topiramate and valproate are potentially efficacious/effective.
  - As initial monotherapy for adults with newly diagnosed or untreated generalized-onset tonic-clonic seizures:

        - Carbamazepine, lamotrigine, oxcarbazepine, phenobarbital, phenytoin, topiramate, and valproate are possibly efficacious/effective.
        - Gabapentin, levetiracetam, and vigabatrin are potentially efficacious/effective.
        - Carbamazepine and phenytoin may precipitate or aggravate generalized-onset tonic-clonic seizures.
    - For children with newly diagnosed or untreated generalized-onset tonic-clonic seizures:
        - Carbamazepine, phenobarbital, phenytoin, topiramate, and valproate are possibly efficacious/effective.
        - Oxcarbazepine is potentially efficacious/effective.
        - Carbamazepine and phenytoin may precipitate or aggravate generalized-onset tonic-clonic seizures.
    - As initial monotherapy for children with newly diagnosed or untreated absence seizures:
        - Ethosuximide and valproate are established as efficacious/effective.
        - Lamotrigine is possibly efficacious/effective.
        - Gabapentin is established as inefficacious/ineffective.
        - Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, tiagabine, and vigabatrin may precipitate or aggravate absence seizures (based on scattered reports).
    - As initial monotherapy for children with benign childhood epilepsy with centrotemporal spikes (BECTS):
        - Carbamazepine and valproate are possibly efficacious/effective.
        - Gabapentin, levetiracetam, oxcarbazepine, and sulthiame (not available in the United States) are potentially efficacious/effective.
    - For patients with newly diagnosed JME:
        - Topiramate and valproate are potentially efficacious/effective.
        - Carbamazepine, gabapentin, oxcarbazepine, phenytoin, tiagabine, and vigabatrin may precipitate or aggravate absence, myoclonic, and in some cases generalized tonic-clonic seizures. There has also been a report that lamotrigine may exacerbate seizures in JME.
    - There is a lack of well-designed randomized trials in epilepsy, particularly for generalized seizures and in the pediatric population.
- A Cochrane systematic review evaluated the efficacy of AED monotherapy for epilepsy (*Nevitt et al 2017*). The review included the use of carbamazepine, phenytoin, valproate, phenobarbital, oxcarbazepine, lamotrigine, gabapentin, topiramate, levetiracetam, and zonisamide for the treatment of partial onset seizures (simple partial, complex partial or secondarily generalized) or generalized tonic-clonic seizures with or without other generalized seizure types.
    - This network meta-analysis showed that for the primary outcome, the time to withdrawal of allocated treatment:
        - For individuals with partial seizures:
            (i) Levetiracetam performed better than carbamazepine and lamotrigine.
            (ii) Lamotrigine performed better than all other treatments (aside from levetiracetam).
            (iii) Carbamazepine performed better than gabapentin and phenobarbital.
        - For individuals with generalized onset seizures, valproate performed better than carbamazepine, topiramate and phenobarbital.
        - For both partial and generalized onset seizures, phenobarbital seems to perform worse than all other treatments.
    - For the secondary outcome, time to first seizure:
        - For individuals with partial seizures, phenobarbital and phenytoin seem to perform better than most other drugs; and carbamazepine performed better than valproate, gabapentin, and lamotrigine.
        - For individuals with generalized seizures, phenytoin seems to work better than most other drugs.
        - There were few notable differences between the newer drugs (oxcarbazepine, topiramate, gabapentin, levetiracetam, and zonisamide) for either partial seizures or generalized seizures.
    - Few notable differences were shown for either partial or generalized seizure types for the secondary outcomes of time to 6-month or 12-month remission of seizures.
    - Overall, direct evidence and network meta-analysis estimates were numerically similar, and effect sizes had overlapping confidence intervals.
    - Data for individuals with generalized seizures are still limited and additional randomized trials are needed.
- The relative efficacy among valproate, lamotrigine, phenytoin, carbamazepine, ethosuximide, topiramate, levetiracetam, and phenobarbital as monotherapy for generalized (n = 7 studies) or absence seizures (n = 3 studies) was evaluated in a systematic review and network meta-analysis (*Campos et al 2018*). The outcomes analyzed were seizure freedom and withdrawal due to inefficacy. Compared to valproate, phenytoin had a lower odds of seizure freedom (OR 0.50; 95% credible Interval [CrI] 0.27 to 0.87) in patients with generalized tonic-clonic seizures. Lamotrigine had the highest

probability of seizure freedom and valproate had the highest probability of withdrawal due to inefficacy in these patients. For absence seizures, ethosuximide and valproate were found to have a higher probability of seizure freedom compared to lamotrigine.

- A meta-analysis estimated the comparative efficacy of achieving seizure freedom with 22 antiepileptic drugs and placebo in children and adolescents (*Rosati et al 2018*). For the treatment of newly diagnosed focal epilepsy (n = 4 studies), point estimates suggested superiority of carbamazepine and lamotrigine; however, this was not statistically significant. For refractory focal epilepsy (n = 9 studies), levetiracetam and perampanel were more effective than placebo in mixed comparisons. Ethosuximide and valproic acid were more effective than lamotrigine for absence seizures. The authors concluded that better designed comparative studies with appropriate length of follow-up, well-defined outcomes, and reliable inclusion criteria are needed to validate these results.
- Approximately 20% to 40% of patients with epilepsy can be considered refractory to drug treatment, referred to as drug-resistant epilepsy. Treatment of drug-resistant epilepsy may include additional anticonvulsant drug trials, epilepsy surgery, vagal nerve stimulation, and dietary changes (the ketogenic diet) (*Sirven 2017*).
  - Combination AED regimens are an option for the treatment of drug-resistant epilepsy. However, robust clinical evidence of suitable combinations of AEDs has been difficult to generate due to the large number of possible combinations of drugs and doses. Examples of combinations for which there is some evidence of efficacy include valproate plus lamotrigine for partial-onset and generalized seizures, valproate plus ethosuximide for absence seizures, and lamotrigine plus topiramate for various seizure types; however, even this evidence is fairly limited. In general, when considering combination therapy, it is recommended to combine medications with different mechanisms of action, and to be mindful of the overall drug load to minimize AEs. Two-drug therapy should be attempted before considering addition of a third drug, and higher numbers of drugs should be avoided as they are associated with a very low likelihood of additional seizure reduction (*Kwan et al 2011*).
  - A meta-analysis examined the efficacy of newer AEDs (eslicarbazepine, brivaracetam, perampanel, and lacosamide) versus levetiracetam as adjunctive therapy for uncontrolled partial-onset seizures. Most patients in this meta-analysis were on at least 2 other AEDs at the time of treatment. In this analysis, eslicarbazepine, lacosamide, and brivaracetam were non-inferior to levetiracetam in terms of efficacy, but all newer AEDs except brivaracetam had worse tolerability profiles than levetiracetam at high doses (*Zhu et al 2017*).
  - A network meta-analysis examined the efficacy of AEDs (including brivaracetam, eslicarbazepine acetate, gabapentin, lacosamide, levetiracetam, lamotrigine, oxcarbazepine, pregabalin, perampanel, rufinamide, tiagabine, topiramate, vigabatrin, and zonisamide) for adjunctive use in patients with refractory partial-onset seizures while using monotherapy (*Zhao et al 2017*). The efficacy outcomes studied were 50% responder rate and state of seizure freedom. The authors concluded that topiramate, levetiracetam, pregabalin, and oxcarbazepine were preferable for their relatively high efficacy and low risk of AEs. Rufinamide was the least preferable medication due to its low efficacy and high risk of AEs.
  - A network meta-analysis was conducted to evaluate the efficacy of 17 newer AEDs for treatment of refractory partial-onset epilepsy with or without secondary generalization (*Hu et al 2018*). The primary outcome was seizure freedom, which was defined as a 100% seizure reduction in the maintenance or double-blind treatment period of the trial. Safety was assessed by the withdrawal rate due to treatment-emergent AEs. Based on results of 54 studies that evaluated the efficacy outcome, the most effective agents included tiagabine, brivaracetam, and valproic acid, and the least effective agents included rufinamide, lamotrigine, and zonisamide. Products with favorable safety included levetiracetam, brivaracetam, and perampanel, while those with the least favorable safety included retigabine, oxcarbazepine, and rufinamide. The authors stated that agents with the best outcomes in terms of efficacy and safety included levetiracetam, vigabatrin, valproic acid, and brivaracetam.
  - Cannibidiol (Epidiolex) was approved in June 2018 for use in pediatric patients 2 years of age and older with LGS or Dravet syndrome (*FDA news release 2018*). It is the first FDA-approved drug for treatment of patients with Dravet syndrome and is the first approved drug that contains a purified substance, cannabidiol, derived from marijuana. Its approval for these 2 indications was based on 3 placebo-controlled trials in patients refractory to other treatments. Epidiolex, along with use of other agents, demonstrated a significant reduction in seizure frequency compared to placebo. To date, no comparative trials have been published.
  - Everolimus tablets for oral suspension (Afinitor Disperz) received an expanded indication for adjunctive use in TSC-associated partial-onset seizures in April 2018. Results of a randomized, double-blind, placebo-controlled study of 366 patients with inadequately controlled seizures on 2 or more AEDs demonstrated a significant reduction in seizure frequency compared to placebo (*French et al 2016*).

- In August 2018, the FDA approved a second drug, stiripentol (Diacomit), for use in the treatment of seizures associated with Dravet syndrome. Two multicenter placebo-controlled studies evaluated the addition of stiripentol to clobazam and valproate therapy in patients 3 years to less than 18 years of age with Dravet syndrome. Responder rates (seizure frequency reduced by 50%) with respect to generalized tonic-clonic seizures were significantly lower with stiripentol compared to placebo (*Diacomit prescribing information 2018).*

CLINICAL GUIDELINES

- **Efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy**. American Academy of Neurology and American Epilepsy Society (*French et al 2004A, Kanner et al, 2018A*).
  - A 2018 update to the 2004 guideline focuses on treatment of new-onset epilepsy with second and third generation AEDs. The 2004 publication summarizes the efficacy, tolerability, and safety of gabapentin, lamotrigine, topiramate, tiagabine, oxcarbazepine, levetiracetam, and zonisamide for the treatment of children and adults with newly diagnosed partial and generalized epilepsies.
  - The recommendations from the 2004 guideline include the following:
    - Patients with newly diagnosed epilepsy who require treatment can be initially treated with standard AEDs such as carbamazepine, phenytoin, valproic acid, or phenobarbital, or on the newer AEDs lamotrigine, gabapentin, oxcarbazepine, or topiramate. Choice will depend on individual patient characteristics.
    - Lamotrigine can be included in the options for children with newly diagnosed absence seizures.
  - The 2018 recommendations include the following :
    - As monotherapy in adult patients with new-onset focal epilepsy or unclassified generalized tonic-clonic seizures:
      - Lamotrigine use should be considered to decrease seizure frequency.
      - Lamotrigine use should be considered and gabapentin use may be considered to decrease seizure frequency in patients aged ≥ 60 years.
      - Levetiracetam use and zonisamide use may be considered to decrease seizure frequency.
      - Vigabatrin appears to be less efficacious than carbamazepine immediate-release and may not be offered; furthermore, the toxicity profile precludes vigabatrin use as first-line therapy.
      - Pregabalin 150 mg per day is possibly less efficacious than lamotrigine 100 mg per day.
      - There is insufficient evidence to consider use of gabapentin, oxcarbazepine, or topiramate over carbamazepine.
      - There is insufficient evidence to consider use of topiramate instead of phenytoin in urgent treatment of new-onset or recurrent focal epilepsy, unclassified generalized tonic-clonic seizures, or generalized epilepsy presenting with generalized tonic-clonic seizures.
      - Data are lacking to support or refute use of third-generation AEDs (eslicarbazepine, ezogabine, lacosamide, perampanel, pregabalin, and rufunamide), clobazam, felbamate, or vigabatrin for new-onset epilepsy.
      - Data are lacking to support or refute use of newer AEDs in treating unclassified generalized tonic-clonic seizures.
    - Ethosuximide or valproic acid should be considered before lamotrigine to decrease seizure frequency in children with absence epilepsy. An exception would be if there are compelling AE-related concerns with use of ethosuximide or valproic acid.
    - The guideline does not address newly approved agents including cannabidiol, everolimus, or stiripentol.
- **Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy**. American Academy of Neurology and American Epilepsy Society (*Kanner et al 2018B*, *French et al 2004B*).
  - A 2018 update to the 2004 guideline focuses on management of treatment-resistant epilepsy with second and third generation AEDs. The 2004 publication summarizes the efficacy, tolerability, and safety of gabapentin, lamotrigine, topiramate, tiagabine, oxcarbazepine, levetiracetam, and zonisamide for the treatment of children and adults with refractory partial and generalized epilepsies.
  - Recommendations from the 2004 guideline include the following:
    - It is appropriate to use gabapentin, lamotrigine, tiagabine, topiramate, oxcarbazepine, levetiracetam, and zonisamide as add-on therapy in patients with refractory epilepsy.
    - Oxcarbazepine, topiramate, and lamotrigine can be used as monotherapy in patients with refractory partial epilepsy.
    - Topiramate may be used for the treatment of refractory generalized tonic-clonic seizures in adults and children.

- Gabapentin, lamotrigine, oxcarbazepine, and topiramate may be used as adjunctive treatment of children with refractory partial seizures.
- Topiramate and lamotrigine may be used to treat drop attacks associated with LGS in adults and children.

○ Recommendations from the 2018 guideline include the following:

- As adjunctive therapy in patients with treatment-resistant adult focal epilepsy (TRAFE):
  - Immediate-release pregabalin and perampanel are established as effective to reduce seizure frequency.
  - Lacosamide, eslicarbazepine, and extended-release topiramate should be considered to decrease seizure frequency.
  - Vigabatrin and rufinamide are effective for decreasing seizure frequency, but are not first-line agents.
  - Ezogabine use should be considered to reduce seizure frequency, but carries a serious risk of skin and retinal discoloration.
  - Clobazam and extended-release oxcarbazepine may be considered to decrease seizure frequency.
- As monotherapy in patients with TRAFE:
  - Eslicarbazepine use may be considered to decrease seizure frequency.
  - Data are insufficient to recommend use of second- and the other third-generation AEDs.
- For add-on therapy for generalized epilepsy, immediate-release and extended-release lamotrigine should be considered as add-on therapy to decrease seizure frequency in adults with treatment-resistant generalized tonic-clonic seizures secondary to generalized epilepsy. Levetiracetam use should be considered to decrease seizure frequency as add-on therapy for treatment-resistant generalized tonic-clonic seizures and for treatment-resistant juvenile myoclonic epilepsy.
- Rufinamide is effective to reduce seizure frequency as add-on therapy for LGS. Clobazam use should be considered as add-on therapy for LGS.
- For add-on therapy in pediatric patients with treatment-resistant focal epilepsy:
  - Levetiracetam use should be considered to decrease seizure frequency (ages 1 month to 16 years).
  - Zonisamide use should be considered to decrease seizure frequency (age 6 to 17 years).
  - Oxcarbazepine use should be considered to decrease seizure frequency (age 1 month to 4 years).
  - Data are unavailable on the efficacy of clobazam, eslicarbazepine, lacosamide, perampanel, rufinamide, tiagabine, or vigabatrin.
- The guideline does not address newly approved agents including cannabidiol, everolimus, or stiripentol.

- **Evidence-based guideline: management of an unprovoked first seizure in adults.** Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society (*Krumholz et al 2015*).
  - This practice guideline makes recommendations based on a consideration of the evidence for prognosis and treatment of adults with an unprovoked first seizure.
  - Recommendations include the following:
    - Adults presenting with an unprovoked first seizure should be informed that the chance for a recurrent seizure is greatest within the first 2 years after a first seizure (21% to 45%).
    - Clinicians should also advise such patients that clinical factors associated with an increased risk of seizure recurrence include a prior brain insult such as a stroke or trauma, an EEG with epileptiform abnormalities, a significant brain-imaging abnormality, or a nocturnal seizure.
    - Clinicians should advise patients that, although immediate AED therapy, as compared with delay of treatment pending a second seizure, is likely to reduce the risk of a seizure recurrence in the 2 years subsequent to a first seizure, it may not improve quality of life.
    - Clinicians should advise patients that over the longer term (> 3 years), immediate AED treatment is unlikely to improve the prognosis for sustained seizure remission.
    - Patients should be advised that their risk for AED AEs ranges from 7% to 31% and that these AEs are predominantly mild and reversible.
  - Immediate AED therapy after an unprovoked first seizure is likely to reduce seizure recurrence risk. A reduction in risk may be important, particularly for adults, for whom seizure recurrences may cause serious psychological and social consequences such as loss of driving privileges and limitations on employment. However, immediate AED treatment is not well accepted and is debated. Decisions should be based on weighing the risk of recurrence against the AEs of AED therapy, and should take patient preferences into account.
  - It is accepted that when a patient has a second or additional seizures, an AED should be initiated because the risk of subsequent seizures is very high.

- **Evidence-based guideline: treatment of convulsive status epilepticus in children and adults.** Guideline Committee of the American Epilepsy Society (*Glauser et al 2016*).
  - This publication provides conclusions and a treatment algorithm based on a structured literature review of randomized trials of anticonvulsant treatments for seizures lasting longer than 5 minutes. A total of 38 trials were included.
  - For treatment in the adult population, conclusions included the following:
    - Intramuscular (IM) midazolam, intravenous (IV) lorazepam, IV diazepam (with or without phenytoin), and IV phenobarbital are established as efficacious at stopping seizures lasting at least 5 minutes.
    - IV lorazepam is more effective than IV phenytoin in stopping seizures lasting at least 10 minutes.
    - There is no difference in efficacy between IV lorazepam followed by IV phenytoin, IV diazepam plus phenytoin followed by IV lorazepam, and IV phenobarbital followed by IV phenytoin.
    - IV valproic acid has similar efficacy to IV phenytoin or continuous IV diazepam as second therapy after failure of a benzodiazepine.
    - Insufficient data exist in adults about the efficacy of levetiracetam as either initial or second therapy.
    - In adults with status epilepticus without established IV access, IM midazolam is established as more effective compared with IV lorazepam.
    - No significant difference in effectiveness has been demonstrated between lorazepam and diazepam in adults with status epilepticus.
  - For treatment in the pediatric population, conclusions included the following:
    - IV lorazepam and IV diazepam are established as efficacious at stopping seizures lasting at least 5 minutes.
    - Rectal diazepam, IM midazolam, intranasal midazolam, and buccal midazolam are probably effective at stopping seizures lasting at least 5 minutes.
    - Insufficient data exist in children about the efficacy of intranasal lorazepam, sublingual lorazepam, rectal lorazepam, valproic acid, levetiracetam, phenobarbital, and phenytoin as initial therapy.
    - IV valproic acid has similar efficacy but better tolerability than IV phenobarbital as second therapy after failure of a benzodiazepine.
    - Insufficient data exist in children regarding the efficacy of phenytoin or levetiracetam as second therapy after failure of a benzodiazepine.
    - In children with status epilepticus, no significant difference in effectiveness has been established between IV lorazepam and IV diazepam.
    - In children with status epilepticus, non-IV midazolam (IM/intranasal/buccal) is probably more effective than diazepam (IV/rectal).
  - Conclusions included the following (age not specified):
    - Insufficient data exist about the comparative efficacy of phenytoin and fosphenytoin. Fosphenytoin is better tolerated compared with phenytoin. When both are available, fosphenytoin is preferred based on tolerability, but phenytoin is an acceptable alternative.
  - The overall treatment algorithm directs that:
    - A benzodiazepine (IM midazolam, IV lorazepam, or IV diazepam) is recommended as the initial therapy of choice in the first phase of treatment (5 to 20 minutes after the beginning of the seizure). Although IV phenobarbital is established as efficacious and well tolerated as initial therapy, its slower rate of administration positions it as an alternative initial therapy. For prehospital settings or where first-line benzodiazepine options are not available, rectal diazepam, intranasal midazolam, and buccal midazolam are reasonable initial therapy alternatives.
    - In the second phase of treatment (from 20 to 40 minutes after the beginning of the seizure), reasonable options include fosphenytoin, valproic acid, and levetiracetam. There is no clear evidence that any of these options is better than the others. Because of AEs, IV phenobarbital is a reasonable second-therapy alternative if none of the 3 recommended therapies are available.
    - There is no clear evidence to guide therapy in the third phase of therapy (≥ 40 minutes after the beginning of the seizure).
- **Evidence-based guideline update: medical treatment of infantile spasms.** Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society (*Go et al 2012*). (Reaffirmed July 18, 2015)
  - This publication provides updated recommendations for the treatment of infantile spasms. The literature review included an evaluation of 26 published articles on this topic.
  - Recommendations include the following:

        - Evidence is insufficient to recommend the use of prednisolone, dexamethasone, and methylprednisolone as being as effective as adrenocorticotropic hormone (ACTH) for short-term treatment of infantile spasms.
        - Low-dose ACTH should be considered as an alternative to high-dose ACTH for treatment of infantile spasms.
        - ACTH or vigabatrin may be offered for short-term treatment of infantile spasms; evidence suggests that ACTH may be offered over vigabatrin.
        - Evidence is insufficient to recommend other therapies (valproic acid, vitamin B6, nitrazepam [not available in the United States], levetiracetam, zonisamide, topiramate, the ketogenic diet, or novel/combination therapies) for treatment of infantile spasms.
        - Hormonal therapy (ACTH or prednisolone) may be considered for use in preference to vigabatrin in infants with cryptogenic infantile spasms, to possibly improve developmental outcome.
        - A shorter lag time to treatment of infantile spasms with either hormonal therapy or vigabatrin may be considered to improve long-term cognitive outcomes.
    - There is a lack of sufficient randomized trials to provide definitive answers to key questions related to treatment of infantile spams.
- **Practice parameter: treatment of the child with a first unprovoked seizure.** Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society (*Hirtz et al 2003*). (Reaffirmed January 23, 2016)
    - This parameter reviews published literature relevant to the decision to begin treatment after a child or adolescent experiences a first unprovoked seizure and presents evidence-based practice recommendations. Treatment during the neonatal period is not addressed.
    - Recommendations include the following:
        - Treatment with AEDs is not indicated for the prevention of the development of epilepsy.
        - Treatment with AEDs may be considered in circumstances where the benefits of reducing the risk of a second seizure outweigh the risks of pharmacologic and psychosocial AEs.
    - The majority of children who experience a first unprovoked seizure will have few or no recurrences. Treatment with AEDs after a first seizure as opposed to after a second seizure has not been shown to improve prognosis for long-term seizure remission.
    - Treatment has been shown in several studies combining both children and adults to reduce the risk of seizure recurrence; however, there is a relative paucity of data from studies involving only children after a first seizure.
- **Summary of recommendations for the management of infantile seizures**. Task force report for the ILAE Commission of Pediatrics (*Wilmshurst et al 2015*).
    - This publication recommends an approach to the standard and optimal management of infants with seizures. When possible, recommendations are evidence-based; however, when no evidence was available, recommendations are based on expert opinion and standard practice.
    - Recommendations/findings include the following:
        - There is no indication for initiation of chronic AEDs for simple febrile seizures. However, in the acute treatment of febrile seizures, it is important to treat seizures lasting 10 minutes or longer.
        - In an otherwise healthy infant, a policy of “wait and see” is reasonable after the first afebrile seizure. However, this is a rare event and close monitoring is essential.
        - Treatment options with established or probable efficacy include the following:
            - Focal seizures: levetiracetam
            - Epileptic spasms: High-dose or low-dose ACTH
            - Dravet syndrome: stiripentol (not available in the United States)
        - Treatment options with possible efficacy include the following:
            - Generalized seizures: levetiracetam, valproate, lamotrigine, topiramate, clobazam
            - Epileptic spasms: prednisone, vigabatrin
            - Benign infantile convulsions: carbamazepine, phenobarbital, valproate
            - Dravet syndrome: topiramate, zonisamide, valproate
            - Benign myoclonic epilepsy of infancy: valproate, topiramate, lamotrigine, clonazepam
            - Provoked or situational seizures: carbamazepine
        - There is no clear evidence supporting an optimal duration of treatment; this is dependent on seizure type.

- **Guidelines on neonatal seizures**. World Health Organization (WHO) (*WHO 2011*).
  - This document was prepared based on a systematic review of the literature and involved cooperation between the WHO, the ILAE, and the International Bureau of Epilepsy (IBE).
  - Recommendations include the following:
    - Phenobarbital should be used as the first-line agent for treatment of neonatal seizures and should be made readily available in all settings.
    - In neonates who continue to have seizures despite administering the maximum tolerated dose of phenobarbital, either a benzodiazepine, phenytoin, or lidocaine may be used as the second-line agent for control of seizures (use of phenytoin or lidocaine requires cardiac monitoring).
    - In neonates with a normal neurological examination and/or normal EEG, stopping AEDs may be considered if the neonate has been seizure-free for > 72 hours; the drug(s) should be reinstituted if seizures recur.
    - In neonates in whom seizure control is achieved with a single AED, the drug can be discontinued abruptly without tapering the dose. In neonates requiring > 1 AED for seizure control, the drugs may be stopped one at a time, with phenobarbital being the last drug to be withdrawn.
- **Practice parameter update: management issues for women with epilepsy – focus on pregnancy (an evidence-based review): teratogenesis and perinatal outcomes.** Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society (*Harden et al 2009A*). (Reaffirmed July 13, 2013)
  - This publication summarizes evidence for selected issues regarding the clinical management of women with epilepsy (WWE) who are pregnant or planning to be pregnant.
  - Recommendations include the following:
    - If possible, avoidance of the use of valproate as part of polytherapy during the first trimester of pregnancy should be considered to decrease the risk of major congenital malformations (MCMs).
    - If possible, avoidance of the use of valproate monotherapy during the first trimester of pregnancy may be considered to decrease the risk of MCMs.
    - To reduce the risk of MCMs, the use of valproate during the first trimester of pregnancy should be avoided, if possible, compared to the use of carbamazepine.
    - To reduce the risk of MCMs, avoidance of the use of polytherapy with valproate during the first trimester of pregnancy, if possible, should be considered, compared to polytherapy without valproate.
    - To reduce the risk of MCMs, avoidance of the use of valproate during the first trimester of pregnancy, if possible, may be considered, compared to the use of phenytoin or lamotrigine.
    - To reduce the risk of MCMs, avoidance of the use of AED polytherapy during the first trimester of pregnancy, if possible, compared to monotherapy should be considered.
    - Limiting the dosage of valproate or lamotrigine during the first trimester, if possible, should be considered to lessen the risk of MCMs.
    - Avoidance of the use of valproate, if possible, should be considered to reduce the risk of neural tube defects and facial clefts, and may be considered to reduce the risk of hypospadias.
    - Avoidance of phenytoin, carbamazepine, and phenobarbital, if possible, may be considered to reduce the risk of specific MCMs: cleft palate for phenytoin use, posterior cleft palate for carbamazepine use, and cardiac malformations for phenobarbital use.
    - Carbamazepine exposure probably does not produce cognitive impairment in offspring of WWE.
    - Avoiding valproate in WWE during pregnancy, if possible, should be considered to reduce the risk of poor cognitive outcomes.
    - Avoiding phenytoin and phenobarbital in WWE during pregnancy, if possible, may be considered to reduce the risk of poor cognitive outcomes.
    - Monotherapy should be considered in place of polytherapy, if possible, for WWE who take AEDs during pregnancy to reduce the risk of poor cognitive outcomes.
    - For WWE who are pregnant, avoidance of valproate, if possible, should be considered compared to carbamazepine to reduce the risk of poor cognitive outcomes.
    - For WWE who are pregnant, avoidance of valproate, if possible, may be considered compared to phenytoin to reduce the risk of poor cognitive outcomes.
  - Valproate has the most data showing an association with risk from in utero exposure. If a change from valproate to another AED is planned, it is prudent to make this change well before pregnancy.

- Although many of the recommendations in this parameter suggest minimizing AED exposure during pregnancy, for most WWE, discontinuing AEDs is not a reasonable or safe option. Discontinuing AEDs may expose the mother and fetus to physical injury from accidents due to seizure activity.

- **Practice parameter update: management issues for women with epilepsy – focus on pregnancy (an evidence-based review): vitamin K, folic acid, blood levels, and breastfeeding.** Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society (*Harden et al 2009B*). (Reaffirmed July 13, 2013)
  - This publication summarizes evidence for selected issues regarding the clinical management of WWE who are pregnant or planning to be pregnant.
  - Recommendations include the following:
    - The fact that phenobarbital, primidone, phenytoin, carbamazepine, levetiracetam, valproate, gabapentin, lamotrigine, oxcarbazepine, and topiramate cross the placenta may be factored into the clinical decision regarding the necessity of AED treatment for a woman with epilepsy.
    - Monitoring of lamotrigine, carbamazepine, and phenytoin levels during pregnancy should be considered.
    - Monitoring of levetiracetam and oxcarbazepine (as monohydroxy derivative) levels during pregnancy may be considered.
    - There is insufficient evidence to support or refute a change in phenobarbital, valproate, primidone, or ethosuximide levels related to pregnancy, but this lack of evidence should not discourage monitoring levels of these AEDs during pregnancy.
    - Valproate, phenobarbital, phenytoin, and carbamazepine may not transfer into breast milk to as great an extent as primidone, levetiracetam, gabapentin, lamotrigine, and topiramate.
  - Although many of the AEDs were shown to cross the placenta or enter breast milk, studies were limited in duration and did not systematically evaluate neonatal symptoms.

- Guidelines also support the use of AEDs for several common non-epilepsy indications:
  - The American Academy of Neurology and American Headache Society state that AEDs with established efficacy for migraine prevention include valproate, divalproex sodium, and topiramate; carbamazepine is noted to be possibly effective (*Silberstein et al 2012*).
  - The American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation state that, for relief of painful diabetic neuropathy, pregabalin is established as effective, and gabapentin and valproate are probably effective (*Bril et al 2011*).
  - The American Academy of Neurology states that gabapentin and pregabalin are of benefit in reducing pain from postherpetic neuralgia (*Dubinsky et al 2004*).
  - American Psychiatric Association guidelines describe the key role of AEDs in the management of bipolar disorder, including the following (*Hirschfeld et al 2002*):
    - First-line pharmacological treatment for more severe manic or mixed episodes is either lithium plus an antipsychotic or valproate plus an antipsychotic; for less ill patients, monotherapy with lithium, valproate, or an antipsychotic may be sufficient. For mixed episodes, valproate may be preferred over lithium. Carbamazepine and oxcarbazepine are alternatives.
    - First-line pharmacological treatment for bipolar depression is either lithium or lamotrigine. When an acute depressive episode of bipolar disorder does not respond to first-line medication treatment, the next steps include adding lamotrigine, bupropion, or paroxetine.
    - The initial treatment for patients who experience rapid cycling should include lithium or valproate; an alternative is lamotrigine.
    - The medications with the best empirical evidence to support their use in maintenance treatment include lithium and valproate; possible alternatives include lamotrigine, carbamazepine, or oxcarbazepine.
    - Note: This guideline was published in 2002 and cannot be assumed to be current; however, AEDs continue to be recommended for both acute (mania or hypomania) and maintenance phases of bipolar disorder *(Post 2017, Stovall 2018).*

SAFETY SUMMARY

- Tolerability and safety are as important as efficacy in determining the overall effectiveness of epilepsy treatment (*Schachter 2018*).

- Common AEs among AEDs include the following (*Schachter 2018*).
  - Systemic AEs:
    - nausea, vomiting, constipation, diarrhea, abdominal pain, anorexia
    - rash, pruritus
    - hyponatremia (carbamazepine, oxcarbazepine)
    - weight gain (ezogabine, pregabalin, valproate), weight loss (felbamate, topiramate, stiripentol)
  - Neurologic AEs:
    - headache
    - somnolence, sedation, drowsiness, lethargy, fatigue
    - dizziness, vertigo
    - tremor, anxiety, nervousness, insomnia
    - aggression, irritability, behavioral changes, hyperactivity
    - attention disturbance, inattention
    - depression, mood alteration
    - confusion, memory impairment
    - ataxia, abnormal coordination, falls
    - blurred or double vision
- Examples of rare but serious AEs include the following (*Schachter 2018*):
  - suicidal ideation and behavior (AEDs as a class, except everolimus)
  - neutropenia, leukopenia, pancytopenia, agranulocytosis, thrombocytopenia, and/or aplastic anemia (brivaracetam, carbamazepine, ethosuximide, felbamate, lacosamide, levetiracetam, oxcarbazepine, phenytoin, phenobarbital, stiripentol, valproate, zonisamide)
  - anaphylaxis or angioedema (brivaracetam, levetiracetam, pregabalin)
  - severe skin rashes, Stevens-Johnson syndrome (SJS), and/or toxic epidermal necrolysis (TEN) (carbamazepine, clobazam, eslicarbazepine, ethosuximide, lamotrigine, levetiracetam, oxcarbazepine, phenytoin, primidone, phenobarbital, rufinamide, tiagabine, valproate, zonisamide)
  - hepatic failure (carbamazepine, ethosuximide, felbamate, phenytoin, primidone, phenobarbital, valproate)
  - hepatocellular injury (cannabidiol)
  - prolonged PR interval, atrioventricular block, and/or changes in QT interval (eslicarbazepine, ezogabine, lacosamide, rufinamide)
  - serum sickness (carbamazepine, ethosuximide, phenytoin, primidone, phenobarbital, valproate)
  - multiorgan hypersensitivity (gabapentin, lacosamide, lamotrigine, oxcarbazepine)
  - severe neuropsychiatric effects/hostility/aggression (perampanel)
  - vision loss (ezogabine)
  - hyponatremia (eslicarbazepine)
  - hemophagocytic lymphohistiocytosis (HLH) (lamotrigine)
- A number of AEDs carry boxed warnings related to potentially serious AEs; these include the following:
  - Carbamazepine:
    - Serious and sometimes fatal dermatologic reactions, including TEN and SJS, have been reported. Studies in patients of Chinese ancestry have found a strong association between the risk of developing SJS/TEN and the presence of HLA-B*1502, an inherited allelic variant of the HLA-B gene. Patients with ancestry in genetically at-risk populations (across broad areas of Asia) should be screened for the presence of HLA-B*1502 prior to initiating treatment with carbamazepine.
    - Aplastic anemia and agranulocytosis have been reported. If a patient exhibits low or decreased white blood cell or platelet counts, the patient should be monitored closely, and discontinuation of the drug should be considered if any evidence of significant bone marrow depression develops.
  - Clobazam, clonazepam, clorazepate, and diazepam:
    - Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Concomitant prescribing should be reserved for use in patients for whom alternative treatment options are inadequate, and patients should be followed for signs and symptoms of respiratory depression and sedation.
  - Ezogabine:
    - Ezogabine can cause retinal and macular abnormalities and may be associated with vision loss. Ezogabine should only be used in patients who have responded inadequately to several alternative treatments and for

whom the benefits outweigh the potential risk of vision loss. Ezogabine should be discontinued in patients who fail to show substantial clinical benefit after adequate titration. All patients taking ezogabine should have baseline and periodic (every 6 months) systematic visual monitoring by an ophthalmic professional. If retinal pigmentary abnormalities or vision changes are detected, ezogabine should be discontinued unless no other suitable treatment options are available and the benefits of treatment outweigh the potential risk of vision loss.

- Felbamate:
  - Use is associated with a marked increase in the incidence of aplastic anemia. Felbamate should only be used in patients whose epilepsy is so severe that the risk of aplastic anemia is deemed acceptable. Routine blood testing cannot be reliably used to reduce the incidence of aplastic anemia, but it will in some cases allow detection of hematologic changes before the syndrome declares itself clinically. Felbamate should be discontinued if any evidence of bone marrow depression occurs.
  - Cases of acute liver failure have been reported. Felbamate should not be prescribed for anyone with a history of hepatic dysfunction. Treatment should be initiated only in individuals without active liver disease and with normal baseline serum transaminases. It has not been proven that periodic serum transaminase testing will prevent serious injury, but it is generally believed that early detection of drug-induced hepatic injury along with immediate withdrawal of the suspect drug enhances the likelihood for recovery. Serum transaminases should be monitored at baseline and periodically thereafter. Felbamate should be discontinued if either AST or ALT become increased to ≥ 2 times the upper limit of normal, or if clinical signs and symptoms suggest liver failure, and should not be considered for retreatment.
- Fosphenytoin and phenytoin:
  - There is a cardiovascular risk associated with rapid IV infusion rates. The rate of administration should not exceed recommendations, and careful cardiac monitoring is required.
- Lamotrigine:
  - Cases of life-threatening serious skin rashes, including SJS and TEN, and/or rash-related death have been caused by lamotrigine. Benign rashes are also caused by lamotrigine; however, it is not possible to predict which rashes will prove to be serious. Lamotrigine should be discontinued at the first sign of a rash, unless the rash is clearly not drug related.
- Perampanel:
  - Serious or life-threatening psychiatric and behavioral AEs including aggression, hostility, irritability, anger, and homicidal ideation and threats have been reported. Patients should be monitored for these reactions and for changes in mood, behavior, or personality. The dose should be reduced if these symptoms occur, and it should be discontinued if symptoms are severe or worsening.
- Valproic acid and divalproex sodium:
  - Hepatoxicity, including fatalities, have been reported, usually during the first 6 months of treatment. Serum liver tests are required and patients should be monitored closely.
  - There is a risk to fetuses exposed in utero, particularly neural tube defects, other major malformations, and decreased intelligence quotient (IQ). Valproate should not be given to a woman of childbearing potential unless the drug is essential to the management of her medical condition, and women should use effective contraception while using valproate.
  - Pancreatitis, including fatal hemorrhagic cases, has occurred. Patients and guardians should be warned that abdominal pain, nausea, vomiting, and/or anorexia can be symptoms of pancreatitis that require prompt medical evaluation.
- Vigabatrin:
  - Vigabatrin can cause permanent bilateral concentric visual field constriction, including tunnel vision that can result in disability. In some cases, vigabatrin may also damage the central retina and may decrease visual acuity. Baseline and periodic vision assessment is recommended. However, this assessment cannot always prevent vision damage, and once detected, vision loss due to vigabatrin is not reversible. Vigabatrin should be withdrawn from patients who fail to show substantial clinical benefit.
  - Due to the risks of vision loss, vigabatrin is available only through a risk evaluation and mitigation strategy (REMS) program (*Vigabatrin REMS 2017*). Healthcare providers who prescribe vigabatrin and pharmacies that dispense the product must be specially certified. Each patient must be enrolled in the REMS program. Prescribers must ensure that periodic visual monitoring is performed and report any AE suggestive of vision loss to the vigabatrin REMS program.

- Everolimus is an antineoplastic, immunosuppressant agent associated with several adverse reactions.

- The most common AE that occurred in trials for TSC-associated partial-onset seizures was stomatitis.
- More serious AEs include:
  - non-infectious pneumonitis
  - infections
  - hypersensitivity reactions
  - angioedema (when taken with an angiotensin converting enzyme inhibitor)
  - renal failure
  - impaired wound healing
  - myelosuppression
  - reduced immune response with vaccination
  - hyperglycemia
  - hyperlipidemia
  - embryo-fetal toxicity

DOSING AND ADMINISTRATION

- General dosing information is provided in Table 3. Dosing may vary based on the specific indication, interacting medications, and the patient's age and renal and hepatic function. Additionally, some medications are recommended to be titrated during initial treatment. Please refer to the prescribing information of the individual products for more detailed information.

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Barbiturates				
Mephobarbital* (Mebaral)‡	tablets	oral	Once daily or divided 3 to 4 times per day	
Pentobarbital (Nembutal†)	injection	IV, IM	Single dose	Acute use only. If needed, additional small increments may be given after the initial dose.
Phenobarbital* (Luminal†, Solfotyn†)	tablets, elixir, injection	oral, IV, IM	2 to 3 times per day	
Primidone (Mysoline)	tablets	oral	3 to 4 times per day	
Benzodiazepines				
Clobazam (Onfi)	tablets, oral suspension	oral	1 or 2 times per day	Daily doses > 5 mg should be given in divided doses 2 times per day.
Clonazepam (Klonopin)	tablets, orally disintegrating tablets (wafers)	oral	3 times per day	
Clorazepate (Tranxene T-Tab)	tablets	oral	2 to 3 times per day	
Diazepam (Diastat, Valium)	tablets, oral solution, oral concentrate, rectal gel, injection	oral, rectal, IV, IM	2 to 4 times per day	For the rectal gel (for acute use), a second dose may be given 4 to 12 hours after the initial dose when required. The injection is also for short-term acute use.
Hydantoins				
Ethotoin (Peganone)	tablets	oral	4 to 6 times per day	

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Fosphenytoin (Cerebyx)	injection	IV, IM	2 times per day or other divided doses based on drug levels	Generally used in acute situations as a loading dose; may be given in divided doses when substituted for oral phenytoin.
Phenytoin (Dilantin, Phenytek)	extended-release capsules, chewable tablets, oral suspension, injection	oral, IV, IM	2 to 4 times per day	Capsules are extended-release and may be suitable for once-daily dosing in some adults.
Miscellaneous				
Brivaracetam (Briviact)	tablets, oral solution, injection	oral, IV	2 times per day	The injection may be used when oral administration is temporarily not feasible.
Cannabidiol	Oral solution	Oral	2 times per day	The provided oral syringe should be used to measure an accurate dose.
Carbamazepine (Carbatrol, Epitol, Equetro, Tegretol, Tegretol-XR)	tablets, chewable tablets, oral suspension, extended-release tablets, extended-release capsules	oral	2 to 4 times per day	Immediate-release tablets are given 2 to 3 times per day and the suspension is given 4 times per day. Carbatrol and Equetro are twice-daily extended-release capsule formulations; these capsules may be opened and sprinkled on soft food. Tegretol-XR is a twice-daily extended-release tablet formulation; these tablets must be swallowed whole.
Divalproex sodium (Depakote, Depakote ER, Depakote Sprinkle)	delayed-release tablets, delayed-release sprinkle capsules, extended-release tablets	oral	2 to 3 times per day (once daily for extended-release tablets)	Delayed-release tablets and extended-release tablets should be swallowed whole. Sprinkle capsules may be opened and sprinkled on soft food. Delayed-release tablet and capsule doses > 250 mg per day should be given in divided doses.
Eslicarbazepine (Aptiom)	tablets	oral	once daily	Tablets may be crushed.
Ethosuximide (Zarontin)	capsules, oral solution/syrup	oral	once daily or in divided doses	
Everolimus (Afinitor Disperz)	tablets for oral suspension	oral	once daily	Should be taken at the same time each day with or without food. Suspension should be prepared using water only and administered immediately after preparation. The suspension should be discarded if not

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				taken within 60 minutes of preparation. Dose adjustments are made based on trough drug concentration.
Ezogabine (Potiga)‡	tablets	oral	3 times per day	Tablets should be swallowed whole.
Felbamate (Felbatol)	tablets, oral suspension	oral	3 or 4 times per day	
Gabapentin (Neurontin)	tablets, capsules, oral solution	oral	3 times per day	Capsules should be swallowed whole.
Lacosamide (Vimpat)	tablets, oral solution, injection	oral, IV	2 times per day	
Lamotrigine (Lamictal, Lamictal ODT, Lamictal XR)	tablets, chewable dispersible tablets, orally disintegrating tablets, extended-release tablets	oral	2 times per day (once daily for extended-release tablets)	Only whole tablets should be administered. Extended-release tablets must not be chewed or crushed.
Levetiracetam (Keppra, Keppra XR, Roweepra, Roweepra XR, Spritam)	tablets, tablets for oral suspension, oral solution, extended-release tablets, injection	oral, IV	2 times per day (once daily for extended-release tablets)	Tablets and extended-release tablets should not be chewed or crushed. Tablets for oral suspension (Spritam) can be dissolved in liquid and swallowed or allowed to disintegrate in the mouth.
Methsuximide (Celontin)	capsules	oral	1 to 4 times per day (*Lexicomp 2017*)	
Oxcarbazepine (Oxtellar XR, Trileptal)	tablets, oral suspension, extended-release tablets	oral	2 times per day (once daily for extended-release tablets)	In conversion of oxcarbazepine immediate-release to Oxtellar XR, higher doses of Oxtellar XR may be necessary. Extended-release tablets must not be chewed or crushed.
Perampanel (Fycompa)	tablets, oral suspension	oral	once daily at bedtime	
Pregabalin (Lyrica)	capsules, oral solution	oral	2 to 3 times per day	
Rufinamide (Banzel)	tablets, oral suspension	oral	2 times per day	Tablets can be administered whole, as half tablets, or crushed.
Stiripentol (Diacomit)	capsules, powder for oral suspension	oral	2 to 3 times per day	Capsules must be swallowed whole with a glass of water during a meal. Powder should be mixed with water and taken immediately after mixing during a meal.
Tiagabine (Gabitril)	tablets	oral	2 to 4 times per day	

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Topiramate (Topamax, Topamax Sprinkle, Topiragen, Trokendi XR, Qudexy XR)	tablets, sprinkle capsules, extended-release capsules, extended-release sprinkle capsules	oral	2 times per day (once daily for extended-release capsule formulations)	Sprinkle capsules may be opened and sprinkled on soft food. Extended-release capsules (Trokendi XR) must not be chewed or crushed, but extended release sprinkle capsules (Qudexy XR) may be sprinkled on soft food.
Valproic acid (Depakene, Stavzor DR‡, Depacon)	capsules, delayed-release capsules, oral solution/ syrup, injection	oral, IV	2 to 4 times per day (*Lexicomp 2017*)	Capsules should be swallowed whole without chewing to avoid local irritation of the mouth and throat. If the total dose exceeds 250 mg, it should be given in divided doses.
Vigabatrin (Sabril)	tablets, powder for oral solution	oral	2 times per day	Powder for oral solution is supplied in individual dose packets to be mixed with water before administration.
Zonisamide (Zonegran)	capsules	oral	1 or 2 times per day	Capsules must be swallowed whole.

* Not FDA approved
† Brand product not currently marketed; generic is available
‡ No brand or generic currently marketed

CONCLUSION

- Several classes of AEDs are available, including barbiturates, benzodiazepines, hydantoins, and miscellaneous agents. These products vary in terms of their indications for specific seizure types and indications other than epilepsy.
- Overall, the anticonvulsants have demonstrated efficacy for their FDA-approved uses. When possible, monotherapy with a single AED is the preferred treatment approach.
- Patients who are refractory to monotherapy may be treated with combination therapy. When considering combination therapy, it is recommended to combine medications with different mechanisms of action and AE profiles.
- Comparative efficacy data for the management of epilepsy are limited.
- Tolerability and safety are as important as efficacy in determining the overall effectiveness of epilepsy treatment. Both systemic AEs and neurologic AEs commonly occur. Some AEDs are associated with rare but serious AEs, and careful patient selection and monitoring are required.
- Epilepsy management can be complex and it is often treated by neurologists. A variety of AEDs should be available to allow clinicians to select the most clinically appropriate agent for individual patients.
- Anticonvulsants are also established as effective for several non-epilepsy indications, including (but not limited to) bipolar disorder, migraine prophylaxis, and neuropathic pain.

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- Zarontin (capsules) [package insert], New York, NY: Pfizer Inc.; May 2016.
- Zarontin (oral solution) [package insert], New York, NY: Pfizer Inc.; May 2016.
- Zhu LN, Chen D, Xu D, Tan G, Wang HJ, Liu L. Newer antiepileptic drugs compared to levetiracetam as adjunctive treatments for uncontrolled focal epilepsy: an indirect comparison. *Seizure*. 2017 Aug 16;51:121-132 (Epub).
- Zhao T, Feng X, Liu J, et al. Evaluate the efficacy and safety of anti-epileptic medications for partial seizures of epilepsy: A network meta-analysis. *J Cell Biochem*. 2017;118(9):2850-2864. doi: 10.1002/jcb.25936.
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Publication Date: September 4, 2018

Prior Authorization Guideline

Guideline Name Pulmonary Arterial Hypertension Agents

1 . Indications

Drug Name: Adcirca (tadalafil) Tablets **Indications** **Pulmonary Arterial Hypertension (PAH)** Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group I) to improve exercise ability. Studies establishing effectiveness included predominately patients with New York Heart Association (NYHA) Functional Class II–III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).
Drug Name: Revatio (sildenafil) Injection, Tablets, Oral Suspension **Indications** **Pulmonary Arterial Hypertension (PAH)** Indicated for the treatment of PAH (WHO Group I) in adults to improve exercise ability and delay clinical worsening. The delay in clinical worsening was demonstrated when Revatio was added to background epoprostenol (Flolan) therapy. Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominately patients with NYHA Functional Class II-III symptoms and idiopathic etiology (71%) or associated with connective tissue disease (25%). Revatio injection is for the continued treatment of patients with PAH who are currently prescribed oral Revatio and who are temporarily unable to take oral medication. Limitation of Use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

2 . Criteria

Alternative Proposed Criteria A:

Product Name: Brand Adcirca tablet, Generic tadalafil tablet, Brand Revatio tablet, Generic sildenafil tablet, Revatio oral suspension, Brand Revatio injection or Generic sildenafil injection.

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	12 Month
Therapy Stage	Initial Authorization and reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 An ICD-10 diagnosis must be submitted on the pharmacy claims from the following list:

ICD-10	Description
I27.20	PULMONARY HYPERTENSION, UNSPECIFIED
I27.21	SECONDARY PULMONARY ARTERIAL HYPERTENSION
I27.22	PULMONARY HYPERTENSION DUE TO LEFT HEART DISE
I27.23	PULMONARY HYPERTENSION DUE TO LUNG DISEASES A
I27.9	PULMONARY HEART DISEASE, UNSPECIFIED

OR

2 Diagnosis of pulmonary arterial hypertension

Proposed Criteria B:

Product Name: Brand Adcirca tablet, Generic tadalafil tablet, Brand Revatio tablet, Generic sildenafil tablet

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of pulmonary arterial hypertension

   AND

2. Pulmonary arterial hypertension is symptomatic

   AND

3. One of the following:
   a. Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization

   OR

   b. Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

   AND

4. Prescribed by or in consultation with one of the following:
   a. Pulmonologist
   b. Cardiologist

Product Name: Brand Revatio injection or Generic sildenafil injection

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of pulmonary arterial hypertension

   AND

2. Pulmonary arterial hypertension is symptomatic

   AND

3. One of the following
   a. Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization

   OR

   b. Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

   AND

4. Prescribed by or in consultation with one of the following:
   a. Pulmonologist
   b. Cardiologist

   AND

5. Patient is unable to take oral medications

Product Name: Revatio oral suspension

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of pulmonary arterial hypertension

   AND

2. Pulmonary arterial hypertension is symptomatic

   AND

3. One of the following:
   a. Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization

   OR

   b. Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

   AND

4. Prescribed by or in consultation with one of the following:
   a. Pulmonologist
   b. Cardiologist

   AND

5. Patient is unable to ingest a solid dosage form (e.g., an oral tablet or capsule) due to one of the following:
   a. Age
   b. Oral-motor difficulties
   c. Dysphagia

Product Name: Brand Adcirca tablet, Generic tadalafil tablet, Brand Revatio injection, Generic sildenafil injection, Brand Revatio tablet, Revatio oral suspension, Generic sildenafil tablet

Diagnosis	All indications listed above
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. Documentation of positive clinical response to therapy

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Pulmonary Arterial Hypertension Medications

Managed Care Organization name: Anthem

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Anthem uses drug specific criteria rather than overall therapeutic class criteria; criteria is accessible in provider web portal– see attached documents

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Jeannine Murray

Signature of individual completing this form: Jeannine M Murray

Anthem Adempas (riociguat)

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

Medications	Quantity Limit
Adempas (riociguat) 0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg	May be subject to quantity limit

APPROVAL CRITERIA

Requests for Adempas (riociguat) may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[2] of pulmonary arterial hypertension (PAH) [World Health Organization (WHO) Group 1][3]; **AND**
II. Individual has WHO functional class II-IV[4] symptoms;

OR

III. Individual has a catheterization-proven diagnosis[2] of chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4)[3]; **AND**
IV. Individual is using for one of the following:
    A. Persistent or recurrent pulmonary hypertension after at least 180 days following surgical treatment with pulmonary endarterectomy; **OR**
    B. Inoperable (via pulmonary endarterectomy) CTEPH;

AND

V. Individual has WHO functional class II-IV[4] symptoms.

Adempas (riociguat) may **not** be approved for the following:

I. Individual has a diagnosis of severe hepatic impairment (Child-Pugh Class C); **OR**
II. Individual is on dialysis or has a creatinine clearance less than 15 mL/min; **OR**
III. Individual has a diagnosis of pulmonary veno-occlusive disease (PVOD); **OR**
IV. Individual has a diagnosis of pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP); **OR**
V. Use in combination with phosphodiesterase (PDE) inhibitors [such as, PDE-5 inhibitors (sildenafil, tadalafil, vardenafil) or nonspecific PDE inhibitors (dipyridamole, theophylline)]; **OR**
VI. Use in combination with nitrates (such as but not limited to, nitroglycerin) or nitric oxide donors (such as but not limited to, amyl nitrite) in any form.

Notes:

1. Adempas (riociguat) has a black box warning for embryo-fetal toxicity. Pregnancy should be excluded prior to start of treatment, monthly during treatment, and 1 month after stopping treatment in females of reproductive potential. Adempas should not be administered to pregnant females due to the potential of causing fetal harm. Pregnancy should be prevented using acceptable means of contraception during treatment and for one month after therapy discontinued. Adempas will be available for all females, regardless of reproductive potential, through a restricted risk evaluation and mitigation strategy (REMS) program. As a component of the Adempas REMS, prescribers, individuals, and pharmacies must enroll in the program.
2. Diagnostic criteria:
    A. PAH: Right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units (ACCF/AHA 2009).
    B. CTEPH (ACCF/AHA 2009, Kim et al. 2013): Pulmonary angiography via right-heart catheterization which shows a mPAP greater than 25 mm Hg caused by thromboemboli in the pulmonary arterial system.
3. WHO Pulmonary Hypertension (PH) Group Classification (ACCF/AHA 2009, Simonneau et al. 2013):
    A. Group 1: Pulmonary arterial hypertension (PAH)
    B. Group 2: PH due to left heart disease
    C. Group 3: PH due to lung diseases and/or hypoxia
    D. Group 4: Chronic thromboembolic PH (CTEPH)
    E. Group 5: Miscellaneous/PH with unclear multifactorial mechanisms
4. WHO functional classification of PH (CHEST 2014):
    A. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
    B. Class II: Slight limitation of physical activity. Comfortable at rest but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    C. Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    D. Class IV: Inability to carry out any physical activity without symptoms. Dyspnea and/or fatigue may be present at rest and discomfort is increased by any physical activity.

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. Accessed January 30, 2017.

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.

Anthem Letairis (ambrisentan)

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

Medications	Quantity Limit
Letairis (ambrisentan) 5mg, 10mg	May be subject to quantity limit

APPROVAL CRITERIA

Requests for Letairis (ambrisentan) may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[2] of pulmonary arterial hypertension (PAH) [World Health Organization (WHO) Group 1][3]; **AND**
II. Individual has WHO functional class II-IV[4] symptoms.

Letairis (ambrisentan) may **not** be approved for the following:

I. Individual has a diagnosis of idiopathic pulmonary fibrosis (IPF); **OR**
II. Individual has a diagnosis of moderate (Child-Pugh Class B) or severe (Child-Pugh Class C) hepatic impairment; **OR**
III. Individual is on dialysis or has a diagnosis of severe renal impairment (creatinine clearance less than 20 mL/min); **OR**
IV. In combination with other endothelin receptor antagonist (ERA) agents, such as but not limited to Opsumit (macitentan) or Tracleer (bosentan); **OR**
V. Individual is initiating therapy and has a diagnosis of clinically significant/severe anemia.

Notes:

1. Letairis (ambrisentan) has a black box warning for embryo-fetal toxicity. Letairis is very likely to produce serious birth defects if used by pregnant women, as this effect has been seen consistently when it is administered to animals. Pregnancy must therefore be excluded before the initiation of treatment and prevented during treatment with acceptable methods of contraception. Monthly pregnancy tests should be obtained during treatment and 1 month post-treatment. Because of the risks of birth defects, Letairis is available for females only through a special restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS). As a component of the Letairis REMS, prescribers, individuals, and pharmacies must enroll in the program.

2. Diagnostic criteria:
    A. PAH: Right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units (ACCF/AHA 2009).
    B. CTEPH: Pulmonary angiography via right-heart catheterization which shows a mPAP greater than 25 mm Hg caused by thromboemboli in the pulmonary arterial system (ACCF/AHA 2009, Kim et al. 2013).

3. WHO Pulmonary Hypertension (PH) Group Classification (ACCF/AHA 2009, Simonneau et al. 2013):
    A. Group 1: Pulmonary arterial hypertension (PAH)
    B. Group 2: PH due to left heart disease
    C. Group 3: PH due to lung diseases and/or hypoxia
    D. Group 4: Chronic thromboembolic PH (CTEPH)
    E. Group 5: Miscellaneous/PH with unclear multifactorial mechanisms

4. WHO functional classification of PH (CHEST 2014):
    A. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
    B. Class II: Slight limitation of physical activity. Comfortable at rest but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    C. Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    D. Class IV: Inability to carry out any physical activity without symptoms. Dyspnea and/or fatigue may be present at rest and discomfort is increased by any physical activity.

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. Accessed January 30, 2017.

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.

Anthem Opsumit (macitentan)

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

Medications	Quantity Limit
Opsumit (macitentan) 10 mg	May be subject to quantity limit

APPROVAL CRITERIA

Requests for Opsumit (macitentan) may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[2] of pulmonary arterial hypertension (PAH) [World Health Organization (WHO) Group 1][3]; **AND**
II. Individual has WHO functional class II-IV[4] symptoms.

Opsumit (macitentan) may not be approved for the following:

I. Individual is initiating therapy and has a diagnosis of clinically significant anemia **OR**
II. In combination with other endothelin receptor antagonist (ERA) agents, such as but not limited to Letairis (ambrisentan) or Tracleer (bosentan).

Notes:

1. Opsumit (macitentan) has a black box warning for embryo-fetal toxicity. Pregnancy should be excluded prior to start of treatment, monthly during treatment, and 1 month after stopping treatment in females of reproductive potential. Opsumit should not be administered to pregnant females due to the potential of causing fetal harm. Pregnancy should be prevented using acceptable means of contraception during treatment and for one month after therapy discontinued. Opsumit will be available for all females, regardless of reproductive potential, through a restricted risk evaluation and mitigation strategy (REMS) program. As a component of the Opsumit REMS, prescribers, individuals, and pharmacies must enroll in the program.

2. Diagnostic criteria:
    A. PAH: Right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units (ACCF/AHA 2009).

B. CTEPH: Pulmonary angiography via right-heart catheterization which shows a mPAP greater than 25 mm Hg caused by thromboemboli in the pulmonary arterial system (ACCF/AHA 2009, Kim et al. 2013).

3. WHO Pulmonary Hypertension (PH) Group Classification (ACCF/AHA 2009, Simonneau et al. 2013):
   A. Group 1: Pulmonary arterial hypertension (PAH)
   B. Group 2: PH due to left heart disease
   C. Group 3: PH due to lung diseases and/or hypoxia
   D. Group 4: Chronic thromboembolic PH (CTEPH)
   E. Group 5: Miscellaneous/PH with unclear multifactorial mechanisms

4. WHO functional classification of PH (CHEST 2014):
   A. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
   B. Class II: Slight limitation of physical activity. Comfortable at rest but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
   C. Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
   D. Class IV: Inability to carry out any physical activity without symptoms. Dyspnea and/or fatigue may be present at rest and discomfort is increased by any physical activity.

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. Accessed January 30, 2017.

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.

Anthem Sildenafil

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

Medications	Comments	Quantity Limit
Viagra (sildenafil)	Requests for Viagra in the treatment of Pulmonary Arterial Hypertension will be reviewed on a case by case basis.	May be subject to quantity limit
Revatio (sildenafil)	N/A	

APPROVAL CRITERIA

Requests for oral Revatio (sildenafil) may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[2] of Pulmonary Arterial Hypertension (PAH) [World Health Organization (WHO Group 1)][3];
AND
II. Individual has WHO functional class II-IV[4] symptoms;

OR
III. Individual has a diagnosis of persistent pulmonary hypertension of the newborn (AHA/ATS 2015);
AND
IV. Individual was started and stabilized on Revatio (sildenafil) in the hospital and requires continued outpatient therapy.

V. Requests for Revatio (sildenafil) suspension may be approved if the following criteria are met in addition to I. and II. OR III. and IV. above:
   A. Individual is unable to swallow the oral tablet dose form due to a clinical condition such as but not limited to the following:
      1. Dysphagia; **OR**
      2. Individual's age.

Requests for Revatio (sildenafil) injection may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[2] of PAH (WHO Group 1)[3]; **AND**
II. Individual has WHO functional class II-IV[4] symptoms; **AND**
III. Individual is temporarily unable to take oral dose forms and requires continued therapy;

OR
IV. Individual has a diagnosis of persistent pulmonary hypertension of the newborn (AHA/ATS 2015); **AND**

V. Individual was started and stabilized on Revatio (sildenafil) in the hospital and requires continued outpatient therapy; **AND**
VI. Individual is temporarily unable to take oral dose forms and requires continued therapy.

Revatio (sildenafil) oral and injectable agents may not be approved for the following:

I. Individuals requesting for the treatment of erectile dysfunction; **OR**
II. Individuals with severe hepatic impairment (Child-Pugh Class C); **OR**
III. Individual has a diagnosis of pulmonary veno-occlusive disease (PVOD); **OR**
IV. Individual has a known hereditary degenerative retinal disorder (such as but not limited to, retinitis pigmentosa); **OR**
V. Use in combination with guanylate cyclase stimulators [such as but not limited to, Adempas (riociguat)]; **AND**
VI. Use in combination with other phosphodiesterase-5 (PDE5) inhibitors [such as but not limited to, Viagra (sildenafil)]; **AND**
VII. Use in combination with organic nitrates, such as but not limited to isosorbide mono/dinitrate or nitroglycerin.

Notes:

1. The addition of Revatio (sildenafil) to Tracleer (bosentan) therapy does not result in any beneficial effect on exercise ability (6-minute walk distance).

2. Diagnostic criteria for PAH (ACCF/AHA 2009): Right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units.

3. WHO Pulmonary Hypertension (PH) Group Classification (ACCF/AHA 2009):
    A. Group 1: Pulmonary arterial hypertension (PAH)
    B. Group 2: PH due to left heart disease
    C. Group 3: PH due to lung diseases and/or hypoxia
    D. Group 4: Chronic thromboembolic PH (CTEPH)
    E. Group 5: Miscellaneous/PH with unclear multifactorial mechanisms

4. WHO functional classification of PH (CHEST 2014):
    A. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
    B. Class II: Slight limitation of physical activity. Conformable at rest but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    C. Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    D. Class IV: Inability to carry out any physical activity without symptoms. Dyspnea and/or fatigue may be present at rest and discomfort is increased by any physical activity.

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

Key References:

Abman SH, Hansmann G, Archer SL, et al. Pediatric Pulmonary Hypertension. Guidelines from the American Heart Association and American Thoracic Society. *Circulation.* 2015; 132. Available from: http://circ.ahajournals.org/content/early/2015/10/29/CIR.0000000000000329. Access on: January 9, 2018.

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 on: January 9, 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.

McLaughlin VV, Archer SL, Badesch, et al. ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension. *Circulation*. 2009; 119:2250-2294. Available from: http://circ.ahajournals.org/content/119/16/2250.full. Accessed on: January 9, 2018.

Taichman DB, Ornelas J, Chung L, et al. Pharmacologic Therapy for Pulmonary Arterial Hypertension in Adults: CHEST Guideline and Expert Panel Report. *CHEST*. 2014; 146(2): 449-475. Available from: http://journal.publications.chestnet.org/data/Journals/CHEST/930614/chest_146_2_449.pdf. Accessed on: January 12, 2017.

Anthem Tadalafil

Override(s)	Approval Duration
Prior Authorization	1 year

Medications	Comments
Cialis (tadalafil)	Requests for Cialis in the treatment of Pulmonary Arterial Hypertension (PAH) will be reviewed on a case by case basis. **ONLY** 2.5mg and 5mg strengths for a diagnosis of Benign Prostatic Hyperplasia (BPH).
Adcirca (tadalafil)	**ONLY** for a diagnosis of PAH

APPROVAL CRITERIA

Requests for Adcirca (tadalafil) may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[1] of Pulmonary Arterial Hypertension (PAH) [World Health Organization (WHO) Group 1][2]; **AND**
II. Individual has WHO functional class II-IV[3] symptoms.

Requests for Adcirca (tadalafil) may not be approved for the following:

I. Individuals requesting for the treatment of benign prostatic hyperplasia and/or erectile dysfunction; **OR**
II. Individual has a diagnosis of severe hepatic impairment (Child-Pugh Class C); **OR**
III. Individual has severe renal impairment (creatinine clearance less than or equal to 30 mL/min) or on dialysis; **OR**
IV. Individual has a diagnosis of pulmonary veno-occlusive disease (PVOD); **OR**
V. Individual has a known hereditary degenerative retinal disorder (such as but not limited to, retinitis pigmentosa); **OR**
VI. Use in combination with guanylate cyclase (GC) stimulators [such as but not limited to, Adempas [riociguat]); **AND**
VII. Use in combination with other phosphodiesterase-5 inhibitors (PDE-5) [such as but not limited to, Cialis (Tadalafil)]; **AND**
VIII. Use in combination with organic nitrates, such as but not limited to, isosorbide mono/dinitrate or nitroglycerin.

Requests for Cialis (tadalafil) 2.5 mg and 5 mg ONLY may be approved if the following criteria are met:

I. Individual has a diagnosis of benign prostatic hyperplasia (BPH); **AND**
II. Individual is using to treat the signs and symptoms of BPH; **AND**
III. Individual has had a previous trial and inadequate response or intolerance to **TWO** preferred agents for BPH;

Preferred agents for BPH**:** finasteride 5 mg (generic Proscar), doxazosin, tamsulosin, terazosin, alfuzosin.

OR

IV. The preferred agents are unacceptable due to concomitant clinical conditions, such as but not limited to the following:
    A. Individual has a documented hypersensitivity to any ingredient in the preferred agents which is not also in Cialis; **OR**
    B. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred agents and acceptable for use with Cialis.

Cialis (tadalafil) 2.5 mg and 5 mg for BPH **may not** be approved for the following:

I. Individual is requesting for the treatment of pulmonary arterial hypertension; **OR**
II. Individual has a diagnosis of severe hepatic impairment (Child-Pugh Class C); **OR**
III. Individual has severe renal impairment (creatinine clearance less than 30 mL/min) or on hemodialysis; **OR**
IV. Individual has a known hereditary degenerative retinal disorder (such as but not limited to, retinitis pigmentosa); **OR**
V. Use in combination with any of the following:
    A. A guanylate cyclase stimulator [such as but not limited to, Adempas (riociguat)]; **OR**
    B. Other phosphodiesterase 5 (PDE5) inhibitor agents [such as but not limited to, Adcirca (tadalafil)]; **OR**
    C. An alpha-blocker agent for the treatment of BPH; **OR**
    D. An organic nitrate, such as but not limited to, isosorbide mono/dinitrate or nitroglycerin;

OR

VI. Individual has any of the following cardiovascular conditions:
    A. Myocardial infarction within the previous 90 days; **OR**
    B. Unstable angina or angina occurring during sexual intercourse; **OR**
    C. Greater than or equal to New York Heart Association (NYHA) Class II heart failure within the previous 6 months; **OR**
    D. Uncontrolled arrhythmias; **OR**
    E. Hypotension (less than 90/50 mmHg) or uncontrolled hypertension; **OR**
    F. Stroke within the previous 6 months.

Notes:

1. Diagnostic criteria for PAH (ACCF/AHA 2009): Complete right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units.

2. WHO Pulmonary Hypertension (PH) Group Classification (ACCF/AHA 2009, Simonneau et al. 2013):
    A. Group 1: Pulmonary arterial hypertension (PAH)
    B. Group 2: PH due to left heart disease
    C. Group 3: PH due to lung diseases and/or hypoxia
    D. Group 4: Chronic thromboembolic PH (CTEPH)
    E. Group 5: Miscellaneous/PH with unclear multifactorial mechanisms.

3. WHO functional classification of PH (CHEST 2014):
    A. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
    B. Class II: Slight limitation of physical activity. Conformable at rest but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    C. Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    D. Class IV: Inability to carry out any physical activity without symptoms. Dyspnea and/or fatigue may be present at rest and discomfort is increased by any physical activity.

4. If Cialis is being utilized concurrently with Proscar (finasteride), to initiate BPH treatment, treatment with Cialis 5 mg once daily is recommended for up to 26 weeks.

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.

Anthem Tracleer (bosentan)

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

Medications	Quantity Limit
Tracleer (bosentan)	May be subject to quantity limit

APPROVAL CRITERIA

Requests for Tracleer (bosentan) may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[3] of pulmonary arterial hypertension (PAH) [World Health Organization (WHO) Group 1][4]; **AND**
II. Individual has WHO functional class II-IV[5] symptoms;

OR

III. Individual has a diagnosis of Eisenmenger's syndrome associated with a catheterization-proven diagnosis[3] of PAH (WHO Group 1)[4] (DrugPoints B IIa); **AND**
IV. Individual has WHO functional class ll-IV[5] symptoms.

Tracleer (bosentan) may **not** be approved for the following:

I. Individual has a diagnosis of moderate (Child-Pugh Class B) or severe (Child-Pugh Class C) hepatic impairment; **OR**
II. Individual is initiating therapy and has elevated [greater than 3 times the upper limit of normal (ULN)] baseline aminotransferase levels; **OR**
III. In combination with other endothelin receptor antagonist (ERA) agents, such as but not limited to Letairis (ambrisentan) or Opsumit (macitentan); **OR**
IV. In the treatment of congestive heart failure with left ventricular dysfunction; **OR**
V. Individual is concomitantly taking cyclosporine A or glyburide.

Notes:

1. In individuals with WHO functional class ll symptoms, the benefits (reduction in rate of clinical deterioration and trend toward improved walk distance) and r isks (hepatotoxicity) of therapy should be considered.
2. Tracleer (bosentan) has black box warnings for risks of hepatotoxicity and embryo-fetal toxicity. Tracleer is available only through a restricted program called the Tracleer REMS Program. The Tracleer REMS program is a component of the Tracleer Risk Evaluation and Mitigation Strategy (REMS). Under the Tracleer REMS, prescribers, individuals, and pharmacies must enroll in the program. Serum aminotransferase levels must be measured prior to initiation of treatment and then monthly. Tracleer should generally be avoided in individuals with elevated aminotransferases (> 3 x ULN) at

baseline because monitoring for hepatotoxicity may be more difficult. If liver aminotransferase elevations are accompanied by clinical symptoms of hepatotoxicity (such as nausea, vomiting, fever, abdominal pain, jaundice, or unusual lethargy or fatigue) or increases in bilirubin ≥ 2 x ULN, treatment should be stopped. Tracleer is likely to cause major birth defects based on animal data. Pregnancy must be excluded before the start of treatment with Tracleer. Throughout treatment and for one month after stopping Tracleer, females of reproductive potential must use two reliable methods of contraception unless the individual has a tubal sterilization or intrauterine device (IUD), in which case no other contraception is needed. Hormonal contraceptives, including oral, injectable, transdermal, and implantable forms should not be used as the sole means of contraception because these may not be effective. Monthly pregnancy tests should be obtained.

3. Diagnostic criteria:
    A. PAH: Right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end- diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units (ACCF/AHA 2009). In pediatric patients, right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg; a pulmonary artery wedge pressure (PAWP) less than 15 mm Hg; and a pulmonary vascular resistance index (PVRI) greater than 2 Wood units (AHA/ATS 2015).
    B. CTEPH: Pulmonary angiography via right-heart catheterization which shows a mPAP greater than 25 mm Hg caused by thromboemboli in the pulmonary arterial system (ACCF/AHA 2009).

4. WHO Pulmonary Hypertension (PH) Group Classification (ACCF/AHA 2009):
    A. Group 1: Pulmonary arterial hypertension (PAH)
    B. Group 2: PH due to left heart disease
    C. Group 3: PH due to lung diseases and/or hypoxia
    D. Group 4: Chronic thromboembolic PH (CTEPH)
    E. Group 5: Miscellaneous/PH with unclear multifactorial mechanisms

5. WHO functional classification of PH (CHEST 2014):
    A. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
    B. Class II: Slight limitation of physical activity. Comfortable at rest but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    C. Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
    D. Class IV: Inability to carry out any physical activity without symptoms. Dyspnea and/or fatigue may be present at rest and discomfort is increased by any physical activity.

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 9, 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 Uptravi (selexipag)

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

Medications	Quantity Limit
Uptravi 200 mcg-800 mcg Titration Pack	May be subject to quantity limit
Uptravi 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1000 mcg, 1200 mcg, 1400 mcg, 1600 mcg	

APPROVAL CRITERIA

Requests for Uptravi (selexipag) may be approved if the following criteria are met:

I. Individual has a catheterization-proven diagnosis[1] of pulmonary arterial hypertension (PAH) [World Health Organization (WHO) Group 1][2]; **AND**
II. Individual has WHO functional class II-IV[3] symptoms.

Uptravi (selexipag) may not be approved for the following:

I. Individual has a diagnosis of severe hepatic impairment (Child-Pugh Class C); **OR**
II. In combination with prostacyclin analogs [such as but not limited to treprostinil (Orenitram, Remodulin, Tyvaso), epoprostenol (Flolan, Veletri), Ventavis (iloprost)]; **OR**
III. Individual is on dialysis or a glomerular filtration rate less than 15 mL/min/1.73 m^2.

Notes:

1. Diagnostic criteria:
   A. PAH: Right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units (ACCF/AHA 2009).
   B. CTEPH: Pulmonary angiography via right-heart catheterization which shows a mPAP greater than 25 mm Hg caused by thromboemboli in the pulmonary arterial system (ACCF/AHA 2009, Kim et al. 2013).

2. WHO Pulmonary Hypertension (PH) Group Classification (ACCF/AHA 2009, Simonneau et al. 2013):
   A. Group 1: Pulmonary arterial hypertension (PAH)

B. Group 2: PH due to left heart disease
C. Group 3: PH due to lung diseases and/or hypoxia
D. Group 4: Chronic thromboembolic PH (CTEPH)
E. Group 5: Miscellaneous/PH with unclear multifactorial mechanisms

3. WHO functional classification of PH (CHEST 2014):
   A. Class I: No limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
   B. Class II: Slight limitation of physical activity. Comfortable at rest but ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
   C. Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
   D. Class IV: Inability to carry out any physical activity without symptoms. Dyspnea and/or fatigue may be present at rest and discomfort is increased by any physical activity.

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. Accessed January 30, 2017.

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.

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Pulmonary Arterial Hypertension Medications

Managed Care Organization name: Health Plan of Nevada

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

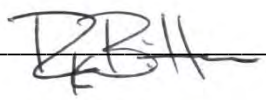
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

HPN does not currently have brand Revatio, brand Adcirca, or generic tadalafil on the Preferred Drug List (PDL). HPN only requires appropriate diagnosis submittal for use of sildenafil tablets or solution (generic Revatio). The PDE-5 inhibitors are the lowest cost agents in the class for treatment of pulmonary hypertension so right-heart catheterization and other requirements may be considered unneeded at this point. HPN also recommends that other pulmonary hypertension agents such as those in the ERA class (Letairis, Tracleer, Opsumit) and similar agents such as Adempas, should have prior authorization for appropriate diagnosis.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

Please print the name of the individual completing this form: Ryan Bitton

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
MCO PRIOR AUTHORIZATION CRITERIA REVIEW FORM

Clinical criteria for drugs or drug classes listed on the appropriate agenda, will be presented at the quarterly Drug Use Review Board meetings. This form will allow Managed Care Organizations to approve or disapprove the proposed criteria and suggest changes to be supported at the quarterly meeting.

DUR Meeting Date: January 24, 2019

Prior Authorization Criteria being reviewed: Pulmonary Arterial Hypertension Medications

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Using Criteria B:

Recommend following additional criteria:

Failure of a trial of a calcium channel blocker (*see Appendix B*), unless member meets one of the following (a or b):

a. Inadequate response or contraindication to acute vasodilator testing;
b. Contraindication or clinically significant adverse effects to a calcium channel blocker are experienced;

Dose does not exceed 60 mg/day (oral formulations) or 30 mg/day (intravenous formulations) in divided doses.

You will have an opportunity to support the recommended changes at the time of the Drug Use Review Board quarterly meeting.

If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

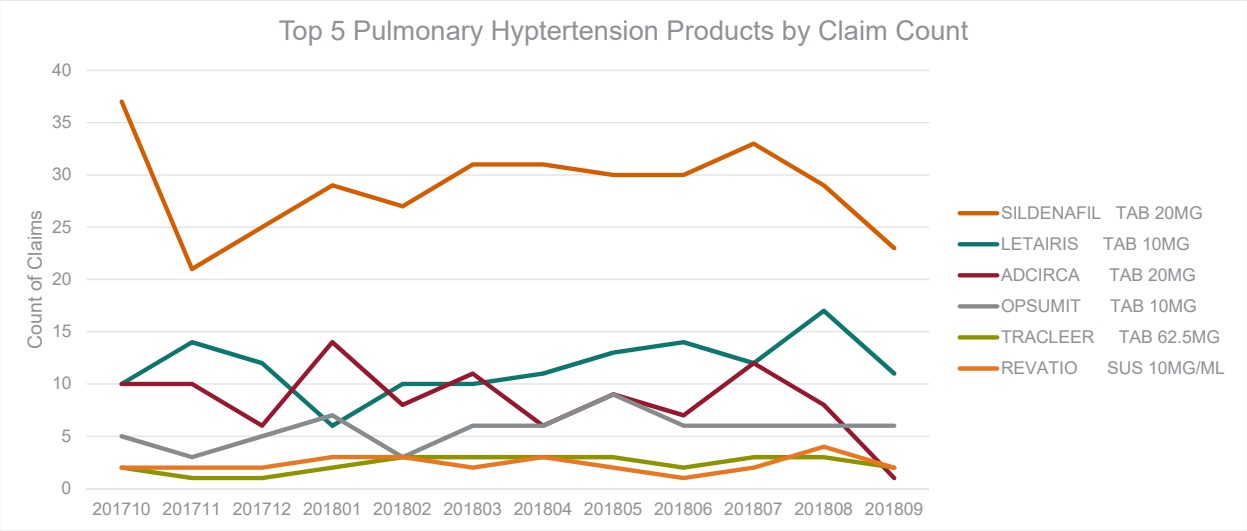
Please print the name of the individual completing this form: _____Tom Beranek_____

Signature of individual completing this form: Tom Beranek

Pulmonary Arterial Hypertension

Summary of Utilization
October 1, 2017 - September 30, 2018
Fee for Service Medicaid

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
ADCIRCA TAB 20MG	99	102	3,095	5,435	$ 319,971.53
ADEMPAS TAB 1.5MG	1	1	30	90	$ 9,762.81
ADEMPAS TAB 1MG	1	1	30	90	$ 9,762.81
LETAIRIS TAB 10MG	131	140	4,299	4,313	$ 1,322,667.15
LETAIRIS TAB 5MG	21	21	750	615	$ 150,438.38
OPSUMIT TAB 10MG	64	68	2,040	2,040	$ 609,565.56
REVATIO SUS 10MG/ML	27	28	908	3,248	$ 140,603.72
REVATIO TAB 20MG	1	2	2	2	$ 93.36
SILDENAFIL TAB 20MG	318	346	9,869	31,811	$ 9,886.46
TADALAFIL TAB 20MG	8	8	240	480	$ 29,323.76
TRACLEER TAB 125MG	13	15	420	840	$ 150,704.55
TRACLEER TAB 32MG	2	2	58	58	$ 10,538.64
TRACLEER TAB 62.5MG	28	28	840	1,380	$ 162,721.90
UPTRAVI TAB 1000MCG	3	3	90	180	$ 31,647.34
UPTRAVI TAB 1600MCG	23	24	720	1,440	$ 386,878.08
UPTRAVI TAB 200MCG	5	5	146	764	$ 132,682.85
UPTRAVI TAB 600MCG	13	14	383	766	$ 206,381.82
UPTRAVI TAB 800MCG	5	5	150	300	$ 66,196.66
Grand Total	**763**	**813**	**24,070**	**53,852**	**$ 3,749,827.38**



Anthem PAH Utilization

Quarter Serviced **4th Quarter 2017**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims-	Sum of Total Days of Therapy	Sum of Total Quantity
ADCIRCA 20 MG TABLET	5	14	420	660
ADEMPAS 0.5 MG TABLET	1	1	30	90
LETAIRIS 10 MG TABLET	1	3	90	90
OPSUMIT 10 MG TABLET	3	8	240	240
SILDENAFIL 20 MG TABLET	8	22	660	1800
UPTRAVI 1,000 MCG TABLET	1	3	90	180
Grand Total	**14**	**51**	**1530**	**3060**

Quarter Serviced **1st Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
ADCIRCA 20 MG TABLET	5	11	330	600
LETAIRIS 10 MG TABLET	1	2	60	60
OPSUMIT 10 MG TABLET	3	7	210	210
SILDENAFIL 20 MG TABLET	9	22	660	1800
UPTRAVI 1,000 MCG TABLET	1	3	90	180
Grand Total	**14**	**45**	**1350**	**2850**

Quarter Serviced **2nd Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
ADCIRCA 20 MG TABLET	6	16	480	870
LETAIRIS 10 MG TABLET	3	6	180	180
OPSUMIT 10 MG TABLET	3	8	240	240
SILDENAFIL 20 MG TABLET	11	28	840	2400
UPTRAVI 1,000 MCG TABLET	1	3	90	180
Grand Total	**17**	**61**	**1830**	**3870**

Quarter Serviced **3rd Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
ADCIRCA 20 MG TABLET	7	12	360	660
ADEMPAS 0.5 MG TABLET	1	1	30	90
ADEMPAS 1 MG TABLET	1	1	30	90
LETAIRIS 10 MG TABLET	3	8	240	240
OPSUMIT 10 MG TABLET	3	7	210	210
SILDENAFIL 20 MG TABLET	9	22	623	1740
TADALAFIL 20 MG TABLET	6	7	210	390
UPTRAVI 1,000 MCG TABLET	1	3	90	180
Grand Total	**17**	**61**	**1793**	**3600**

Pulmonary Arterial Hypertension HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
ADCIRCA TAB 20MG	4	11	30	510
ADEMPAS TAB 2.5MG	3	8	30	720
LETAIRIS TAB 10MG	6	16	30	480
LETAIRIS TAB 5MG	1	1	30	46
OPSUMIT TAB 10MG	5	14	30	420
SILDENAFIL TAB 20MG	9	19	30	2,340
UPTRAVI TAB 1000MCG	1	3	30	180
UPTRAVI TAB 1400MCG	1	3	30	180
Total	30	75	240	4,876
01/01/18 - 03/31/18 - Q1				
ADCIRCA TAB 20MG	5	11	30	540
ADEMPAS TAB 2.5MG	3	9	30	810
LETAIRIS TAB 10MG	7	19	30	570
OPSUMIT TAB 10MG	5	15	30	450
SILDENAFIL TAB 20MG	10	25	30	3,180
UPTRAVI TAB 1000MCG	1	2	30	120
UPTRAVI TAB 1400MCG	1	3	30	180
UPTRAVI TAB 200MCG	1	2	28	280
Total	33	86	238	6,130
04/01/18 - 06/30/18 - Q2				
ADCIRCA TAB 20MG	7	16	30	780
ADEMPAS TAB 2.5MG	3	8	30	720
LETAIRIS TAB 10MG	7	20	30	600
OPSUMIT TAB 10MG	6	15	30	450
REVATIO SUS 10MG/ML	1	1	30	112
SILDENAFIL TAB 20MG	14	24	67	2,633
TRACLEER TAB 32MG	1	1	28	14
UPTRAVI TAB 1400MCG	1	3	30	180
UPTRAVI TAB 200/800	1	3	28	600
Total	41	91	303	6,089

Pulmonary Arterial Hypertension HPN Utilization

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/01/18 - 09/30/18 - Q3				
ADCIRCA TAB 20MG	6	10	30	390
ADEMPAS TAB 2.5MG	3	5	30	450
LETAIRIS TAB 10MG	7	18	30	540
OPSUMIT TAB 10MG	7	19	30	570
REVATIO SUS 10MG/ML	1	1	30	112
SILDENAFIL TAB 20MG	13	30	68	3,029
TADALAFIL TAB 20MG	5	5	30	240
UPTRAVI TAB 1400MCG	1	3	30	180
UPTRAVI TAB 200/800	1	1	28	200
Total	44	92	306	5,711
Grand Total	148	344	1,087	22,806

Pulmonary Arterial Hypertension Utilization – Q4 2017 – Q3 2018

SilverSummit Healthplan

Report Date Range	Medication Name	Total Claims	Unique Members	Number of Units	Days Supply
10/01/2017 - 09/30/2018	Letairis Tab 10 mg	9	3	270	270
10/01/2017 - 09/30/2018	Sildenafil Tab 20 mg	9	1	864	270
10/01/2017 - 09/30/2018	Adcirca Tab 20 mg	6	1	360	180
10/01/2017 - 09/30/2018	Total PAH claims	24	5	1494	720

Therapeutic Class Overview
Pulmonary Arterial Hypertension Agents

INTRODUCTION

- Pulmonary arterial hypertension (PAH), a subtype of pulmonary hypertension (PH), is a chronic, life-threatening disease that is characterized by increased resistance in the pulmonary circulation caused by progressive pulmonary artery remodeling and constriction of the pulmonary vasculature (*Buckley et al 2013, Wu et al 2013*).
  - PH is defined as a mean pulmonary arterial pressure (mPAP) of ≥ 25 mmHg at rest. Normal pulmonary arterial systolic pressure ranges from 15 to 30 mmHg, diastolic pressure from 4 to 12 mmHg, and normal mPAP is ≤ 20 mmHg (*Rubin et al 2018*).
  - PAH often manifests with clinical symptoms such as shortness of breath and decreased functional capacity, and eventually leads to right heart failure and death (*Gomberg-Maitland et al 2011*).
- Early recognition of PAH is essential and the gold standard for the clinical diagnosis of PAH is right heart catheterization (*Buckley et al 2013*).
- The World Health Organization (WHO) classifies PH into 5 groups:
  - Group 1 – PAH
  - Group 2 – PH secondary to heart disease
  - Group 3 – PH secondary to lung diseases and/or hypoxia
  - Group 4 – Chronic thromboembolic PH (CTEPH)
  - Group 5 – PH with unclear or multifactorial etiologies
- WHO Group I encompasses PAH, including idiopathic PAH, heritable PAH, drug- and toxin-induced PAH, and PAH associated with other disorders such as connective tissue disease, portal hypertension, human immunodeficiency virus infection, congenital heart disease, and schistosomiasis (*Simonneau et al 2013*).
- In addition to the diagnostic classification, patients may be stratified according to their WHO functional capacity, which was adapted from the New York Heart Association (NYHA) classification of left heart failure. A brief description of these functional classes (FC) is as follows (*Stringham et al 2010*):
  - Class I: No limitation of physical activity
  - Class II: Slight limitation of physical activity
  - Class III: Marked limitation of physical activity
  - Class IV: Inability to carry out any physical activity without symptoms
- The prevalence of WHO Group 1 PAH has been estimated at 7 to 26 cases per million adults (*Pogue et al 2016*). The disease has a poor prognosis and an approximate mortality rate of 15% within 1 year on therapy (*McLaughlin et al 2009*). The median survival in the 1980s was 2.8 years; this had improved to 7 years in the late 2000s (*Pogue et al 2016*).
- CTEPH (WHO Group 4) is a leading cause of severe PH that results from thrombus formation leading to fibrous stenosis or complete obliteration of pulmonary arteries.
  - The incidence of CTEPH is uncertain, but it occurs in up to 4% of patients after an acute pulmonary embolism (*Simonneau et al 2009*).
- Specific agents to treat PAH primarily target 3 pathways critical to its pathobiology: the prostacyclin, endothelin, and nitric oxide pathways (*Wu et al 2013*). There are currently 10 molecular entities within 5 therapeutic classes that are Food and Drug Administration (FDA)-approved for the treatment of PAH (*Lexicomp 2018*).
  - Drugs active within the prostacyclin pathway are the prostacyclin analogues (PCAs) or prostanoids (intravenous [IV] epoprostenol; inhaled iloprost; and IV, subcutaneous [SC], inhaled, and oral treprostinil) and a prostacyclin receptor agonist (oral selexipag).
  - Drugs active within the endothelin pathway are the endothelin receptor antagonists (ERAs) (oral ambrisentan, oral bosentan, and oral macitentan).
  - Drugs active within the nitric oxide pathway are the phosphodiesterase-type-5 (PDE-5) inhibitors (IV and oral sildenafil and oral tadalafil) and a soluble guanylate cyclase (sGC) stimulator (oral riociguat).
- The goals of treatment include improvement in the patient's symptoms, quality of life (QOL), and survival. The optimal therapy for a patient should be individualized, taking into account many factors including severity of illness, route of administration, side effects, comorbid illness, treatment goals, and clinician preference (*McLaughlin et al 2009*).

- Initial management of PAH includes the use of warfarin, diuretics, and/or oxygen depending on the patient's diagnosis and symptoms. Prior to the initiation of advanced therapy, patients with PAH should undergo a vasoreactivity test. Oral calcium channel blockers (CCBs) are indicated only for patients who have a positive acute vasodilator response to testing (*Galiè et al 2015[b], McLaughlin et al 2009, Taichman et al 2014*).
- For patients who do not have a positive acute vasodilator response to testing and are considered low to moderate risk based on clinical assessment, oral mono- or combination therapy with certain agents are recommended. These include ERAs, PDE-5 inhibitors, an sGC stimulator, and a prostacyclin receptor (IP) agonist. In patients with high risk disease, continuous treatment with an IV PCA therapy (epoprostenol or treprostinil) would be recommended. Combination therapy may be considered if patients are not responding adequately to monotherapy or are not candidates for monotherapy (*Barst, 2009, Galiè et al 2015[b], McLaughlin et al 2009, Taichman et al 2014*).
- The PAH agents are FDA-approved for the treatment of patients with WHO Group I PAH; however, there are differences in the study populations for which their FDA-approvals were based (*McLaughlin et al 2009*).
- Adempas (riociguat) is a first-in-class sGC stimulator with a dual mode of action involving endogenous nitric oxide that leads to increased generation of cyclic guanosine monophosphate (cGMP) with subsequent vasodilation. This agent has the additional FDA approval for treating adults with persistent/recurrent CTEPH (WHO Group 4) after surgical treatment or inoperable CTEPH. Adempas is the first and only drug to be FDA-approved in the treatment of CTEPH. Pulmonary endarterectomy is curative for CTEPH, but it is technically demanding which may limit access to its use as a treatment (*Archer 2013*).
- In PAH, prostacyclin synthase is reduced resulting in inadequate production of prostacyclin I_2, a potent vasodilator with antiproliferative effects and an inhibitor of platelet aggregation (*McLaughlin et al 2009*). The PCAs, iloprost and treprostinil, were developed as chemically stable alternatives to epoprostenol, which requires continuous IV infusion due to its lack of stability (*Asaki et al 2015*). Orenitram (treprostinil) is the first FDA-approved oral PCA. It may represent a more convenient dosage form to the other treprostinil formulations (Remodulin and Tyvaso). However, patients with more severe PAH are likely to receive infused PCA rather than oral therapy (*McLaughlin et al 2009*). Among these agents, epoprostenol IV is the only agent that has demonstrated improved patient survival in high risk PAH patients (*Galiè et al 2015[b]*). Uptravi (selexipag) works at the same pathway as the PCAs, but activates the IP receptor, also known as the prostacyclin receptor. Orenitram and Uptravi are the only orally administered agents that work within the prostacyclin pathway (*Asaki et al 2015*).
- Endothelial dysfunction in PAH causes increased production of endothelin-1 resulting in vasoconstriction, which is mediated by the endothelin receptors, ET_A and ET_B. Stimulation of ET_A causes vasoconstriction and cell proliferation, while stimulation of ET_B results in vasodilatation, antiproliferation and endothelin-1 clearance. The ERAs (Letairis [ambrisentan], Opsumit [macitentan], and Tracleer [bosentan]) competitively bind to both receptors with different affinities. Letairis and Opsumit are highly selective for the ET_A receptor, while Tracleer is slightly selective for the ET_A receptor over the ET_B receptor. In addition, Opsumit has a pharmacologically active metabolite and is considered "tissue-targeting" because it displays high affinity and sustained occupancy at the ET receptors in human pulmonary arterial smooth muscles. However, the clinical significance of receptor affinities of the ERAs has not been established (*McLaughlin et al 2009*).
- In patients with PAH, there is also an impaired release of nitric oxide by the vascular endothelium, thereby reducing cGMP concentrations. The PDE-5 enzyme is the predominant phosphodiesterase in the pulmonary vasculature and is responsible for the degradation of cGMP. The PDE-5 inhibitors, Revatio (sildenafil) and Adcirca (tadalafil), increase the concentrations of cGMP resulting in relaxation of the pulmonary vascular bed.
- Medispan class: Cardiovascular Agents, Miscellaneous – Prostaglandin Vasodilators; Pulmonary Hypertension: Endothelin Receptor Antagonists, Phosphodiesterase Inhibitors, Prostacyclin Receptor Agonist, and Soluble Guanylate Cyclase Stimulator.

Table 1. Medications Included Within Class Review

Drug	Generic Availability
ERAs	
Letairis (ambrisentan)	-
Opsumit (macitentan)	-
Tracleer (bosentan)	-
PDE-5 inhibitors	
Adcirca (tadalafil)	✔
Revatio (sildenafil)	✔ *
Prostacyclin receptor agonist	
Uptravi (selexipag)	-
PCAs	
Flolan (epoprostenol)	✔
Veletri (epoprostenol)	-
Orenitram (treprostinil)	-
Remodulin (treprostinil)	-**
Tyvaso (treprostinil)	-
Ventavis (iloprost)	-
sGC stimulator	
Adempas (riociguat)	-

*Revatio tablet and IV formulations are currently available generically; however, the oral suspension is brand-only.
**A generic was approved by the FDA but has not yet been launched by its manufacturer (Sandoz); settlement agreements may apply.

(*Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018*)

INDICATIONS

Table 2. FDA-approved Indications

Indication	Adcirca (tadalafil)	Adempas (riociguat)	Flolan (epoprostenol)	Letairis (ambrisentan)	Opsumit (macitentan)	Orenitram (treprostinil)	Remodulin (treprostinil)	Revatio (sildenafil)	Tracleer (bosentan)	Tyvaso (treprostinil)	Uptravi (selexipag)	Veletri (epoprostenol)	Ventavis (iloprost)
Treatment of PAH (WHO Group I) to improve exercise ability and delay clinical worsening				✔ *				✔ §	✔ †				
Treatment of PAH (WHO Group I) to improve exercise ability/diminish symptoms associated with exercise	✔ ¶		✔ ≠			✔ ¶¶	✔ ₴			✔ Ω		✔ ₳	
Treatment of PAH (WHO Group I) to delay/reduce risks of disease progression and reduce risk of hospitalization					✔ **						✔ ‡		

Treatment of PAH (WHO Group I) to improve exercise capacity, to improve WHO FC, and to delay clinical worsening		✔											
Treatment of PAH (WHO Group I) to improve a composite endpoint of exercise tolerance, symptoms, and lack of deterioration													✔ ¥
For patients who require transition from epoprostenol, to reduce the rate of clinical deterioration; risks and benefits of each drug should be carefully considered prior to transition							✔						
Treatment of persistent/recurrent CTEPH (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO FC		✔											
Treatment of PAH (WHO Group I), in combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability				✔ *									
Treatment of PAH (WHO Group I) in pediatric patients aged ≥ 3 years with idiopathic or congenital PAH to improve pulmonary vascular resistance, which is expected to improve exercise ability									✔				

Abbreviations: CTEPH=chronic thromboembolic pulmonary hypertension; FC=functional class; NYHA=New York Heart Association, PAH=pulmonary arterial hypertension, WHO=World Health Organization.

*Studies establishing effectiveness included predominantly patients with WHO FC II to III symptoms and etiologies of idiopathic or heritable PAH (60%) or PAH associated with connective tissue diseases (34%).

§The delay in clinical worsening was demonstrated when Revatio was added to background epoprostenol therapy. Studies establishing effectiveness were short-term (12 to 16 weeks) and included predominately patients with NYHA FC II to III symptoms and idiopathic etiology (71%) or associated with connective tissue disease (25%).

†Studies establishing effectiveness included predominately patients with WHO FC II to IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital systemic-to-pulmonary shunts (18%).

¶Studies establishing effectiveness included predominately patients with NYHA FC II to III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

≠Studies included predominately patients with NYHA FC III to IV symptoms and etiologies of idiopathic or heritable PAH (49%) or PAH associated with connective tissue diseases (51%).
¶¶The study that established effectiveness included predominantly patients with WHO FC II to III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%). As the sole vasodilator, the effect on exercise is small. Orenitram has not been shown to add to other vasodilator therapy.
ƧStudies establishing effectiveness included predominately patients with NYHA FC II to IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary shunts (23%), and PAH associated with connective tissue diseases (19%).
ΩStudies establishing effectiveness included predominately patients with NYHA FC III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).
₳Studies establishing effectiveness included predominately patients with NYHA FC III to IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.
**Effectiveness was established in a long-term study in PAH patients with predominantly WHO FC II to III symptoms treated for an average of 2 years. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%).
‖Efficacy was shown in patients on Adempas monotherapy or in combination with endothelin receptor antagonists or prostanoids. Studies establishing effectiveness included predominately patients with WHO FC II to III and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (25%).
¥Studies establishing effectiveness included predominately patients with NYHA FC III to IV symptoms and etiologies of idiopathic or heritable PAH (65%) or PAH associated with connective tissue diseases (23%).
‡Effectiveness was established in a long-term study in PAH patients with WHO FC II to III symptoms. Patients had idiopathic PAH (58%), PAH associated with connective tissue diseases (29%), and PAH associated with congenital systemic-to-pulmonary shunts (10%).

(*Prescribing information: Adcirca 2017, Adempas 2018, Flolan 2018, Letairis, 2015, Opsumit 2018, Orenitram 2017, Remodulin 2018, Revatio 2018, Tracleer 2018, Tyvaso 2017, Uptravi 2017, Veletri 2018, Ventavis 2017*)

NOTE: Information on indications, mechanism of action, pharmacokinetics, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

Adcirca (tadalafil)

- Adcirca was evaluated in the PHIRST study, a 16-week, randomized, double-blind, placebo-controlled trial consisting of 405 patients with predominantly WHO FC II or III symptoms. Treatment with Adcirca significantly improved exercise capacity, as measured by the 6MWD and reduced clinical worsening compared to placebo (*Galiè et al 2009*). In a 52-week extension trial, PHIRST-2, the improvements in 6MWD observed at the end of PHIRST appeared to be maintained through week 52 of PHIRST-2 (68 weeks total). In addition, 34% of patients enrolled in PHIRST-2 experienced an improvement in WHO FC compared to baseline of the PHIRST trial (*Oudiz et al 2012*).

Adempas (riociguat)

- The efficacy and safety of Adempas were evaluated in CHEST-1, a multinational, multicenter, double-blind,16-week trial in 261 adult patients with CTEPH. The majority of patients were WHO FC II (31%) or class III (64%). The primary endpoint of CHEST-1 was change from baseline in 6MWD after 16 weeks. Secondary endpoints included changes from baseline in pulmonary vascular resistance (PVR), N-terminal pro-brain natriuretic peptide (NT-proBNP) level, WHO FC, time to clinical worsening, Borg dyspnea score, QOL variables, and safety. Improvements in walking distance occurred beginning at week 2. At week 16, the placebo adjusted mean increase in 6MWD within the Adempas group was 46 m (95% confidence interval [CI], 25 m to 67 m; $p < 0.001$) (*Ghofrani et al 2013[a]*).
  - An open-label, non-comparative, extension study (CHEST-2) included 237 patients who completed CHEST-1. CHEST-2 consisted of an 8-week, double-blind dose-adjustment phase, followed by an open-label study phase that continued until Adempas received official approval and became commercially available. At the March 2013 cut-off date, 211 patients (89%) were receiving ongoing treatment, and 179 (76%) had received over 1 year of treatment. The safety profile of Adempas in CHEST-2 was similar to CHEST-1, with no new safety signals. Improvements in 6MWD and WHO FC observed in CHEST-1 persisted for up to 1 year in CHEST-2. In the observed population at 1 year, mean±standard deviation (SD) 6MWD had changed by 51±62 m (n = 172) versus CHEST-1 baseline (n = 237), and WHO FC had improved, stabilized, or worsened in 47, 50, or 3% of patients (n = 176) versus CHEST-1 baseline (n = 236). Of patients treated for 1 year in CHEST-2, 145 (92%) out of 157 were continuing to receive monotherapy, and 12 (8%) patients were receiving additional PH-specific medication (8 [5%] were receiving ERAs and 4 [3%] were receiving prostanoids). No patient required additional treatment with both an ERA and prostanoid at 1 year (Simmoneau et al 2015). An exploratory analysis noted a significant association with overall survival for

6MWD and NT-proBNP concentration at baseline (p = 0.0199, and 0.0183, respectively), and at follow-up (p = 0.0385, and 0.0068, respectively). Additionally, short-term improvements were associated with long-term survival and worsening-free survival. At 2 years, the overall survival rate was 93% (95% CI, 89 to 96%) and the rate of clinical worsening-free survival was 82% (95% CI, 77 to 87%) (*Simonneau et al 2016*). Due to lack of a control group and because certain outcomes were considered exploratory, data from this study must be interpreted cautiously.

- The efficacy and safety of Adempas were also evaluated in PATENT-1, a multinational, multicenter, double-blind, 12-week trial in 443 adult patients with PAH as defined by PVR > 300 dyn*sec*cm^{-5} and a PAP_{mean} > 25 mmHg. In this study, 50% of the patients were treatment-naïve with respect to PAH therapy, 44% were pre-treated with an ERA, and 6% were pretreated with a PCA (inhaled, oral, or SC). Patients were randomized to 1 of 3 treatment groups: placebo (n = 126), an exploratory capped titration arm of Adempas 1.5 mg 3 times daily (n = 63), or a capped maximum dose of Adempas 2.5 mg 3 times daily (n = 254). The primary endpoint of PATENT-1 was change from baseline in 6MWD after 12 weeks in the Adempas 2.5 mg group compared to placebo. Secondary endpoints included changes from baseline in PVR, NT-proBNP level, WHO FC, time to clinical worsening, Borg dyspnea score, QOL variables, and safety. At week 12, the placebo-adjusted mean increase in 6MWD within the Adempas 2.5 mg treatment group was 36 m (95% CI, 20 m to 52 m, p < 0.001). The group receiving the capped dose at 1.5 mg was excluded from the efficacy analysis (*Ghofrani et al 2013[b]*).
  - An open-label, non-comparative, extension study (PATENT-2) included 396 patients who completed PATENT-1. PATENT-2 consisted of an 8-week, double-blind dose-adjustment phase, followed by an open-label study phase that continues until all patients have transitioned to the commercially available drug. A total of 197 patients received Adempas monotherapy and 199 received Adempas in combination with an ERA or prostanoid, or both. The primary objective of the study was to assess the safety and tolerability of long-term Adempas treatment. Assessments took place at entry to PATENT-2, at weeks 2, 4, 6, 8, and 12, and every 3 months thereafter. At the March 2013 data cut-off, 324 patients (82%) were receiving ongoing treatment and 84% had received 1 year or more of treatment. Mean treatment duration was 95 weeks (median 91 weeks), and cumulative treatment exposure was 718 patient-years (Rubin et al 2015). An exploratory analysis concluded that there was a significant association between overall survival and 6MWD, NT-proBNP concentration, and WHO FC at baseline (p = 0.0006, 0.0225, and 0.0191, respectively), and at follow-up (p = 0.021, 0.0056, and 0.0048, respectively). Additionally, short-term improvements were associated with long-term survival and worsening-free survival. The estimated survival rate was 97% (95% CI, 95 to 98%) and rate of clinical worsening-free survival was 88% (95% CI, 85 to 91%) at 1 year and 79% (95% CI, 74 to 82%) at 2 years (*Ghofrani et al 2016*). Certain outcomes were considered exploratory, so data from this study must be interpreted cautiously.

Flolan (epoprostenol)

- The safety and efficacy of chronically-infused Flolan were evaluated in 2 similar, open-label, randomized trials of 8 to12 weeks' duration comparing Flolan plus conventional therapy (eg, anticoagulants, oral vasodilators, diuretics, digoxin, oxygen) with conventional therapy alone in idiopathic or heritable PAH (NYHA Class II to IV) patients (n = 106). The average Flolan dose was 9.2 ng/kg/min at the trials' end. A statistically significant improvement was observed in the 6MWD in patients receiving Flolan plus conventional therapy for 8 to 12 weeks compared with those receiving conventional therapy alone. Improvements were noted as early as week 1. Increases in exercise capacity were accompanied by statistically significant improvement in dyspnea and fatigue, as measured by the Chronic Heart Failure Questionnaire and the Dyspnea Fatigue Index, respectively.
- The efficacy of chronically-infused Flolan in PAH and scleroderma spectrum of diseases (NYHA Class II to IV) was evaluated in an open-label, randomized, 12-week trial (n = 111) comparing Flolan plus conventional therapy with conventional therapy alone. The mean Flolan dose was 11.2 ng/kg/min at the end of week 12. Statistically significant improvement was observed in the 6MWD in patients receiving continuous Flolan plus conventional therapy for 12 weeks compared to those receiving conventional therapy alone. Increases in exercise capacity were accompanied by statistically significant improvement in dyspnea and fatigue, as measured by Borg Dyspnea Index and Dyspnea Fatigue Index. At week 12, the NYHA FC improved in 41% of patients treated with Flolan plus conventional therapy compared to none of the patients treated with conventional therapy alone. However, the majority of patients in both treatment groups showed no change in FC, with 4% of the Flolan plus conventional therapy group and 27% of conventional therapy group alone worsening.

Letairis (ambrisentan)

- The safety and efficacy of Letairis in the treatment of PAH were established in the ARIES trials. ARIES-1 and ARIES-2 were 12-week, randomized, double-blind, placebo-controlled trials that compared Letairis to placebo in 394 patients. Compared to placebo, treatment with Letairis resulted in a significant increase in exercise capacity as measured by 6MWD (*Galiè et al 2008[a]*). ARIES-E was the open-label extension study for ARIES-1 and ARIES-2. After 1 year of treatment, there was an improvement in 6MWD in the 2.5, 5 and 10 mg Letairis groups (25, 28 and 37 m, respectively). After 2 years of treatment, the improvement was sustained in the 5 and 10 mg groups (23 and 28 m), but not the 2.5 mg group (7 m) (*Oudiz et al 2009*).
- ARIES-3 was a long-term, open-label, single-arm, safety, and efficacy study of Letairis in patients with PH receiving Letairis 5 mg once daily for 24 weeks. The primary endpoint was change from baseline in 6MWD at week 24. Secondary efficacy endpoints included change in plasma NT-proBNP, Borg Dyspnea Index, WHO FC, time to clinical worsening of PAH, survival and adverse events (AEs). A total of 224 patients with PH due to idiopathic and familial PAH (31%), connective tissue disease (18%), chronic hypoxemia (22%), chronic thromboembolic disease (13%), or other etiologies (16%) were enrolled, and 53% of patients received stable background PAH therapies. After 24 weeks of therapy, there was an increase in 6MWD of 21 m (95% CI, 12 to 29), and a decrease in NT-proBNP of -26% (95% CI, -34 to -16%) observed in the overall population compared to baseline. However, increases in 6MWD were not observed in several non-Group 1 PH subpopulations. Peripheral edema, headache, and dyspnea were the most common AEs (*Badesch et al 2012*).
- The AMBITION trial (n = 610) was a double-blind, randomized, Phase 3/4 trial, which compared combination treatment with Letairis plus Adcirca to monotherapy with each in patients with WHO FC II or III symptoms. The study protocol was amended during the trial resulting in 17% of the initial protocol patients being excluded from the analysis, and treatment was administered significantly longer in the combination group vs. monotherapy groups (p = 0.03). Results demonstrated that patients receiving combination therapy had significantly fewer clinical failure events (defined as death, hospitalization for worsening PAH, disease progression, or unsatisfactory long-term clinical response) compared to patients receiving individual monotherapy (combination vs. pooled-monotherapy group, hazard ratio [HR] 0.5; 95% CI, 0.35 to 0.72; p < 0.001). Primary event outcomes were primarily driven by hospitalization. No significant differences were observed in terms of change in FC or all-cause death. The most common AEs that occurred more often with combination treatment included peripheral edema, headache, nasal congestion, anemia, and bronchitis (*Galiè et al 2015[a]*). Based on results from the AMBITION trial, the FDA-approved Letairis in combination with Adcirca to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.

Opsumit (macitentan)

- The efficacy and safety of Opsumit on progression of PAH were demonstrated in a multicenter, Phase 3, event-driven, placebo-controlled trial (SERAPHIN) in 742 patients with symptomatic PAH (WHO FC II, III, or IV) with or without concomitant use of oral PDE-5 inhibitors, oral or inhaled PCAs, CCBs, or L-arginine for the 3 month period prior to randomization. Patients were randomized to placebo (n = 250), Opsumit 3 mg once daily (n = 250), or Opsumit 10 mg once daily (n = 242). The mean treatment durations were 85.3, 99.5, and 103.9 weeks in the placebo, Opsumit 3 mg, and Opsumit 10 mg groups, respectively. The primary study endpoint was time to the first occurrence of death, a significant morbidity event (defined as atrial septostomy, lung transplantation, initiation of IV or SC PCAs), or other worsening of PAH (defined as a sustained ≥ 15% decrease from baseline in 6MWD, worsening of PAH symptoms as determined by worsening of WHO FC, and need for additional treatment of PAH) during the double-blind treatment plus 7 days. Pre-specified secondary endpoints included change from baseline to month 6 in the 6MWD and percentage of patients with improvement in WHO FC. Other critical pre-specified secondary endpoints were time to PAH death or PAH hospitalization. The primary endpoint occurred in 46.4%, 38%, and 31.4% of the patients in the placebo, Opsumit 3 mg, and Opsumit 10 mg groups, respectively. Opsumit 10 mg once daily therapy resulted in a 45% reduction compared to placebo (HR, 0.55; 97.5% CI, 0.39 to 0.76; p < 0.001) in the occurrence of the primary endpoint to the end of the double-blind treatment. The beneficial effect of Opsumit 10 mg was primarily due to its reduction in clinical worsening (*Pulido et al 2013*).
  - In a sub-group analysis of the effect of Opsumit on hospitalizations, there were 117 (46.8%), 104 (41.6%), and 90 (37.2%) patients in the placebo, Opsumit 3 mg and 10 mg groups, respectively, who were hospitalized for any cause at least once during double-blind treatment, and they experienced a total of 171, 159, and 135 all-cause hospitalizations, respectively. Compared with that of placebo, the risk of all-cause hospitalization with Opsumit 3 mg was reduced by 18.9% (HR, 0.811; 95% CI, 0.623 to 1.057; p = 0.1208) and with Opsumit 10 mg by 32.3% (HR,

0.677; 95% CI, 0.514 to 0.891; p = 0.0051). Compared with placebo, the rate of PAH-related hospitalization was reduced by 44.5% in the Opsumit 3 mg group (p = 0.0004) and by 49.8% in the Opsumit 10 mg group (p < 0.0001). The mean number of annual hospital days for PAH-related hospitalizations was reduced by 53.3% in the Opsumit 3 mg arm (p = 0.0001) and by 52.3% in the Opsumit 10 mg arm (p = 0.0003). Due to the exploratory nature of this endpoint and small population, data from this study must be interpreted cautiously (*Channick et al 2015*).

Remodulin (treprostinil)

- The safety and efficacy of Remodulin were evaluated in 2 identical 12-week, multi-center, randomized, placebo-controlled, double-blind trials in a total of 470 patients with NYHA Class II, III, and IV PAH. Remodulin was administered SC at an average dose of 9.3 ng/kg/min. The effect on the 6MWD was small and did not achieve statistical significance at 12 weeks. For the combined populations, the median change from baseline for patients on Remodulin was 10 m and the median change from baseline on placebo was 0 m from a baseline of approximately 345 m. Remodulin significantly improved the Borg dyspnea score during the 6-minute walk test. Remodulin also consistently improved indices of dyspnea, fatigue, and signs and symptoms of PH. However, these results were difficult to interpret in the context of incomplete blinding to treatment assignment resulting from infusion site symptoms.

Orenitram (treprostinil)

- The efficacy and safety of Orenitram were evaluated in 3 multi-center, randomized, placebo-controlled, double-blind trials in 349 patients (FREEDOM-M), 350 patients (FREEDOM-C), and 310 patients (FREEDOM-C2).
  - FREEDOM-M compared twice daily administration of Orenitram with placebo in patients newly diagnosed with PAH and not receiving any background PAH treatment. The dose titration was based on patient's clinical response and tolerability. The primary endpoint was change in 6MWD over 12 weeks. The Orenitram group showed a significant improvement in 6MWD of 23 m (p = 0.0125). More than 50% of patients had an improvement of ≥ 20 m, and over 30% of patients had an improvement of > 50 m (*Jing et al 2013*). Orenitram demonstrated AEs typical of prostacyclin treatments (*Waxman 2013*).
  - FREEDOM-C and FREEDOM-C2 failed to meet the primary endpoint of improved 6MWD (*Tapson et al 2012, Tapson et al 2013*).

Revatio (sildenafil)

- The safety and efficacy of Revatio were evaluated in the SUPER-1 study, a 12-week, randomized, double-blind, placebo-controlled trial consisting of 278 patients with predominantly WHO FC II or III symptoms. Compared to placebo, Revatio significantly improved exercise capacity, as measured by the 6MWD, WHO FC symptoms and hemodynamics (*Galiè et al 2005*). In a 3-year extension study (SUPER-2), 46% of patients increased 6MWD relative to SUPER-1 baseline, 18% decreased 6MWD from baseline, 19% had died and 17% discontinued treatment or were lost to follow-up (*Rubin et al 2011*). The addition of Revatio to epoprostenol was evaluated in PACES, a 16-week, randomized, double-blind, placebo-controlled trial consisting of 267 patients receiving epoprostenol with predominantly WHO FC II or III symptoms. Revatio added to epoprostenol improved exercise capacity, hemodynamic measurements and time to clinical worsening more than epoprostenol plus placebo (*Simonneau et al 2008*).

Tracleer (bosentan)

- Tracleer was originally FDA-approved in PAH patients with WHO FC III and IV symptoms based on the results from 2 randomized, double-blind, placebo-controlled trials in 32 (Study 351) and 213 (BREATHE-1) patients treated for 16 and 12 weeks, respectively. In both studies, significant increases in the 6MWD were observed in all Tracleer groups compared to placebo. Tracleer was also associated with a significant reduction in dyspnea during walk tests and a significant improvement in WHO FC symptoms (*Channick et al 2001, Rubin et al 2002*). The FDA-approved indication was subsequently expanded to include patients with WHO FC II symptoms based on the results of the EARLY study consisting of 168 patients. In this 26-week study, treatment with Tracleer resulted in an increase in the 6MWD of 11.2 m compared to a decrease of 7.9 m in the placebo group; however, the difference was not statistically significant. The study did show a significant delay in clinical worsening and a lower incidence of worsening FC symptoms in the Tracleer group compared to placebo (*Galiè et al 2008[b], McLaughlin et al 2006*).
  - The results of an open-label extension phase of the EARLY trial suggested that the majority of patients exposed to long-term Tracleer therapy maintained or improved their FC. Approximately 20% of patients discontinued treatment because of AEs, which were most commonly PAH worsening (defined as death or initiation of IV or SC PCAs) and

elevated liver enzymes. Due to lack of a control group, data from this study must be interpreted cautiously (*Simmoneau et al 2014*).

- The COMPASS-2 trial (n = 334) was a prospective, double-blind, randomized controlled trial consisting of symptomatic PAH patients ranging from WHO FC II to IV who were taking stable Revatio doses (mean dose, 60 mg) for ≥ 3 months. Patients were randomized to Tracleer 125 mg twice daily plus Revatio or placebo plus Revatio for 16 weeks. There was no difference in the primary endpoint, time to the first morbidity/mortality event (defined as time to all-cause death, hospitalization for worsening PAH, initiation of IV prostanoid, atrial septostomy, lung transplant, or worsening PAH). There were also no significant differences in the individual measures of the primary endpoint; however, observed benefits were seen in terms of the mean 6MWD test. A high drop-out rate was observed during the trial; therefore, study power was reduced (*McLaughlin et al 2015*).

Tyvaso (treprostinil)

- The safety and efficacy of Tyvaso were evaluated in TRIUMPH I, a 12-week, multi-center, randomized, placebo-controlled, double-blind trial in WHO Group I PAH (98% NYHA Class III) patients who were receiving either Tracleer or Revatio (n = 235) for at least 3 months prior to study initiation. Patients received either placebo or Tyvaso in 4 daily treatments with a target dose of 9 breaths (54 mcg) per session. The primary endpoint, 6MWD, was measured at peak exposure (10 to 60 minutes post dose) and 3 to 5 hours after Tracleer or 30 to 120 minutes after Revatio. Patients receiving Tyvaso had a placebo-corrected median change from baseline in peak 6MWD of 20 meters (m) at week 12 ($p < 0.001$). The 6MWD measured at trough exposure (measured 4 hours after dosing) improved by 14 m.
- In a long-term follow-up of patients who were treated with Tyvaso in the pivotal study and the open-label extension (n = 206), Kaplan-Meier estimates of survival at 1, 2, and 3 years were 97%, 91%, and 82%, respectively. Of note, these observations were uncontrolled and therefore cannot be compared to the control group to determine the long-term effect of Tyvaso on mortality.

Uptravi (selexipag)

- The safety and efficacy of Uptravi were evaluated in the GRIPHON study (n = 1,156), a randomized, double-blind, placebo-controlled trial consisting of patients with predominantly idiopathic PAH, and WHO FC II or III symptoms. The median duration of treatment varied from 1.2 to 1.4 years for placebo and Uptravi, respectively, and treatment end was defined as 7 days after the last day of treatment intake. Compared to placebo, Uptravi significantly reduced the composite endpoint signifying the time to progression of PAH, defined as all-cause death or a PAH complication (27% vs. 41.6%; HR, 0.6; 99% CI, 0.46 to 0.78; $p < 0.001$); however, there were no differences in mortality between groups. The reduction in PAH complications was primarily driven by a reduction in disease progression (17.2% vs. 6.6%) and PAH-related hospitalization (18.7% vs. 13.6%). The safety of Uptravi compared to other agents in class is not clear. The GRIPHON pre-specified sub-group analysis did not stratify AEs by background treatment, but the study allowed stable doses of PDE-5 inhibitors and/or an ERA which accounted for ~80% of patients within the placebo baseline group. Those AEs that occurred significantly more often with Uptravi treatment included headache, diarrhea, jaw pain, nausea, myalgia, vomiting, extremity pain, flushing ($p < 0.001$ for all AEs), anemia ($p = 0.05$), and hyperthyroidism ($p = 0.004$) (*Sitbon et al 2015*).
- Frost and colleagues demonstrated that transitioning patients from inhaled treprostinil to Uptravi was effective and safe (*Frost et al 2018*). Of 34 enrolled patients, 32 (94.1%) stopped inhaled treprostinil and were receiving Uptravi, with 28 patients (82.4%) meeting all criteria for sustained treatment transition. In general, patients remained clinically stable throughout therapy and reported improved outcomes.

Veletri (epoprostenol)

- Please refer to the clinical efficacy summary for Flolan above.

Ventavis (iloprost)

- The efficacy of Ventavis was evaluated in a 12-week, randomized, multicenter, double-blind, placebo-controlled trial consisting of 203 patients with NYHA Class III PAH (majority), Class IV PAH, or CTEPH. Patients received 2.5 or 5 mcg of Ventavis 6 to 9 times daily during waking hours. The difference in the primary composite endpoint (10% increase in 6MWD 30 minutes after dose, improvement by at least one NYHA class compared to baseline, and no death or deterioration of PH) was statistically significant (19% vs. 4% placebo, $p = 0.0033$). The results for the CTEPH patients were not included in the aforementioned results, since there was inadequate evidence of benefit in this

patient population. The placebo-corrected difference in the 6MWD in Ventavis patients at 12 weeks was 40 m ($p < 0.01$).

- The safety of Ventavis was evaluated in a prospective, 2 year, open-label study with 63 PAH patients. Patients received Ventavis 2 to 4 mcg 6 to 9 times daily. Thirty-six patients completed at least 630 days of therapy, 19 patients dropped out prematurely, and 8 patients died. AEs were mild to moderate, the most common of which were cough and flushing. Two-year survival was found to be 87% [95% CI, 76% to 98%] (*Olschewski et al 2010*).

Meta-analyses and systematic reviews

- The results of a meta-analysis of 18 randomized controlled trials (n = 4,363) suggested that all oral PAH therapies confer a therapeutic benefit. More specifically, the findings showed:
  - PDE-5 inhibitors were associated with a statically significant reduction in mortality (relative risk [RR], 0.22; 95% CI, 0.07 to 0.71; p = 0.011), while other drugs only showed a trend toward reducing mortality.
  - Compared with placebo, ERAs, PDE-5 inhibitors, and riociguat significantly reduced clinical worsening, ameliorated WHO function class, and increased 6MWD. Oral prostanoids only showed a mild effect on 6MWD (19.88 m; 95% CI, 10.12 to 29.64, p = 0), and did not have any effect on reducing mortality and clinical worsening. Additionally, oral prostanoids significantly increased the incidence of treatment discontinuation due to AEs (RR, 3.41; 95% CI, 2.06 to 5.63; p = 0) (*Zheng et al 2014[a]*).
- A meta-analysis of 14 randomized controlled trials (n = 2,244) that evaluated the improvement in overall survival with use of oral, SC, IV, and inhaled PCAs, suggested the following:
  - Only IV PCAs showed a survival benefit (RR, 0.36; 95% CI, 0.16 to 0.79; p = 0.011), while oral (RR, 0.73; 95% CI, 0.32 to 1.66; p = 0.446), inhaled (RR, 0.28; 95% CI, 0.05 to 1.67; p = 0.162), and SC administration (RR, 0.91; 95% CI, 0.38 to 2.20; p = 0.837) did not show a benefit.
  - Overall mortality in the 14 studies was 3.30% (74 of 2,244 patients) with 2.52% (30 of 1,189 patients) mortality in the PCA-treated group and 4.17% (44 of 1,055 patients) mortality in the placebo group. The cumulative RR estimate of death showed a significant reduction of 44% (RR, 0.56; 95% CI, 0.35 to 0.88; p = 0.01), and no heterogeneity ($I^2 = 0.0\%$; p = 0.84) was detected among studies (*Zheng et al 2014[b]*).
- The results of a meta-analysis of 21 randomized controlled trials (n = 5,105) suggested that there was a reduction in the number of combined clinical worsening events (defined as all-cause mortality, lung or heart-lung transplant, hospitalization for PAH, and escalation of treatment) in patients with PAH with oral treatments, but showed less favorable effects on life expectancy in the short-term follow-up. Results demonstrated:
  - All classes reduced clinical worsening compared to placebo, including oral prostanoids (odds ratio [OR], 0.616; 95% CI, 0.419 to 0.906; p = 0.014), ERAs (OR, 0.504; 95% CI, 0.409 to 0.621; p < 0.001), PDE-5 inhibitors (OR, 0.468; 95% CI, 0.329 to 0.664; p < 0.001), and Adempas (OR, 0.277; 95% CI, 0.098 to 0.782; p = 0.015).
  - There were no significant reductions in mortality with any class versus placebo (*Zhang et al 2015*).
- A meta-analysis of 5 randomized controlled trials (n = 962) of < 16 weeks duration in adults and children treated with an sGC stimulator determined the following (all comparisons are vs. placebo):
  - sGC stimulators improve PAP in patients with PAH (who are treatment naïve or receiving a prostanoid or ERA) or those with recurrent or inoperable CTEPH.
  - Pooled analysis showed a mean difference in 6MWD of 30.13 m (95% CI, 5.29 to 54.96; $I^2 = 64\%$). On subgroup analysis, for PAH, there was no effect on 6MWD (11.91 m; 95% CI, -44.92 to 68.75; $I^2 = 77\%$), and for CTEPH, sGC stimulators improved 6MWD by a mean difference of 45 m (95% CI, 23.87 to 66.13; $I^2 = 0\%$).
  - The secondary outcome of mortality showed no change on pooled analysis.
  - Although pooled results demonstrated an increase (improvement) in WHO FC (OR, 1.53; 95% CI, 0.87 to 2.72; $I^2 = 49\%$), the results did not reach statistical significance. Also, there was no effect on clinical worsening (OR, 0.45; 95% CI, 0.17 to 1.14; $I^2 = 54\%$) or a reduction in MAP (−2.77 mmHg; 95% CI, −4.96 to −0.58; $I^2 = 49\%$). The pooled analysis did not show any significant difference in serious AEs (OR, 1.12; 95% CI, 0.66 to 1.90; $I^2 = 39\%$).
  - sGC stimulators should not be taken by people also receiving PDE-5 inhibitors or nitrates due to the risks of hypotension, and there is currently no evidence supporting their use in pulmonary hypertension associated with left heart disease (*Wardle et al 2016*).
- Several additional meta-analyses have been conducted evaluating ERAs, PDE-5 inhibitors, and PCAs. Notable observations in meta-analyses include the following:
  - Survival benefit was seen more with IV PCAs, especially in patients with more severe disease, compared with other routes such as oral and inhalation (*Ryerson et al 2010*).

- ERAs (Letairis and Tracleer) may have a somewhat lower effect on exercise tolerance in patients with connective tissue diseases, whereas PDE-5 inhibitors (Revatio and Adcirca) and the PCA epoprostenol showed consistent effects regardless of the presence or absence of connective tissue diseases (*Kuwana et al 2013*).
- Combination therapy appears to improve exercise capacity and reduce the risk of clinical worsening in PAH patients compared with monotherapy (*Zhu et al 2012*).
- Favorable effects on clinical events were not predicted by changes in the 6MWD (*Savarese et al 2012*). In addition, pulmonary hemodynamics correlated with exercise capacity, but not with clinical events (*Savarese et al 2013*).
- According to an Agency for Healthcare Research and Quality meta-analysis, prostacyclin analogues showed a statistically significant improvement in mortality. In addition, all drug classes improved 6MWD, but comparisons between agents were inconclusive. Combination therapy also improved 6MWD compared with monotherapy, but comparisons between specific regimens were inconclusive. Patients taking ERAs and PDE-5 inhibitors had a lower risk of hospitalization than those taking placebo, while the reduction in patients taking PCAs compared with placebo was similar, but not statistically significant (*McCrory et al 2013*).
- A meta-analysis including 15 RCTs comparing combination and monotherapy for the treatment of PAH found that the absolute risk reduction of clinical worsening was relatively constant beyond a 6 to 12-month treatment duration, and cast doubt on the need for trials of longer duration for measuring treatment efficacy in this population (*Lajoie et al 2017*).

CLINICAL GUIDELINES

- Several published clinical guidelines on PAH are available.
  - The Chest Guideline and Expert Panel Report on pharmacologic therapy for PAH provides several options for initial and subsequent therapy (*Taichman et al 2014*).
    - Initial therapy: For patients in WHO FC II or III, monotherapy with an ERA, PDE-5 inhibitor, or sGC stimulator is recommended. In WHO FC III patients with evidence of rapid progression or markers of poor prognosis, a parenteral prostanoid should be considered. For patients in WHO FC IV, a parenteral PCA is recommended; however, if patients are unable or unwilling to manage a parenteral product, an alternative is an inhaled PCA combined with an ERA.
    - Subsequent therapy: For patients in WHO FC III who have evidence of progression or markers of poor prognosis, addition of an inhaled or parenteral prostanoid should be considered. In patients in WHO FC III or IV, if clinical status is unacceptable, a second (and if needed, a third) class of PAH therapy can be added.
  - The European Society of Cardiology (ESC)/European Respiratory Society (ERS) guidelines for the diagnosis and treatment of PH (*Galiè et al 2015[b]*) provide several options for both monotherapy and combination therapy of PAH.
    - Monotherapy: For patients in WHO FC II, recommendations include an ERA, a PDE-5 inhibitor, an sGC stimulator, or a prostacyclin receptor agonist. For patients in WHO FC III, the same medications may be used, and another option is a PCA. PCAs (eg, epoprostenol) are generally preferred for patients in WHO FC IV.
    - Initial drug combination therapy: Only the combination of Adcirca and Letairis has a category I recommendation for patients in WHO FC II and III; this combination also has a category IIb recommendation for patients in WHO FC IV. Other double- and triple-therapy combinations are also options, including other ERA and PDE-5 inhibitor combinations (WHO FC II, III, and IV) and some combinations of oral therapies with parenteral PCAs (WHO FC III and IV).
    - Sequential drug combination therapy: Several options are provided for sequential combination therapy. Oral combinations are commonly recommended for patients in WHO FC II and III, including Opsumit added to Revatio, Adempas added to Tracleer, and Uptravi added to an ERA and/or a PDE-5 inhibitor. Other oral combinations and combinations of oral therapies with inhaled or parenteral agents may also be used in patients in WHO FC II, III, and/or IV, but in most cases these recommendations are not as strong.
  - A 2018 scientific statement on the evaluation and management of right-sided heart failure from the American Heart Association (AHA) summarizes data for the use of prostacyclin analogs, PDE-5 inhibitors, and endothelin receptor agonists in patients with PAH (*Konstam et al 2018*). However, specific recommendations concerning the use of these agents in the PAH population are not provided in this document.
  - Reputable society groups agree that evidence supporting pediatric treatment is lacking. The AHA and American Thoracic Society (ATS) recently published a guideline on pediatric PH. This guideline states that in pediatric patients with lower-risk PAH, oral therapy with either a PDE-5 inhibitor or an ERA is recommended, and in pediatric

patients with higher-risk PAH, IV or SC PCAs should be initiated without delay (*Abman et al 2015*). A recent expert consensus statement from the European Pediatric Pulmonary Vascular Disease Network, the International Society of Heart and Lung Transplantation, and the German Society of Pediatric Cardiology reaffirm the AHA/ATS guideline. Additionally, early combination therapy with oral PAH drugs in treatment-naïve children who are FC II or III may be considered (*Hansmann et al 2016*).

SAFETY SUMMARY

- sGC Stimulator
  - Adempas has a boxed warning due to embryo-fetal toxicity. It is contraindicated in pregnancy because it may cause fetal harm when administered to pregnant women.
  - Females can only receive Adempas through the Adempas REMS Program, a restricted distribution program that requires enrollment and certification of prescribers, patients, and pharmacies. The program also requires females of reproductive potential to comply with pregnancy testing and contraception requirements.
  - Adempas is contraindicated in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias.
  - Additional contraindications for Adempas include co-administration with nitrates or nitric oxide donors and PDE-inhibitors (specific and non-specific).
  - Warnings and precautions for Adempas include symptomatic hypotension, bleeding, and pulmonary edema in patients with veno-occlusive disease (if confirmed, treatment should be discontinued).
  - The most common AEs associated with Adempas include headache, dyspepsia and gastritis, dizziness, nausea, diarrhea, hypotension, vomiting, anemia, gastroesophageal reflux disease, and constipation.
- ERAs
  - The ERAs (Letairis, Opsumit, and Tracleer) have boxed warnings for embryo-fetal toxicity and/or risks of teratogenicity due to the potential for fetal harm when administered to women who are or may become pregnant.
  - The Letairis and Opsumit REMS programs, respectively, are designed in the same manner as the Adempas REMS program described above.
  - The Tracleer Access Program (T.A.P.) program has been re-listed as the Tracleer REMS program. As a requirement of the REMS, healthcare professionals who prescribe or dispense Tracleer must enroll and comply with the requirements. Requirements include monthly reviews of pregnancy tests in women of reproductive potential, and liver enzymes and bilirubin in all patients. All patients must understand the risks and complete an enrollment form.
  - Letairis has an additional contraindication for idiopathic pulmonary fibrosis (IPF).
  - Tracleer has an additional boxed warning for risks of hepatotoxicity and birth defects. Throughout treatment and for 1 month after stopping Tracleer, females of reproductive potential must use 2 reliable methods of contraception unless the patient has had a tubal sterilization or had an intrauterine device (IUD) inserted.
  - Drug Reaction with Eosinophilia and Systematic Symptoms (DRESS), anaphylaxis, rash, and angioedema have been reported with Tracleer.
  - Warnings and precautions for Adcirca and Revatio include prolonged erection (for more than 4 hours), hearing loss, and vision loss (in 1 or both eyes), all of which require immediate medical attention.
  - Pulmonary edema/fluid retention has been reported during postmarketing surveillance of Letairis and Tracleer. Fluid retention may occur within weeks after starting Letairis and is more common when Letairis is used in combination with Adcirca than with Letairis or Adcirca alone.
  - Use of Opsumit and Tracleer should be avoided in patients taking potent inhibitors or inducers of CYP3A.
  - Decreases in sperm count, decreased hemoglobin and hematocrit levels, and pulmonary edema (associated with pulmonary veno-occlusive disease (PVOD) have been observed in patients taking ERAs.
- PDE-5 Inhibitors
  - All PDE-5 inhibitor products have a contraindication for use in patients on nitrates as well as a warning with concomitant alpha blocker use due to resulting hypotension. The patient should allow 48 hours to elapse between the last dose of Adcirca and taking nitrates. Additionally, Revatio and Adcirca are contraindicated for concomitant use with the sGC stimulator, Adempas.
  - In August 2012, the prescribing information for Revatio was updated with a warning stating that the use of Revatio in pediatric patients is not recommended due to increased mortality associated with higher doses and noted that lower doses are not effective in improving exercise capacity. The FDA clarified the warning related to pediatric use

of Revatio in March 2014, stating it was not intended to suggest that Revatio never be used in children. The FDA acknowledged there may be situations in which the benefit-to-risk profile may be acceptable in individual children, for example, when other treatment options are limited, in which case Revatio can be used with close monitoring (FDA Drug Safety Communication, 2014).
  - Co-administration of Revatio or Adcirca with potent CYP3A inhibitors is not recommended. Co-administration of Adcirca with potent CYP3A inducers is not recommended.
  - Blood pressure lowering effects are increased when Adcirca is taken with alcohol.
  - Revatio and Adcirca are generally well tolerated with headaches, myalgia, flushing, and dyspepsia being the most common AEs reported for both products.
  - Stevens-Johnson syndrome and exfoliative dermatitis have been reported with Adcirca, and anaphylactic reaction, anaphylactic shock and anaphylactoid reaction have been reported with Revatio.
  - Vision loss, including permanent vision loss because of non-arteritic anterior ischemic optic neuropathy has been reported with the use of PDE-5 inhibitors.
- Prostacyclin Receptor Agonist
  - Uptravi has a warning/precaution to consider PVOD if acute pulmonary edema develops.
  - Uptravi is not recommended in patients with severe hepatic impairment (Child-Pugh Class C) and has not been studied in dialysis patients (or with eGFR < 15 mL/min/1.73m^2).
  - Concomitant administration of Uptravi is contraindicated with strong inhibitors of CYP2C8 (eg, gemfibrozil).
  - The most common AEs reported with Uptravi are headache, diarrhea, jaw pain, nausea, myalgia, vomiting, pain in extremity, and flushing. These AEs are more frequent during the dose titration phase.
- PCAs
  - Orenitram is contraindicated for use in patients with severe hepatic impairment (Child-Pugh Class C).
  - Flolan and Veletri are contraindicated in patients with heart failure due to severe left ventricular dysfunction. Additionally, Veletri is contraindicated in patients with pulmonary edema, stating that the development of pulmonary edema during dose initiation may be associated with pulmonary veno-occlusive disease.
  - Orenitram and Tyvaso both carry a warning/precaution related to an increased risk of bleeding, particularly in patients receiving anticoagulants. Additional warnings and precautions for Tyvaso include symptomatic hypotension, possible Tyvaso dose changes when inhibitors or inducers of CYP2C8 are added or withdrawn, and a possible increase in exposure or a decrease in tolerability with hepatic or renal impairment. Orenitram should be avoided in patients with blind-end pouches (diverticulosis).
  - The safety of Tyvaso and Ventavis has not been established in patients with significant underlying lung disease (eg, asthma, chronic obstructive pulmonary disease, acute pulmonary infections). Patients with acute pulmonary infections who are taking Tyvaso should be carefully monitored to detect any worsening of lung disease and loss of drug effect. Ventavis can induce bronchospasm.
  - Hypotension leading to syncope has been observed with Ventavis. It should not be administered in patients with a systolic blood pressure below 85 mmHg.
  - Flolan and Ventavis carry additional warnings and precautions regarding pulmonary edema. If signs of pulmonary edema occur, treatment should be stopped because this could be a sign of pulmonary venous hypertension or pulmonary veno-occlusive disease.
  - With Flolan, Orenitram, Remodulin, and Veletri, abrupt withdrawal (including interruptions in drug delivery) or sudden large reductions in the dose can worsen PAH symptoms (or cause rebound PH in patients taking Flolan).
  - Flolan carries additional warnings and precautions that include vasodilation reactions and an increased risk of bleeding.
  - Flolan, Remodulin, and Veletri are administered via an indwelling central venous catheter. This route of administration is associated with blood stream infections (BSI) and sepsis, which may be fatal. During long-term follow-up, sepsis was reported at a rate of 0.3 infections per patient per year in patients treated with Flolan. In an open-label study of IV Remodulin using an external infusion pump (n = 47), there were 7 catheter-related line infections during approximately 35 patient years, or about one BSI event per 5 years of use. A Centers for Disease Control and Prevention survey of 7 sites that used IV Remodulin for the treatment of PAH found approximately one BSI event per 3 years of use. In an open-label study of an implantable pump (n = 60), there were 2 BSIs related to the implant procedure during approximately 265 patient-years. Continuous SC infusion (undiluted) is the preferred mode of administration of Remodulin. VELTERI was associated with chills/fever/sepsis/flu-like symptoms in 25% of patients in controlled trials for idiopathic or heritable PAH.

- Remodulin and Tyvaso exposure may increase or decrease when administered with strong inhibitors or inducers of CYP2C8.
- AEs reported with Tyvaso include cough, headache, throat irritation/pharyngolaryngeal pain, nausea, flushing, and syncope. AEs with Remodulin include infusion site pain, infusion site reaction, headache, diarrhea, nausea, rash, jaw pain, vasodilation, dizziness, edema, pruritus, and hypotension. The most common AEs reported with Orenitram include headache, diarrhea, nausea, and flushing.
- AEs associated with Ventavis include vasodilation (flushing), increased cough, headache, trismus, insomnia, nausea, hypotension, vomiting, increased alkaline phosphatase, flu syndrome, back pain, tongue pain, palpitations, syncope, increased gamma-glutamyl transpeptidase, muscle cramps, hemoptysis, and pneumonia.
- The most common AEs reported with Flolan and Veletri include dizziness, jaw pain, nausea, vomiting, headache, hypotension, flushing, and musculoskeletal pain.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Adcirca (tadalafil)	Tablet: 20 mg	Oral	Daily	Dividing the dose over the course of the day is not recommended.
Adempas (riociguat)	Tablet: 0.5, 1, 1.5, 2, and 2.5 mg	Oral	Three times daily	Patients who smoke may tolerate higher doses. If they stop smoking, dose decreases may be required. Lower starting doses should be considered in patients unable to tolerate the hypotensive effects and patients receiving strong CYP and P-gp/BCRP inhibitors. Adempas may be crushed and mixed with water or soft foods immediately before administration. Discontinue at least 24 hours prior to administering a PDE-5 inhibitor. Pregnancy test required prior to treatment initiation and monthly during treatment.
Flolan (epoprostenol)	Powder for injection: 0.5 and 1.5 mg	IV	Continuous infusion; Initiate infusion through a central venous catheter at 2 ng/kg/min; increase in increments of 1 to 2 ng/kg/min at intervals of at least 15 minutes based on clinical response	Abrupt withdrawal or sudden large reductions in infusion rates should be avoided. Continuous chronic infusion is administered through a central venous catheter. Temporary peripheral IV infusion may be used until central access is established.
Letairis (ambrisentan)	Tablet: 5 and 10 mg	Oral	Once daily (with or without tadalafil daily); titrate at 4-week intervals	Doses > 10 mg once daily have not been studied. Tablets should not be split, crushed, or chewed.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				Pregnancy test required prior to treatment initiation and monthly during treatment.
Opsumit (macitentan)	Tablet: 10 mg	Oral	Once daily	Doses > 10 mg once daily are not recommended.
Orenitram (treprostinil)	Extended-release tablet: 0.125, 0.25, 1, 2.5 mg, and 5 mg	Oral	Twice or 3 times daily; maximum dose is determined by tolerability; titrate not more than every 3 to 4 days as tolerated	Should be taken with food. Tablets should be swallowed whole. Coadministration with CYP2C8 inhibitors (eg, gemfibrozil) and the presence of mild hepatic impairment require a lower starting dose.
Remodulin (treprostinil)	Multi-dose vials for injection: 1, 2.5, 5, 10 mg/mL	SC, IV	Continuous infusion; initial dose for patients new to therapy: 1.25 ng/kg/min; increase in increments of 1.25 to 2.5 ng/kg/min at weekly intervals, depending on clinical response	SC is preferred, although administration via a central IV line can be performed if SC administration is not tolerated. An implantable IV infusion pump has recently been approved for use with Remodulin (Implantable System for Remodulin or ISR). Refer to the pump manufacturer's manual for specific instructions for use.
Revatio (sildenafil)	Tablet: 20 mg Powder for oral suspension: 10 mg/mL Solution for injection: 10 mg/12.5 mL	Oral, IV	Oral: 3 times daily approximately 4 to 6 hours apart Injection: IV bolus 3 times daily	Doses above 20 mg 3 times daily are not recommended. Revatio 10 mg injection dose is predicted to be the equivalent of a 20 mg oral dose. Revatio injection is for continued treatment of patients who are temporarily unable to take oral treatment. Oral suspension expires within 60 days of reconstitution.
Tracleer (bosentan)	Tablet: 62.5 and 125 mg Tablet for oral suspension: 32 mg	Oral	Twice daily (age and weigh based dosing) Concurrent ritonavir: Once daily or every other day in patients who have been receiving ritonavir for ≥ 10 days; discontinue Tracleer at least 36 hours prior to initiation of ritonavir; resume	Tablets for oral suspension should be dispersed in a minimal amount of water immediately before administration. Pregnancy test required prior to treatment initiation, monthly during treatment, and one month after stopping. Initiation should be avoided in patients with aminotransferases > 3x ULN. Doses > 125 mg twice daily do not

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			Tracleer 10 days following ritonavir initiation	have additional benefit sufficient to offset the increased risk of hepatotoxicity.
Tyvaso (treprostinil)	Inhalation solution (solution, refill, and starter solution): 0.6 mg/mL (1.74 mg per 2.9 mL)	Inhale	3 breaths per treatment session, 4 times a day (4 hours apart); titrate by an additional 3 breaths per session in 1 to 2 week intervals; maximum: 9 breaths per treatment session, 4 times daily	Inhalation system consists of an ultrasonic, pulsed delivery device and its accessories.
Uptravi (selexipag)	Tablet: 200, 400, 600, 800, 1000, 1200, 1400, and 1600 mcg Therapy pack: 200/800 mcg	Oral	Twice daily; titrate dose weekly	Swallow tablets whole. Food may improve tolerability.
Veletri (epoprostenol)	Powder for injection: 0.5 and 1.5 mg	IV	Continuous infusion; Initiate infusion at 2 ng/kg/min; increase in increments of 2 ng/kg/min at intervals of at least 15 minutes based on clinical response If symptoms persist or recur after improving, increase in increments of 1 to 2 ng/kg/min at intervals of at least 15 minutes	Abrupt withdrawal or sudden large reductions in infusion rates should be avoided. Continuous chronic infusion is administered through a central venous catheter. Temporary peripheral IV infusion may be used until central access is established.
Ventavis (Iloprost)	Inhalation solution: 10 and 20 mcg	Inhale	Administered 6 to 9 times per day (no more than once every 2 hours); maximum: 9 times daily	Ventavis is intended to be inhaled using the I-neb Adaptive Aerosol Delivery (AAD) System. The 20 mcg/mL concentration is for patients who are maintained at the 5 mcg dose and who have repeatedly experienced extended treatment times, which could result in incomplete dosing. Vital signs should be monitored while initiating Ventavis.

Abbreviations: CYP = cytochrome P450; IV = intravenous; P-gp/BCRP = P-glycoprotein/breast cancer resistance protein; SC = subcutaneous

CONCLUSION

- Pulmonary arterial hypertension (PAH) is a life-threatening disorder that is associated with a poor prognosis.
- There are 5 classes of drugs that are used in the management of PAH, including endothelin receptor antagonists (ERAs), phosphodiesterase (PDE)-5 inhibitors, a prostacyclin analog (PCA), a prostacyclin receptor agonist, and a soluble guanylate cyclase (sGC) stimulator.
- All of the PAH agents have shown improved pulmonary hemodynamics and exercise capacity in PAH patients as compared to placebo. Their effects on mortality have not been adequately demonstrated.
- Most trials for PAH have been relatively short-term trials (12 to 18 weeks) that evaluated changes in exercise capacity using the 6-minute walk distance (6MWD) as a primary endpoint. However, recently there has been a preference toward longer, event-driven trials that evaluate composite clinical worsening events (*LeVarge et al 2015*). Published event-driven trials include SERAPHIN, GRIPHON, AMBITION, and COMPASS-2 (*Galiè et al 2015[a], McLaughlin et al 2015, Pulido et al 2013, Sitbon et al 2015*).
- Clinical trials have demonstrated the safety and efficacy of the individual PAH agents; however, there is limited data comparing the agents within classes or between classes. Data are conflicting regarding the benefits of combination vs. monotherapy (*Barst, 2009, McLaughlin et al 2009, Galiè et al 2015[b], Taichman et al 2014*). Two recent trials evaluating this include the AMBITION and COMPASS-2 trials. The AMBITION trial has demonstrated that combination treatment with Letairis and Adcirca resulted in reduced disease progression and hospitalization in mainly FC II and III PAH patients compared to monotherapy (*Galiè et al 2015[a]*). However, the COMPASS-2 trial demonstrated no difference between Tracleer plus Revatio versus Revatio monotherapy for most endpoints with the exception of the mean 6MWD test (*McLaughlin et al 2015*).
- Adempas is the first and only drug to be FDA-approved in the treatment of CTEPH. Pulmonary endarterectomy can be curative for CTEPH, but it is technically demanding which may limit access to its use as a treatment. Adempas is dosed 3 times daily, which is more frequent than several other oral treatments for PAH.
- The ERAs (Letairis, Opsumit, and Tracleer) competitively bind to both receptors with different affinities. Letairis and Opsumit are highly selective for the ET_A receptor, while Tracleer is slightly selective for the ET_A receptor over the ET_B receptor. In addition, Opsumit has a pharmacologically active metabolite and is considered “tissue-targeting” because it displays high affinity and sustained occupancy at the ET receptors in human pulmonary arterial smooth muscles. However, the clinical significance of receptor affinities of the ERAs has not been established.
- The PDE-5 inhibitors (Adcirca and Revatio) are generally well tolerated; the most common side effects include headache, myalgia, flushing, dizziness, and gastrointestinal upset. Both products are contraindicated for use in patients on nitrates and have warnings about their use in patients on alpha-adrenergic inhibitors. Use of Adcirca with potent CYP3A inhibitors or inducers may significantly alter serum levels of Adcirca and is not recommended. Use of Adcirca in patients who are using an sGC stimulator may potentiate the hypotensive effects of sGC stimulators and is not recommended. Use of Revatio with potent CYP3A inhibitors is not recommended as they may significantly alter serum levels of Revatio.
- In addition to the oral formulation, Revatio is available in an oral suspension formulation and an intravenous formulation. Currently, Revatio tablets and intravenous formulation are available generically.
- Adcirca is taken just once a day compared to 3 times a day with Revatio.
- Orenitram is the first oral PCA approved by the FDA. The PCAs are frequently reserved for more severe forms of PAH. As the first oral option in this subclass for treatment of PAH, Orenitram may offer a more convenient alternative dosage form leading to earlier PCA initiation in treatment. Orenitram is dosed twice daily and requires dosage titration every 3 to 4 days. Orenitram did not demonstrate added benefit when added to other vasodilator therapy.
- Uptravi is a first-in-class prostacyclin receptor agonist, which works within the same pathway as Orenitram. Based on results from the GRIPHON trial, Uptravi has reduced disease progression and hospitalization. This is in contrast to Orenitram, which has only improved exercise tolerability. Unlike Orenitram, Uptravi has also demonstrated efficacy when combined with a PDE-5 inhibitor and/or an ERA. The safety of Uptravi compared to other oral agents in the class is not clear. The GRIPHON pre-specified sub-group analysis did not stratify AEs by background treatment, but the study allowed stable doses of PDE-5 inhibitors and/or an ERA throughout the trial. Background treatment was used by ~80% of patients within the placebo baseline group. Those AEs reported significantly more often with Uptravi treatment include headache, diarrhea, jaw pain, nausea, myalgia, vomiting, extremity pain, flushing, anemia, and hyperthyroidism (*Sitbon et al 2015*). Based on indirect trial evidence, the proportion of patients discontinuing Uptravi vs. placebo (14% vs. 7%) due to AEs in the GRIPHON trial was higher than those within the Orenitram labeling vs.

placebo (4% vs. 3%) (*Orenitram prescribing information 2014, Sitbon et al 2015*). Overall, it is not clear how the Uptravi safety profile compares to other agents in class due to different study populations. Head-to-head trials are needed to confirm safety risks and differences.

- The 2014 CHEST Guideline and Expert Panel Report update identifies PDE-5 inhibitors, ERAs, the oral PCA, and the sGC stimulator as viable alternatives in treating PAH adults with varying severity levels (FC II to IV) based primarily on consensus opinions (*Taichman et al 2014*).
- The 2015 European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines stratifies PAH treatment by low or intermediate risk or high risk patients. In adult patients with low or intermediate risk (FC II to III), initial monotherapy or initial oral combination therapy is recommended. Based on the AMBITION trial, guidelines state that initial combination treatment with ambrisentan plus tadalafil has proven to be superior to initial monotherapy with ambrisentan or tadalafil in delaying clinical failure. In adult patients with high risk (FC IV), initial combination therapy including IV PCAs are recommended with epoprostenol IV considered first-line due to the mortality benefits in trials (*Galiè et al 2015[b]*).
- Reputable society group guidelines agree that there is a lack of randomized trials in pediatric patients, making it difficult to deliver strong guidelines (*Abman et al 2015, Galiè et al 2015[b], Hansmann et al 2016*). The 2015 American Heart Association and American Thoracic Society guidelines recommend oral therapy with either a PDE-5 inhibitor or an ERA in lower risk PAH pediatric patients. In pediatric patients with higher-risk PAH, IV and SC PCAs should be initiated immediately with a goal to transition patients to oral or inhaled therapy after the patient is asymptomatic and stable (*Abman et al 2015*). The 2015 ESC/ERS guidelines recommend that pediatric treatment follows adult guidelines taking in account risks (*Galiè et al 2015[b]*). The European Pediatric Pulmonary Vascular Disease Network, the International Society of Heart and Lung Transplantation, and the German Society of Pediatric Cardiology reaffirm much of the aforementioned guidance, but also stipulate that early combination therapy with two oral PAH drugs in treatment-naïve children who are FC II or III may be considered (*Hansmann et al 2016*).
- A 2018 scientific statement on the evaluation and management of right-sided heart failure from the American Heart Association (AHA) summarizes data for the use of prostacyclin analogs, PDE-5 inhibitors, and endothelin receptor agonists in patients with PAH (*Konstam et al 2018*). However, specific recommendations concerning the use of these agents in the PAH population are not provided in this document.

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Prior Authorizations for Over $10,000 Limit

Count of Prior Authorization Requests
August 6, 2018 - Semptember 30, 2018
Fee for Service Medicaid

Year Month Received	CASE STATUS	DRUG NAME	Number of PA Req
August 2018			
	Resolved-Approved		42
		ACTIMMUNE	1
		AFINITOR	2
		BOSULIF	1
		CRYSVITA	2
		FREESTYLE LIBRE/READER/FLASH MONITORING SYSTEM	1
		GLASSIA	1
		IBRANCE	3
		IMBRUVICA	2
		JADENU	1
		JAKAFI	2
		KISQALI	1
		KUVAN	1
		OCTAGAM	3
		ORFADIN	1
		POMALYST	1
		PRIVIGEN	1
		PROMACTA	1
		RAVICTI	1
		REMODULIN	1
		REVLIMID	3
		RITUXAN	1
		SPRYCEL	1
		SUBSYS	1
		SYMDEKO	1
		TASIGNA	1
		TOBI PODHALER	2
		TYVASO REFILL	2
		VERZENIO	1
		ZEJULA	1
		ZEMAIRA	1
	Resolved-Denied		7
		AFINITOR	1
		FREESTYLE LIBRE/SENSOR/FLASH MONITORING SYSTEM	1
		JADENU	1
		OCTAGAM	2
		PERJETA	1
		PRIVIGEN	1
September 2018			
	Resolved-Approved		36
		AFINITOR	4
		AUBAGIO	1
		CALQUENCE	1
		GAMMAGARD LIQUID	1
		H.P. ACTHAR	1
		HUMULIN R U-500 KWIKPEN	1
		HYDROCODONE/ACETAMINOPHEN	1
		IBRANCE	3
		JYNARQUE	1
		NERLYNX	2
		OPDIVO	1
		ORENITRAM	2
		PRIVIGEN	1
		SABRIL	2
		TAGRISSO	1
		TASIGNA	2
		TOBI PODHALER	4
		TRACLEER	1

	TRIPTODUR	1
	TYVASO REFILL	1
	UPTRAVI	1
	VIGABATRIN	1
	VOTRIENT	1
	XTANDI	1
Resolved-Denied		7
	AFINITOR	2
	AMPHETAMINE/DEXTROAMPHETAMINE	1
	FREESTYLE LIBRE/READER/FLASH MONITORING SYSTEM	1
	HUMIRA PEN-CD/UC/HS STARTER	1
	ORENITRAM	1
	PRIVIGEN	1
Grand Total		**92**

>$10,000 Claim Prior Authorizations

October 1, 2017 - September 30, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 09/30/2018				
No Data to Report				
Total				
Grand Total				

No rejects exist for claims where the sole reason for the rejection was >$10,000. HPN processed 734 claims in the timeframe that were greater than $10,000 per month, however, these drugs were either non-formulary or required clinical prior authorization.

Prior Authorizations over $10,000- Q4 2017–Q3 2018

SilverSummith Healthplan

Drug Name	Total PA Requests over $10,000	Approvals	Denials
Glecaprevir-Pibrentasvir	98	42	56

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%

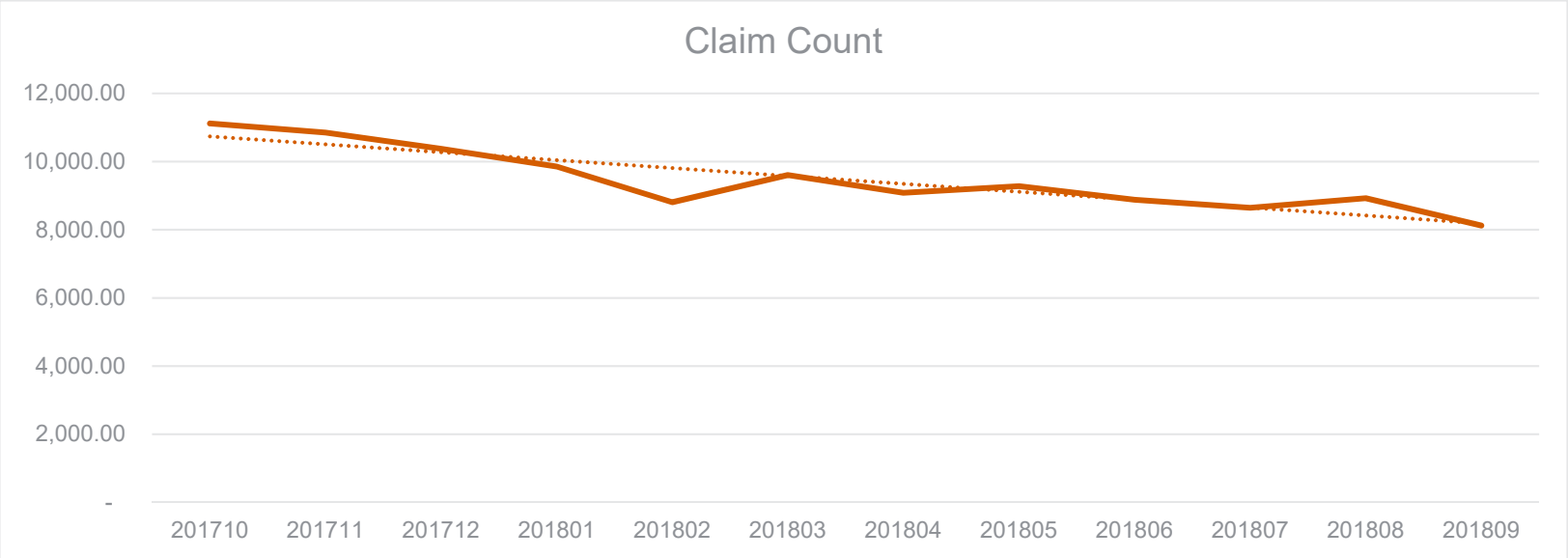
Opioid Utilization

Overall Summary

October 1, 2017 - September 30, 2018

Fee for Service Medicaid

Year Month Filled	Member Count	Claim Count	Claims per member	Sum of Days Supply	Sum of Qty	Qty Per Member	Sum of Pd Amt
201710	8,522.00	11,118.00	1.30	240,713	872,643	102.40	$ 554,505.93
201711	8,249.00	10,850.00	1.32	235,523	849,815	103.02	$ 533,639.90
201712	7,994.00	10,376.00	1.30	230,877	830,180	103.85	$ 517,566.02
201801	7,603.00	9,855.00	1.30	231,217	804,608	105.83	$ 493,763.50
201802	7,038.00	8,806.00	1.25	210,422	722,200	102.61	$ 478,220.23
201803	7,354.00	9,608.00	1.31	229,041	788,008	107.15	$ 499,561.42
201804	7,131.00	9,085.00	1.27	217,778	741,507	103.98	$ 518,396.35
201805	7,134.00	9,280.00	1.30	218,275	745,255	104.47	$ 495,513.76
201806	6,993.00	8,881.00	1.27	210,508	716,192	102.42	$ 480,838.76
201807	6,821.00	8,645.00	1.27	207,372	707,467	103.72	$ 429,541.24
201808	6,903.00	8,926.00	1.29	210,370	711,044	103.00	$ 502,248.79
201809	6,551.00	8,123.00	1.24	193,595	660,770	100.87	$ 427,165.78



Opioid Utilization by Member

Top 25 Members and Prescribers
October 1, 2017 - September 30, 2018
Fee for Service Medicaid

Member Enc ID	Enc NPI	Count of Claim	Sum of Qty	Sum of Days	Sum of Due Amt
1A		58	728	362	$ 6,209.41
	AAA	58	728	362	$ 6,209.41
2A		56	4320	735	$ 1,314.33
	YY	56	4320	735	$ 1,314.33
3A		54	630	339	$ 5,427.12
	C	54	630	339	$ 5,427.12
4A		54	766	383	$ 6,463.64
	VV	54	766	383	$ 6,463.64
5A		52	2730	1260	$ 90,293.99
	KKK	49	2590	1170	$ 90,101.68
	MMM	3	140	90	$ 192.31
6A		46	2282	635	$ 1,206.62
	BBB	4	196	56	$ 103.04
	DDD	42	2086	579	$ 1,103.58
7A		43	2820	600	$ 1,050.69
	JJ	1	120	30	$ 42.84
	PP	42	2700	570	$ 1,007.85
8A		43	1170	286	$ 1,117.65
	WW	43	1170	286	$ 1,117.65
9A		41	6660	1183	$ 4,130.33
	OOO	41	6660	1183	$ 4,130.33
10A		41	1035	531	$ 6,671.69
	FF	1	12	1	$ 8.99
	VV	40	1023	530	$ 6,662.70
11A		41	4910	1230	$ 3,599.66
	JJJ	41	4910	1230	$ 3,599.66
12A		41	6150	1020	$ 2,972.37
	HH	6	810	150	$ 306.64
	D	35	5340	870	$ 2,665.73
13A		39	2698	1184	$ 1,291.63
	GG	1	28	14	$ 21.04
	LL	5	360	150	$ 168.52
	TT	32	2250	990	$ 1,070.07
	GGG	1	60	30	$ 32.00
14A		39	658	625	$ 7,053.79
	VV	39	658	625	$ 7,053.79
15A		39	2367	1078	$ 1,276.90
	DD	37	2187	1018	$ 1,233.15
	UU	2	180	60	$ 43.75
16A		38	3408	897	$ 1,667.61
	RR	3	220	33	$ 62.03
	SS	18	1614	516	$ 454.68
	CCC	17	1574	348	$ 1,150.90

17A		38	998	439	$	6,606.64
	MM	29	882	381	$	5,606.50
	XX	9	116	58	$	1,000.14
18A		38	2420	1140	$	2,331.76
	II	3	200	90	$	187.80
	EEE	15	1000	450	$	935.12
	HHH	2	20	60	$	132.31
	LLL	15	1000	450	$	903.19
	NNN	3	200	90	$	173.34
19A		38	2628	776	$	843.18
	OO	18	1326	404	$	419.09
	FFF	8	840	240	$	225.93
	III	12	462	132	$	198.16
20A		37	4890	1110	$	927.87
	C	37	4890	1110	$	927.87
21A		37	4110	1110	$	2,015.74
	QQ	37	4110	1110	$	2,015.74
22A		36	1192	298	$	670.93
	KK	35	1072	268	$	636.59
	ZZ	1	120	30	$	34.34
23A		36	2280	1080	$	1,173.72
	C	36	2280	1080	$	1,173.72
24A		36	3420	1080	$	2,166.28
	A	8	660	240	$	1,107.61
	EE	4	360	120	$	562.41
	MM	24	2400	720	$	496.26
25A		36	2226	1014	$	13,128.26
	A	34	2072	954	$	12,381.21
	EE	2	154	60	$	747.05

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
10/1/17 - 9/30/18	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
7/1/17 - 6/30/18	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
4/1/17 - 3/31/18	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 Prescribers and Utilizers 10/1/17-9/30/18

Prescriber	Claim Count	Sum of Total Days of Therapy	Sum of Total Quantity
11PA-surg	1662	47240	160768
18PA-surg	1387	38385	129959
14PA	1234	34637	109189
18NP	1080	32043	95336
11MD-anesth	915	25396	76557
11MD-rehb	869	25590	81577
13MD-rehb	822	22302	71572
19PA	764	21477	71289
14MD-IM	756	20138	73443
18NP	747	22000	61979

Member	Claim Count	Sum of Total Days of Therapy	Sum of Total Quantity
1	43	1199	4025
2	39	1055	3706
3	39	1054	4218
4	39	1170	3120
5	39	1090	2605
6	37	865	1994
7	36	1070	2260
8	34	1020	1500
9	34	1020	2970
10	34	982	2102

Top Opioid Prescribers Utilizers HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Opioid Utilization					
Year/Month Filled	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Amt Paid
201710	13,360	16,222	316,587	1,143,199	NA
201711	12,616	15,208	301,465	1,085,609	NA
201712	11,993	14,210	286,168	1,028,453	NA
201801	10,810	12,872	288,713	978,757	NA
201802	9,755	11,303	256,794	859,846	NA
201803	9,848	11,733	264,807	888,464	NA
201804	9,313	10,918	245,148	822,394	NA
201805	9,440	11,384	254,968	850,249	NA
201806	8,980	10,646	235,066	791,575	NA
201807	8,864	10,627	233,676	783,145	NA
201808	9,077	11,055	239,965	800,105	NA
201809	8,583	10,086	218,157	724,588	NA
201810	8,927	10,858	236,199	780,746	NA
201811	8,320	9,911	220,459	730,009	NA

Top Opioid Prescriber Utilizers HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 10 Opioid Prescribers by Member Count					Q3 2018 - Current		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
A	PAIN MANAGEMENT	LAS VEGAS	NEVADA	562	1,197	187	104,640
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	464	910	223	78,946
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	340	849	217	77,353
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	315	511	106	48,564
E	PAIN MANAGEMENT & ER MEDICINE	LAS VEGAS	NEVADA	298	446	96	42,453
F	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	259	363	116	27,575
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	256	538	155	51,427
H	PAIN MANAGEMENT	LAS VEGAS	NEVADA	246	324	137	29,138
I	ORAL SURGERY	LAS VEGAS	NEVADA	215	235	37	4,647
J	ORAL SURGERY	LAS VEGAS	NEVADA	213	222	36	3,106

Top 10 Opioid Prescribers by Member Count					Q2 2018 - Previous		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	467	937	200	81,224
K	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	460	1,024	183	90,096
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	375	682	134	66,813
E	PAIN MANAGEMENT & ER MEDICINE	LAS VEGAS	NEVADA	320	491	60	46,309
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	280	650	205	61,076
F	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	252	327	301	24,534
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	579	96	56,370
L	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	386	94	38,493
M	PAIN MANAGEMENT	LAS VEGAS	NEVADA	236	500	177	47,747
N	PAIN MANAGEMENT	LAS VEGAS	NEVADA	235	339	169	30,771

Top Opioid Prescriber Utilizers HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 10 Opioid Prescribers by Claim Count					Q3 2018 - Current		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
A	PAIN MANAGEMENT	LAS VEGAS	NEVADA	562	1,197	187	104,640
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	462	908	193	78,766
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	340	849	217	77,353
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	256	538	155	51,427
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	315	511	106	48,564
O	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	189	508	207	57,612
E	PAIN MANAGEMENT & ER MEDICINE	LAS VEGAS	NEVADA	298	446	96	42,453
P	GENERAL PRACTICE	LAS VEGAS	NEVADA	119	416	61	39,504
Q	PHYSICAL MEDICINE/REHAB	LAS VEGAS	NEVADA	183	366	200	31,826
F	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	259	363	116	27,575

Top 10 Opioid Prescribers by Claim Count					Q2 2018 - Previous		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
K	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	460	1,024	183	90,096
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	465	933	170	80,864
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	375	682	134	66,813
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	280	650	205	61,076
O	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	196	647	162	75,848
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	579	96	56,370
M	PAIN MANAGEMENT	LAS VEGAS	NEVADA	236	500	177	47,747
E	PAIN MANAGEMENT & ER MEDICINE	LAS VEGAS	NEVADA	320	491	60	46,309
P	GENERAL PRACTICE	LAS VEGAS	NEVADA	128	437	107	42,328
L	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	386	94	38,493

Top Opioid Prescriber Utilizers HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 10 Opioid Prescribers by Days Supply					Q3 2018 - Current		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
R	INTERNAL MEDICINE	LAS VEGAS	NEVADA	103	194	253	18,135
S	FAMILY PRACTICE	LAS VEGAS	NEVADA	110	234	242	15,490
T	FAMILY PRACTICE	LAS VEGAS	NEVADA	66	104	226	5,799
C	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	340	849	217	77,353
U	PAIN MANAGEMENT	LAS VEGAS	NEVADA	58	149	209	13,866
O	INTERNAL MEDICINE	LAS VEGAS	NEVADA	189	508	207	57,612
Q	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	183	366	200	31,826
B	PHYSICAL MEDICINE REHAB	LAS VEGAS	NEVADA	462	908	193	78,766
A	PAIN MANAGEMENT	LAS VEGAS	NEVADA	562	1,197	187	104,640
V	FAMILY PRACTICE	LAS VEGAS	NEVADA	53	126	176	15,569

Top 10 Opioid Prescribers by Days Supply					Q2 2018 - Previous		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
F	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	252	327	301	24,534
W	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	75	141	222	10,627
T	FAMILY PRACTICE	LAS VEGAS	NEVADA	74	115	216	6,628
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	280	650	205	61,076
X	FAMILY PRACTICE	LAS VEGAS	NEVADA	81	142	205	10,583
Y	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	467	937	200	81,224
K	FAMILY PRACTICE	LAS VEGAS	NEVADA	62	161	188	14,253
M	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	460	1,024	183	90,096
S	PAIN MANAGEMENT	LAS VEGAS	NEVADA	236	500	177	47,747
Z	FAMILY PRACTICE	LAS VEGAS	NEVADA	117	230	176	16,011

Top Opioid Prescriber Utilizers HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 10 Opioid Prescribers by Sum of Qty					Q3 2018 - Current		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
A	PAIN MANAGEMENT	LAS VEGAS	NEVADA	562	1,197	187	104,640
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	462	908	193	78,766
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	340	849	217	77,353
O	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	189	508	207	57,612
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	256	538	155	51,427
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	315	511	106	48,564
E	PAIN MANAGEMENT & ER MEDICINE	LAS VEGAS	NEVADA	298	446	96	42,453
P	GENERAL PRACTICE	LAS VEGAS	NEVADA	119	416	61	39,504
AA	PAIN MANAGEMENT	LAS VEGAS	NEVADA	204	353	88	35,316
L	PAIN MANAGEMENT	LAS VEGAS	NEVADA	207	339	91	32,646

Top 10 Opioid Prescribers by Sum of Qty					Q2 2018 - Previous		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
K	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	460	1,024	183	90,096
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	465	933	170	80,864
O	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	196	647	162	75,848
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	375	682	134	66,813
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	280	650	205	61,076
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	579	96	56,370
M	PAIN MANAGEMENT	LAS VEGAS	NEVADA	236	500	177	47,747
E	PAIN MANAGEMENT & ER MEDICINE	LAS VEGAS	NEVADA	320	491	60	46,309
P	GENERAL PRACTICE	LAS VEGAS	NEVADA	128	437	107	42,328
L	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	386	94	38,493

Top Opioid Prescriber Utilizers HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 10 Opioid Prescribers by Paid Amount					Q3 2018 - Current		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
S	FAMILY PRACTICE	LAS VEGAS	NEVADA	110	234	242	15,490
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	340	849	217	77,353
O	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	189	508	207	57,612
AB	INTERNAL MEDICINE	LAS VEGAS	NEVADA	56	175	130	5,855
A	PAIN MANAGEMENT	LAS VEGAS	NEVADA	562	1,197	187	104,640
AC	PAIN MANAGEMENT & ER MEDICINE	LAS VEGAS	NEVADA	58	115	93	3,676
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	256	538	155	51,427
N	PAIN MANAGEMENT	LAS VEGAS	NEVADA	158	267	75	25,085
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	462	908	193	78,766
Z	INTERNAL MEDICINE	HENDERSON	NEVADA	49	82	114	3,604

Top 10 Opioid Prescribers by Paid Amount					Q2 2018 - Previous		
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity
S	FAMILY PRACTICE	LAS VEGAS	NEVADA	117	230	176	16,011
O	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	196	647	162	75,848
C	PAIN MANAGEMENT	LAS VEGAS	NEVADA	280	650	205	61,076
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	579	96	56,370
AB	INTERNAL MEDICINE	LAS VEGAS	NEVADA	57	166	156	5,896
B	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	465	933	170	80,864
M	PAIN MANAGEMENT	LAS VEGAS	NEVADA	236	500	177	47,747
K	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	460	1,024	183	90,096
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	375	682	134	66,813
AC	FAMILY MEDICINE & ADDICTION MED	LAS VEGAS	NEVADA	75	133	87	3,231

Report Summary: Provider B saw member 2222265620. Provider C saw the following members - 22222656516, 22222656517 and 22222656522.

Opioid Utilization by Member

Top 15 Members by Claim Count
October 1, 2017 - September 30, 2018
Health Plan of Nevada

Encrypted Member ID	Count of Claims	Sum of Qty
22222656510	**73**	**2,562**
HYDROCO/APAP TAB 10-325MG	50	1,584
HYDROCO/APAP TAB 5-325MG	23	978
22222656511	**51**	**1,450**
HYDROCO/APAP TAB 5-325MG	2	20
OXYCOD/APAP TAB 10-325MG	39	1,170
OXYCOD/APAP TAB 7.5-325	10	260
22222656512	**43**	**855**
OXYCOD/APAP TAB 10-325MG	43	855
22222656513	**43**	**1,517**
BUT/APAP/CAF CAP CODEINE	12	360
BUTORPHANOL SOL 10MG/ML	21	53
HYDROCO/APAP TAB 5-325MG	1	24
OXYCOD/APAP TAB 5-325MG	9	1,080
22222656514	**42**	**1,265**
HYDROCO/APAP TAB 10-325MG	1	42
HYDROCO/APAP TAB 5-325MG	4	112
OXYCOD/APAP TAB 10-325MG	4	200
OXYCOD/APAP TAB 5-325MG	29	729
OXYCOD/APAP TAB 7.5-325	4	182
22222656515	**41**	**3,830**
MORPHINE SUL TAB 15MG ER	14	1,185
MORPHINE SUL TAB 30MG ER	14	1,185
OXYCODONE TAB 15MG	13	1,460
22222656516	**40**	**3,450**
OXYCODONE TAB 15MG	10	420
OXYCODONE TAB 30MG	12	2,010
OXYMORPHONE TAB 20MG ER	6	300
OXYMORPHONE TAB 40MG ER	12	720
22222656517	**40**	**4,840**
ASCOMP/COD CAP 30MG	13	1,560
HYDROCO/APAP TAB 10-325MG	1	10
MORPHINE SUL TAB 30MG ER	12	1,080
OXYCOD/APAP TAB 5-325MG	2	390
OXYCOD/APAP TAB 7.5-325	12	1,800

Opioid Utilization by Member

Top 15 Members by Claim Count

October 1, 2017 - September 30, 2018

Encrypted Member ID	Count of Claims	Sum of Qty
22222656518	**39**	**3,830**
APAP/CODEINE TAB 300-30MG	2	20
METHADONE TAB 10MG	14	1,230
OXYCODONE TAB 15MG	1	45
OXYCODONE TAB 30MG	15	1,695
SUBSYS SPR 600MCG	2	240
SUBSYS SPR 800MCG	5	600
22222656519	**38**	**5,310**
HYDROCO/APAP TAB 10-325MG	25	3,750
MORPHINE SUL TAB 200MG ER	13	1,560
22222656520	**38**	**1,809**
HYDROCO/APAP TAB 10-325MG	2	112
METHADONE TAB 10MG	18	1,016
OXYCOD/APAP TAB 10-325MG	17	621
OXYCOD/APAP TAB 7.5-325	1	60
22222656521	**37**	**5,190**
HYDROMORPHON TAB 8MG	12	1,440
MORPHINE SUL TAB 60MG ER	13	1,950
OXYCOD/APAP TAB 10-325MG	12	1,800
22222656522	**37**	**4,680**
HYDROCO/APAP TAB 10-325MG	12	2400
MORPHINE SUL TAB 100MG ER	12	720
OXYCODONE TAB 30MG	13	1,560
22222656523	**37**	**108**
BUTORPHANOL SOL 10MG/ML	37	108
22222656524	**37**	**6,283**
BUT/APAP/CAF CAP CODEINE	4	360
HYDROMORPHON TAB 8MG	12	2,160
OXYCODONE TAB 5MG	21	3,763
Grand Total	**636**	**46,978**

Highlighted members saw providers on the top 10 list. Member 2222265620 saw provider B. All other highlighed members saw provider C.

Top 10 Opioid Prescriber Reports for Nevada SSHP

Top 10 Opioid Prescribers by Unique Util

10/1/2017 - 9/30/2018

Rank	Physician NPI	Unique Utilizers	Claim Count	Sum Metric Qty	Sum Days Supply
1	*******014	268	470	38,447	13,584
2	*******941	236	822	72,885	24,096
3	*******730	200	900	82,034	26,628
4	*******870	152	754	70,057	21,989
5	*******552	116	130	2,524	726
6	*******005	106	121	2,444	596
7	*******686	84	407	36,167	11,415
8	*******756	80	528	54,368	15,509
9	*******491	75	280	26,293	8,183
10	*******195	74	598	32,553	14,848

Top 10 Opioid Prescribers by Claim Count

10/1/2017 - 9/30/2018

Rank	Physician NPI	Unique Utilizers	Claim Count	Sum Metric Qty	Sum Days Supply
1	*******730	200	900	82,034	26,628
2	*******941	236	822	72,885	24,096
3	*******870	152	754	70,057	21,989
4	*******195	74	598	32,553	14,848
5	*******709	45	593	16,183	9,010
6	*******756	80	528	54,368	15,509
7	*******014	268	470	38,447	13,584
8	*******686	84	407	36,167	11,415
9	*******634	35	376	34,583	10,946
10	*******504	56	369	33,464	11,012

Top 10 Opioid Prescribers by Sum Days Supply

10/1/2017 - 9/30/2018

Rank	Physician NPI	Unique Utilizers	Claim Count	Sum Metric Qty	Sum Days Supply
1	*******730	200	900	82,034	26,628
2	*******941	236	822	72,885	24,096
3	*******870	152	754	70,057	21,989
4	*******756	80	528	54,368	15,509
5	*******195	74	598	32,553	14,848
6	*******014	268	470	38,447	13,584
7	*******686	84	407	36,167	11,415
8	*******504	56	369	33,464	11,012
9	*******634	35	376	34,583	10,946
10	*******709	45	593	16,183	9,010

Top 10 Opioid Prescribers by Sum Metric Quantity

10/1/2017 - 9/30/2018

Rank	Physician NPI	Unique Utilizers	Claim Count	Sum Metric Qty	Sum Days Supply
1	*******730	200	900	82,034	26,628
2	*******941	236	822	72,885	24,096
3	*******870	152	754	70,057	21,989
4	*******756	80	528	54,368	15,509
5	*******014	268	470	38,447	13,584
6	*******686	84	407	36,167	11,415
7	*******634	35	376	34,583	10,946
8	*******504	56	369	33,464	11,012
9	*******195	74	598	32,553	14,848
10	*******709	45	593	16,183	9,010

Top 10 Opioid Prescribers by Billed Amount

10/1/2017 - 9/30/2018

Rank	Physician NPI	Unique Utilizers	Claim Count	Sum Metric Qty	Sum Days Supply
1	*******195	74	598	32,553	14,848
2	*******709	45	593	16,183	9,010
3	*******730	200	900	82,034	26,628
4	*******756	80	528	54,368	15,509
5	*******870	152	754	70,057	21,989
6	*******941	236	822	72,885	24,096
7	*******504	56	369	33,464	11,012
8	*******686	84	407	36,167	11,415
9	*******634	35	376	34,583	10,946
10	*******014	268	470	38,447	13,584

Opioid Utilization by Member

Top 25 Members

October 1, 2017 - September 30, 2018

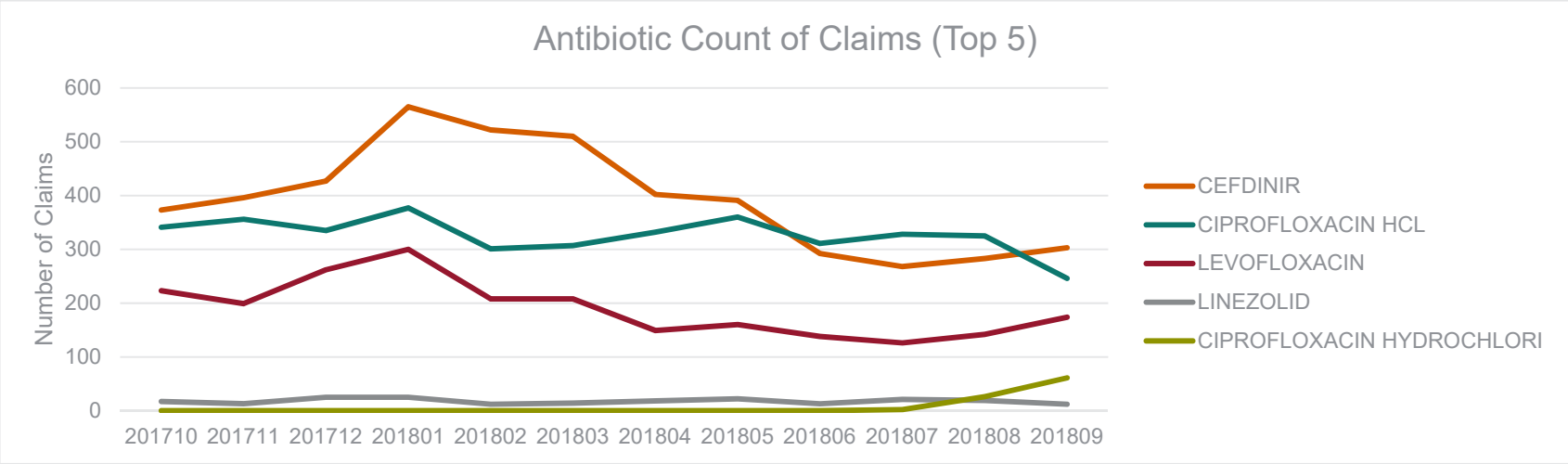
Silversummit Healthplan

Member	Enc NPI	Count of Claim	Sum of Qty	Sum of Days	Billed Amt
A		34	654	328	$4,749
B	*******686	29	3179	1027	$9,312
C	*******709	28	846	444	$5,925
D	*******686	28	2940	840	$1,692
	*******196				
	*******634				
E	*******565	28	2566	934	$1,478
F	*******709	27	956	478	$6,201
G	*******709	26	952	476	$6,303
H	*******709	26	839	442	$5,779
I	*******686	26	3030	1020	$5,591
	*******634				
J	*******686	26	2340	865	$3,135
K	*******686	26	2790	850	$2,053
	*******756				
	*******504				
L	*******941	26	1891	945	$1,492
	*******730				
	*******014				
M	*******709	25	898	464	$6,085
N	*******756	25	3645	1045	$4,591
	*******504				
	*******686				
O		25	492	365	$1,955
P	*******305	25	2346	827	$1,488
	*******635				
Q	*******756	25	3114	962	$1,245
	*******504				
R	*******504	25	3870	990	$1,042
	*******686				
S		25	2530	844	$904
T	*******756	24	2460	950	$8,773
	*******504				
U	*******756	24	2185	957	$7,870
	*******504				
V	*******635	24	1206	603	$7,633
	*******634				
	*******195				
W	*******305	24	1815	825	$3,031
	*******635				
	*******050				
X	*******686	24	3492	963	$1,722
Y	*******634	24	2280	900	$1,687

Antibiotic Agents Considered for Prior Authorization

Summary of Utilization
October 1, 2017 - September 30, 2018
Fee for Service Medicaid

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
AVELOX	15	15	306	306	$ 9,228.57
BAXDELA	7	7	91	182	$ 12,356.19
CEFDINIR	4,650	4,732	46,135	263,973	$ 117,049.90
CEFIXIME	1	1	14	50	$ 142.25
CEFPODOXIME PROXETIL	75	75	863	2,492	$ 11,739.06
CIPRO	15	19	237	2,400	$ 3,356.04
CIPROFLOXACIN ER	5	5	82	131	$ 800.06
CIPROFLOXACIN HCL	3,794	3,919	32,312	62,838	$ 43,443.42
CIPROFLOXACIN HYDROCHLORI	88	89	718	1,380	$ 1,045.89
LEVOFLOXACIN	2,205	2,289	18,986	21,109	$ 29,029.04
LINEZOLID	198	211	2,742	7,773	$ 31,324.85
MOXIFLOXACIN HCL	1	1	7	7	$ 1.25
SIVEXTRO	3	4	34	34	$ 11,540.44
SUPRAX	2	2	56	6	$ 186.89
Grand Total	**11,059**	**11,369**	**102,583**	**362,681**	**$ 271,243.85**



Anthem Antibiotic Utilization

Quarter Serviced **4th Quarter 2017**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
CEFDINIR 125 MG/5 ML SUSP	434	443	4428	36940
CEFDINIR 250 MG/5 ML SUSP	1051	1083	11271	82140
CEFDINIR 300 MG CAPSULE	388	396	3711	7363
CEFPODOXIME 100 MG TABLET	6	7	102	203
CEFPODOXIME 200 MG TABLET	12	14	111	192
CIPRO 5% SUSPENSION	1	1	10	100
CIPROFLOXACIN ER 500 MG TABLET	6	7	64	78
CIPROFLOXACIN HCL 250 MG TAB	116	122	750	1391
CIPROFLOXACIN HCL 500 MG TAB	1013	1047	7959	15810
CIPROFLOXACIN HCL 750 MG TAB	7	7	84	168
LEVOFLOXACIN 250 MG TABLET	12	12	88	102
LEVOFLOXACIN 500 MG TABLET	249	274	2406	2402
LEVOFLOXACIN 750 MG TABLET	231	242	1873	1871
LEVOFLOXACIN 750 MG/150 ML-D5W	1	2	10	1500
MOXIFLOXACIN HCL 400 MG TABLET	1	1	21	21
OFLOXACIN 400 MG TABLET	1	1	7	14
SUPRAX 400 MG CAPSULE	1	1	1	1
Grand Total	**3439**	**3660**	**32896**	**150296**

Quarter Serviced **1st Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
CEFDINIR 125 MG/5 ML SUSP	568	584	5741	49340
CEFDINIR 250 MG/5 ML SUSP	1356	1390	14422	104020
CEFDINIR 300 MG CAPSULE	486	495	4481	8884
CEFPODOXIME 100 MG TABLET	7	9	131	272
CEFPODOXIME 200 MG TABLET	9	9	79	154
CIPROFLOXACIN ER 500 MG TABLET	1	1	14	28
CIPROFLOXACIN HCL 250 MG TAB	102	109	773	1337
CIPROFLOXACIN HCL 500 MG TAB	961	986	7465	14730
CIPROFLOXACIN HCL 750 MG TAB	18	19	230	444
LEVOFLOXACIN 25 MG/ML SOLUTION	2	2	24	400
LEVOFLOXACIN 250 MG TABLET	12	13	110	125
LEVOFLOXACIN 500 MG TABLET	364	389	3244	3248
LEVOFLOXACIN 750 MG TABLET	254	270	2042	2024
MOXIFLOXACIN HCL 400 MG TABLET	4	5	67	67
Grand Total	**4020**	**4281**	**38823**	**185073**

Quarter Serviced **2nd Quarter 2018**

Row Labels	Distinct Count of Subscriber ID Client	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
BAXDELA 450 MG TABLET	1	1	14	28
CEFDINIR 125 MG/5 ML SUSP	302	307	3140	25780
CEFDINIR 250 MG/5 ML SUSP	808	826	8606	61760
CEFDINIR 300 MG CAPSULE	407	412	3638	7244
CEFIXIME 100 MG/5 ML SUSP	1	1	3	50
CEFIXIME 200 MG/5 ML SUSP	1	1	3	50
CEFPODOXIME 100 MG TABLET	2	4	97	194

Anthem Antibiotic Utilization Q2 continued

CEFPODOXIME 200 MG TABLET	9	9	77	147
CIPRO 10% SUSPENSION	1	1	10	100
CIPRO 5% SUSPENSION	1	1	7	100
CIPROFLOXACIN HCL 250 MG TAB	108	112	729	1283
CIPROFLOXACIN HCL 500 MG TAB	940	967	7419	14731
CIPROFLOXACIN HCL 750 MG TAB	17	20	197	386
LEVOFLOXACIN 250 MG TABLET	10	10	99	103
LEVOFLOXACIN 500 MG TABLET	215	227	1946	1948
LEVOFLOXACIN 750 MG TABLET	182	195	1453	1445
MOXIFLOXACIN HCL 400 MG TABLET	2	2	15	15
SUPRAX 400 MG CAPSULE	2	2	11	11
Grand Total	**2933**	**3098**	**27464**	**115375**

Quarter Serviced **3rd Quarter 2018**

Row Labels	**Distinct Count of Subscriber ID Client**	**Count of Claims**	**Sum of Total Days of Therapy**	**Sum of Total Quantity**
BAXDELA 450 MG TABLET	3	4	55	100
CEFDINIR 125 MG/5 ML SUSP	214	220	2144	19320
CEFDINIR 250 MG/5 ML SUSP	565	574	5889	44000
CEFDINIR 300 MG CAPSULE	348	353	3105	6135
CEFPODOXIME 100 MG TABLET	3	5	111	222
CEFPODOXIME 200 MG TABLET	9	10	65	129
CIPRO 10% SUSPENSION	1	1	14	200
CIPROFLOXACIN HCL 250 MG TAB	91	94	555	1052
CIPROFLOXACIN HCL 500 MG TAB	968	1007	7628	15012
CIPROFLOXACIN HCL 750 MG TAB	8	9	98	180
LEVOFLOXACIN 250 MG TABLET	7	7	55	55
LEVOFLOXACIN 500 MG TABLET	185	193	1627	1620
LEVOFLOXACIN 750 MG TABLET	159	162	1146	1143
MOXIFLOXACIN HCL 400 MG TABLET	3	3	11	11
SUPRAX 400 MG CAPSULE	1	1	1	1
Grand Total	**2505**	**2643**	**22504**	**89180**

Antibiotic Utilization HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
10/01/17 - 12/31/2017 - Q4				
CEFDINIR	2,739	2,837	668	179,093
CEFPODOXIME	7	7	25	110
CIPRO	5	5	27	600
CIPROFLOXACIN	2,064	2,142	450	32,195
LEVOFLOXACIN	757	787	227	6,400
MOXIFLOXACIN	3	3	26	26
OFLOXACIN	0	0	0	0
SUPRAX	8	8	5	11
Total	5,583	5,789	1,428	218,435
01/01/18 - 03/31/18 - Q1				
CEFDINIR	3,436	3,559	681	223,918
CEFPODOXIME	16	16	57	228
CIPRO	2	2	7	200
CIPROFLOXACIN	1,915	1,996	379	29,989
LEVOFLOXACIN	947	970	277	7,846
MOXIFLOXACIN	11	11	45	90
OFLOXACIN	3	3	10	60
SUPRAX	12	12	38	20
Total	6,342	6,569	1,494	262,351
04/01/18 - 06/30/18 - Q2				
BAXDELA	1	1	10	20
CEFDINIR	2,375	2,449	681	147,598
CEFPODOXIME	7	7	41	88
CIPRO	6	6	27	600
CIPROFLOXACIN	1,921	1,997	407	29,878
LEVOFLOXACIN	641	661	276	5,433
MOXIFLOXACIN	10	11	41	80
OFLOXACIN	2	2	20	40
SUPRAX	16	19	58	76
Total	4,979	5,153	1,561	183,813

Antibiotic Utilization HPN

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty
07/01/18 - 09/30/18 - Q3				
BAXDELA	4	4	24	90
CEFDINIR	1,776	1,812	605	101,885
CEFPODOXIME	3	3	22	44
CIPRO	6	6	29	800
CIPROFLOXACIN	1,822	1,887	455	28,412
LEVOFLOXACIN	533	555	275	4,689
MOXIFLOXACIN	8	8	42	59
OFLOXACIN	1	2	14	56
SUPRAX	27	28	44	155
Total	4,180	4,305	1,510	136,190
Grand Total	**21,084**	**21,816**	**5,993**	**800,789**

Antibiotic Utilization – Q4 2017 – Q3 2018

SilverSummit Healthplan

Report Date Range	Medication Name	Total Claims	Unique Members	Number of Units	Days Supply
10/01/2017 - 09/30/2018	BAXDELA TAB 450MG	3	1	48	24
10/01/2017 - 09/30/2018	CEFDINIR CAP 300MG	412	382	6998	3509
10/01/2017 - 09/30/2018	CEFDINIR SUS 125/5ML	191	165	14700	1707
10/01/2017 - 09/30/2018	CEFDINIR SUS 250/5ML	443	381	31120	4201
10/01/2017 - 09/30/2018	CEFIXIME SUS 100/5ML	3	3	250	25
10/01/2017 - 09/30/2018	CEFPODO PROX SUS 100/5ML	1	1	100	5
10/01/2017 - 09/30/2018	CEFPODOXIME TAB 100MG	1	1	10	10
10/01/2017 - 09/30/2018	CEFPODOXIME TAB 200MG	9	9	126	63
10/01/2017 - 09/30/2018	CIPROFLOXACN TAB 1000MG	1	1	7	7
10/01/2017 - 09/30/2018	CIPROFLOXACN TAB 250MG	105	99	1420	691
10/01/2017 - 09/30/2018	CIPROFLOXACN TAB 500MG	1153	1029	17321	8759
10/01/2017 - 09/30/2018	CIPROFLOXACN TAB 750MG	19	19	374	191

Antibiotic Utilization – Q4 2017 – Q3 2018

SilverSummit Healthplan

Report Date Range	Medication Name	Total Claims	Unique Members	Number of Units	Days Supply
10/01/2017 - 09/30/2018	LEVOFLOXACIN TAB 250MG	9	9	75	61
10/01/2017 - 09/30/2018	LEVOFLOXACIN TAB 500MG	347	290	2860	2861
10/01/2017 - 09/30/2018	LEVOFLOXACIN TAB 750MG	216	189	1630	1636
10/01/2017 - 09/30/2018	MOXIFLOXACIN TAB 400MG	2	2	14	14
10/01/2017 - 09/30/2018	SUPRAX CAP 400MG	8	8	8	8
10/01/2017 - 09/30/2018	Total Antibiotic Utilization	2924	2422	77121	23779

Standard DUR Reports

Top 10 Drug Group by Paid Amt

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

Q3 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
85	HEMATOLOGICAL AGENTS - MISC.*	2,772	$ 10,980,075.38
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,869	$ 6,081,838.84
12	ANTIVIRALS*	3,714	$ 5,728,664.69
27	ANTIDIABETICS*	19,368	$ 5,669,898.77
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	4,231	$ 5,499,965.07
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	36,854	$ 4,706,609.02
72	ANTICONVULSANTS*	43,828	$ 4,329,026.00
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	5,171	$ 3,109,117.15
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	4,983	$ 2,587,362.48
90	DERMATOLOGICALS*	17,606	$ 2,551,149.79

Top 10 Drug Group by Claim Count

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

Q3 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
72	ANTICONVULSANTS*	43,828	$4,329,026.00
65	ANALGESICS - OPIOID*	42,326	$1,466,739.72
58	ANTIDEPRESSANTS*	42,012	$857,657.59
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	36,854	$4,706,609.02
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,869	$6,081,838.84
36	ANTIHYPERTENSIVES*	23,739	$354,882.84
66	ANALGESICS - ANTI-INFLAMMATORY*	23,196	$2,081,646.37
57	ANTIANXIETY AGENTS*	22,944	$258,456.70
49	ULCER DRUGS/ANTISPASMODICS/ANTICHOLINERG	21,056	$1,081,522.85
39	ANTIHYPERLIPIDEMICS*	20,393	$693,603.80

Top 10 Drug Classes by Paid Amt

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

Q3 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	92	$ 10,329,174.40
1210	ANTIRETROVIRALS**	2,019	$ 3,314,300.79
2710	INSULIN**	6,311	$ 3,305,392.81
4420	SYMPATHOMIMETICS**	25,641	$ 3,223,541.22
7260	ANTICONVULSANTS - MISC.**	32,833	$ 2,866,386.19
1235	HEPATITIS AGENTS**	160	$ 2,350,142.71
2135	ANTINEOPLASTIC - ANTIBODIES**	413	$ 2,329,086.98
5907	BENZISOXAZOLES**	6,888	$ 2,245,231.90
5940	ANTIPSYCHOTICS - MISC.**	3,009	$ 1,876,016.67
3090	METABOLIC MODIFIERS**	2,683	$ 1,838,633.21

Nevada Medicaid
Fee for Service Medicaid

Top 10 Drug Classes by Claim Count

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 (NSA	24,850	$ 309,860.44
6510	OPIOID AGONISTS**	20,482	$ 878,117.97
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSF	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 (NSA	23,818	$ 310,320.48
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSF	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

Q3 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
7260	ANTICONVULSANTS - MISC.**	32,833	$ 2,866,386.19
4420	SYMPATHOMIMETICS**	25,641	$ 3,223,541.22
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSA	22,728	$ 352,648.43
6599	OPIOID COMBINATIONS**	22,518	$ 457,097.97
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSF	19,411	$ 244,582.10
6510	OPIOID AGONISTS**	18,737	$ 743,067.69
3940	HMG COA REDUCTASE INHIBITORS**	17,145	$ 355,837.96
7510	CENTRAL MUSCLE RELAXANTS**	15,374	$ 255,797.44
5710	BENZODIAZEPINES**	14,478	$ 143,102.81
2210	GLUCOCORTICOSTEROIDS**	12,319	$ 283,733.09

Anthem Blue Cross Blue Shield

Top 10 Therapeutic Classes 10/1/2017-9/30/2018

Therapeutic Chapter Description	Rx Count Rank	Rx Count	Ing Cost Rank
ANTIDEPRESSANT AGENTS	1	97,978	14
NSAIDS/COX II INHIBITORS	2	90,732	17
ANTICONVULSANTS	3	70,214	9
ANTIHISTAMINES	4	62,583	35
BETA AGONISTS INHALERS	5	59,567	10
VITAMINS & HEMATINICS	6	59,105	62
LIPID/CHOLESTEROL LOWERING AGENTS	7	57,136	22
PENICILLINS	8	56,695	40
NON-INSULIN HYPOGLYCEMIC AGENTS	9	54,857	5
COMBINATION NARCOTIC /ANALGESICS	10	51,163	16

Program Trends HPN Top 10 Classes

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 10 Drug Classes by Paid Amount		Q3 2018
Drug Class Name	Count of Claims	Pharmacy Paid
ANALGESICS - ANTI-INFLAMMATORY	322	NA
ANTIVIRALS	87	NA
ANTIVIRALS	330	NA
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	15,188	NA
ANTIDIABETICS	1,969	NA
ANTIVIRALS	286	NA
ANTIDIABETICS	2,446	NA
ANTIVIRALS	409	NA
DIAGNOSTIC PRODUCTS	5,568	NA
ANTIVIRALS	335	NA

Top 10 Drug Classes by Paid Amount		Q2 2018
Drug Class Name	Count of Claims	Pharmacy Paid
ANALGESICS - ANTI-INFLAMMATORY	336	NA
ANTIVIRALS	103	NA
ANTIVIRALS	348	NA
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	16,029	NA
ANTIDIABETICS	2,028	NA
ANTIVIRALS	297	NA
ANTIVIRALS	429	NA
ANTIDIABETICS	1,173	NA
DIAGNOSTIC PRODUCTS	5,933	NA
ANTIDIABETICS	2,292	NA

Top 10 Drug Classes by Claim Count		Q3 2018
Drug Class Name	Count of Claims	Pharmacy Paid
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	15,188	NA
TOPICAL NASAL PRODUCT	9,870	NA
ANALGESICS - ANTI-INFLAMMATORY	9,591	NA
ANALGESICS - OPIOID	6,806	NA
ANTICONVULSANTS	6,751	NA
ANTIHYPERLIPIDEMICS	5,739	NA
ANTIDIABETICS	5,704	NA
CALCIUM CHANNEL BLOCKER	5,629	NA
DIAGNOSTIC PRODUCTS	5,568	NA
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	5,456	NA

Top 10 Drug Classes by Claim Count		Q2 2018
Drug Class Name	Count of Claims	Pharmacy Paid
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	16,029	NA
TOPICAL NASAL PRODUCT	12,258	NA
ANALGESICS - ANTI-INFLAMMATORY	8,398	NA
ANALGESICS - OPIOID	7,362	NA
ANTICONVULSANTS	6,961	NA
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	6,016	NA
DIAGNOSTIC PRODUCTS	5,933	NA
CALCIUM CHANNEL BLOCKER	5,888	NA
ANTIDIABETICS	5,813	NA
ANTIHISTAMINE	5,733	NA

Top 10 Drug Class By Claim Volume- Q4 2017–Q3 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBE	RANK NAME	CLAIM COUNT	UTILIZER COUNT
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	1	Nonsteroidal Anti-inflammatory Agents (NSAIDs)	19,979	10,278
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	2	Anticonvulsants - Misc.	15,072	3,466
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	3	Selective Serotonin Reuptake Inhibitors (SSRIs)	13,572	3,479
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	4	Sympathomimetics	13,345	5,159
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	5	Opioid Combinations	12,457	5,226
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	6	HMG CoA Reductase Inhibitors	11,182	2,632
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	7	Central Muscle Relaxants	9,439	3,507
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	8	ACE Inhibitors	7,613	2,099
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	9	Aminopenicillins	7,093	5,785
Top Drug Class By Claim Volume	10/01/2017 - 09/30/2018	10	Proton Pump Inhibitors	6,983	2,242

Top 10 Drug Class By Spend- Q4 2017–Q3 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBER	RANK NAME	CLAIM COUNT	UTILIZER COUNT
Top Drug Class By Spend	10/01/2017 - 09/30/2018	1	Antiretrovirals	2,563	353
Top Drug Class By Spend	10/01/2017 - 09/30/2018	2	Insulin	3,973	774
Top Drug Class By Spend	10/01/2017 - 09/30/2018	3	Hepatitis Agents	114	48
Top Drug Class By Spend	10/01/2017 - 09/30/2018	4	Sympathomimetics	13,345	5,159
Top Drug Class By Spend	10/01/2017 - 09/30/2018	5	Multiple Sclerosis Agents	116	23
Top Drug Class By Spend	10/01/2017 - 09/30/2018	6	Anticonvulsants - Misc.	15,072	3,466
Top Drug Class By Spend	10/01/2017 - 09/30/2018	7	Antipsychotics - Misc.	861	256
Top Drug Class By Spend	10/01/2017 - 09/30/2018	8	Opioid Partial Agonists	2,075	281
Top Drug Class By Spend	10/01/2017 - 09/30/2018	9	Incretin Mimetic Agents (GLP-1 Receptor Agonists)	780	179
Top Drug Class By Spend	10/01/2017 - 09/30/2018	10	Antineoplastic Enzyme Inhibitors	41	11

Top 50 Drugs by Paid Amount - Q1 2018

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 Paid Amount - Q2 2018

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 Paid Amount - Q3 2018

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	20	$ 5,388,761.11	100,308	15
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	7	$ 2,721,665.34	180,000	26
5907005010	PALIPERIDONE PALMITATE	696	$ 1,801,189.62	1	22
7470005000	NUSINERSEN	12	$ 1,500,122.04	3	17
5940002310	LURASIDONE HCL	1299	$ 1,469,307.00	17	15
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	9	$ 1,346,693.93	94,698	29
6627001500	ADALIMUMAB	188	$ 1,101,645.50	1	8
4420101010	ALBUTEROL SULFATE	16424	$ 1,087,879.95	30	14
2710400300	INSULIN GLARGINE	2324	$ 1,073,009.54	13	31
1235990265	SOFOSBUVIR-VELPATASVIR	47	$ 1,022,932.03	14	14
7260005700	PREGABALIN	2433	$ 989,791.36	45	19
1910002010	IMMUNE GLOBULIN (HUMAN) IV	183	$ 916,639.75	360	5
4420990270	FLUTICASONE-SALMETEROL	2252	$ 887,216.81	42	23
9410003000	GLUCOSE BLOOD	6467	$ 861,270.50	77	25
3090522510	CINACALCET HCL	1827	$ 797,720.87	88	2
5925001500	ARIPIPRAZOLE	4501	$ 789,521.62	22	18
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	333	$ 735,892.09	17	17
4530402000	DORNASE ALFA	199	$ 728,809.10	39	13
1235990235	GLECAPREVIR-PIBRENTASVIR	56	$ 712,823.43	45	15
4927002510	ESOMEPRAZOLE MAGNESIUM	2359	$ 710,546.22	24	23
7210000700	CLOBAZAM	431	$ 679,127.17	80	16
3010002000	SOMATROPIN	163	$ 671,537.33	2	8
8240157000	PEGFILGRASTIM	115	$ 659,341.07	0	2
2710400500	INSULIN LISPRO	1019	$ 620,849.08	11	24
7260003600	LACOSAMIDE	986	$ 598,552.60	52	14
2135305300	PEMBROLIZUMAB	57	$ 579,840.40	9	1
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2270	$ 558,923.63	8	24
2135304100	NIVOLUMAB	80	$ 550,977.34	23	1
2710400200	INSULIN ASPART	1019	$ 542,807.25	12	24
1235990240	LEDIPASVIR-SOFOSBUVIR	21	$ 538,673.56	10	10
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	1584	$ 518,024.62	21	24
8580005000	ECULIZUMAB	24	$ 508,794.00	90	1
9085990208	LIDOCAINE-EMOLLIENT	45	$ 499,843.70	1	8
6240552500	DIMETHYL FUMARATE	61	$ 479,381.12	16	8
3090523010	ETELCALCETIDE HCL	328	$ 439,789.99	15	1
6110002510	LISDEXAMFETAMINE DIMESYLATE	1575	$ 435,923.85	22	22
5925002000	BREXPIPRAZOLE	459	$ 425,893.81	13	13
2755007010	SITAGLIPTIN PHOSPHATE	803	$ 399,879.02	37	36
6240506000	OCRELIZUMAB	18	$ 391,129.67	11	5
4016000700	AMBRISENTAN	43	$ 389,633.94	20	21
7460003500	ETEPLIRSEN	6	$ 384,061.02	27	9
4530990230	LUMACAFTOR-IVACAFTOR	21	$ 376,729.20	36	9
7217008500	VIGABATRIN	34	$ 374,690.32	70	18
1210301510	DOLUTEGRAVIR SODIUM	233	$ 368,871.09	18	17
5940001810	CARIPRAZINE HCL	333	$ 354,728.23	12	12
2710400600	INSULIN DETEMIR	882	$ 350,780.86	11	25
1210990229	EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	222	$ 350,329.49	21	21
1210990315	ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	126	$ 343,086.21	22	22
2717001500	DULAGLUTIDE	377	$ 338,742.86	2	25
8240101510	DARBEPOETIN ALFA	156	$ 336,934.74	1	1

Top 50 Drugs by Claim Count - Q1 2018

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

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

Top 50 Drugs by Claim Count - Q3 2018

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
4420101010	ALBUTEROL SULFATE	16424	$ 1,087,879.95	30	14
6599170210	HYDROCODONE-ACETAMINOPHEN	14277	$ 214,270.24	50	14
7260003000	GABAPENTIN	13702	$ 191,616.45	70	22
3940001010	ATORVASTATIN CALCIUM	10709	$ 114,036.44	30	30
6610002000	IBUPROFEN	10249	$ 99,289.07	42	12
3610003000	LISINOPRIL	8402	$ 68,597.43	46	42
2810001010	LEVOTHYROXINE SODIUM	8188	$ 140,638.44	33	33
5915307010	QUETIAPINE FUMARATE	8147	$ 146,302.08	30	21
5812008010	TRAZODONE HCL	7998	$ 90,517.93	31	24
5710001000	ALPRAZOLAM	7706	$ 81,533.28	45	20
3400000310	AMLODIPINE BESYLATE	7355	$ 51,328.90	39	38
6599000220	OXYCODONE W/ ACETAMINOPHEN	7317	$ 220,253.58	48	13
7720203200	CHOLECALCIFEROL	7049	$ 56,568.40	26	25
5025006505	ONDANSETRON HCL	6944	$ 32,402.13	4	2
6510007510	OXYCODONE HCL	6860	$ 247,978.05	65	17
5816007010	SERTRALINE HCL	6611	$ 74,040.63	29	24
2725005000	METFORMIN HCL	6539	$ 141,601.04	84	42
9410003000	GLUCOSE BLOOD	6467	$ 861,270.50	77	25
4450505010	MONTELUKAST SODIUM	6290	$ 91,680.66	26	25
7975001000	SODIUM CHLORIDE	6178	$ 14,640.40	453	1
4220003230	FLUTICASONE PROPIONATE (NASAL)	5967	$ 70,930.20	13	26
6410001000	ASPIRIN	5923	$ 33,044.14	21	20
6510005510	MORPHINE SULFATE	5783	$ 132,859.44	19	8
5907007000	RISPERIDONE	5647	$ 78,170.92	36	21
7510005010	CYCLOBENZAPRINE HCL	5132	$ 48,824.27	39	17
4927007010	PANTOPRAZOLE SODIUM	5076	$ 48,782.61	24	23
5025006500	ONDANSETRON	4913	$ 48,736.19	6	3
7250001010	DIVALPROEX SODIUM	4875	$ 143,368.20	53	19
0120001010	AMOXICILLIN	4580	$ 50,966.46	48	6
5816004000	FLUOXETINE HCL	4504	$ 79,217.67	30	23
5925001500	ARIPIPRAZOLE	4501	$ 789,521.62	22	18
3320003010	METOPROLOL TARTRATE	4491	$ 36,958.39	64	34
4155003000	LORATADINE	4433	$ 49,575.64	31	20
4920002010	RANITIDINE HCL	4423	$ 62,371.77	55	28
7510009010	TIZANIDINE HCL	4386	$ 89,102.74	48	20
2210004500	PREDNISONE	4231	$ 36,327.49	16	9
7260004000	LAMOTRIGINE	4214	$ 216,968.30	39	20
5710006000	LORAZEPAM	4212	$ 36,776.72	15	7
4155002010	CETIRIZINE HCL	4077	$ 46,595.32	39	20
7210001000	CLONAZEPAM	3974	$ 42,910.61	36	18
7260004300	LEVETIRACETAM	3938	$ 168,525.19	124	21
3615004020	LOSARTAN POTASSIUM	3911	$ 30,921.80	44	42
6610005200	MELOXICAM	3893	$ 34,619.53	29	25
4920003000	FAMOTIDINE	3774	$ 31,115.54	24	16
5830004010	BUPROPION HCL	3751	$ 76,764.18	30	22
3720003000	FUROSEMIDE	3722	$ 28,498.08	37	30
6610003710	KETOROLAC TROMETHAMINE	3620	$ 15,247.75	2	1
7720203000	ERGOCALCIFEROL	3523	$ 37,484.13	5	29
9720202500	LANCETS	3487	$ 58,585.04	76	27
7260007500	TOPIRAMATE	3371	$ 165,530.40	45	22

Anthem Blue Cross Blue Shield 10/1/2017-9/30/2018

Top 50 drugs

Drug Name	Rx Count	Rx Count
VENTOLIN HFA	1	40,261
IBU	2	18,218
TRUE METRIX GLUCOSE TEST STRIP	3	14,945
LORATADINE	4	12,236
VITAMIN D2	5	11,600
AMOXICILLIN	6	11,465
AZITHROMYCIN	7	11,079
ALBUTEROL SULFATE	8	10,315
BASAGLAR KWIKPEN U-100	9	9,244
MONTELUKAST SODIUM	10	8,632
AMOXICILLIN	11	8,417
GABAPENTIN	12	8,090
ONDANSETRON ODT	13	8,075
NAPROXEN	14	8,054
METFORMIN HCL	15	7,657
ATORVASTATIN CALCIUM	16	7,624
METFORMIN HCL	17	7,119
LORATADINE	18	6,996
OMEPRAZOLE	19	6,922
IBUPROFEN	20	6,386
ATORVASTATIN CALCIUM	21	6,332
TRAZODONE HCL	22	6,291
AMOXICILLIN-CLAVULANATE POTASS	23	6,179
CYCLOBENZAPRINE HCL	24	6,128
PROMETHAZINE-DM	25	6,104
HYDROCODONE-ACETAMINOPHEN	26	6,018
CEPHALEXIN	27	5,967
TRAZODONE HCL	28	5,957
HYDROCHLOROTHIAZIDE	29	5,824
LISINOPRIL	30	5,772
MONTELUKAST SODIUM	31	5,771
HYDROCODONE-ACETAMINOPHEN	32	5,758
TRAMADOL HCL	33	5,631
SERTRALINE HCL	34	5,493
MELOXICAM	35	5,391
PREDNISONE	36	5,168
LISINOPRIL	37	4,893
SERTRALINE HCL	38	4,872
FLUCONAZOLE	39	4,755
IBUPROFEN	40	4,746
IBU	41	4,699
METRONIDAZOLE	42	4,629
CHILDREN'S LORATADINE	43	4,588
PREDNISOLONE	44	4,578

Anthem Top 50 Drugs continued

POLYETHYLENE GLYCOL 3350	45	4,567
ATORVASTATIN CALCIUM	46	4,418
AMLODIPINE BESYLATE	47	4,370
FLUTICASONE PROPIONATE	48	4,147
MUPIROCIN	49	4,130
CHILDREN'S LORATADINE	50	4,127

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q4 2017	
Drug Name	Count of Claims	Pharmacy Paid
ELBASVIR-GRAZOPREVIR	116	NA
ADALIMUMAB	375	NA
SOFOSBUVIR-VELPATASVIR	52	NA
GLUCOSE BLOOD	9,668	NA
ALBUTEROL SULFATE	18401	NA
INSULIN GLARGINE	2,174	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOV	337	NA
ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	317	NA
INSULIN LISPRO	1179	NA
INSULIN GLARGINE	2,121	NA
EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	442	NA
DIMETHYL FUMARATE	79	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOVDF	161	NA
ETANERCEPT	95	NA
INSULIN LISPRO	851	NA
INSULIN ASPART	709	NA
DOLUTEGRAVIR SODIUM	270	NA
FLUTICASONE FUROATE-VILANTEROL	1,189	NA
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	121	NA
OXYCODONE W/ ACETAMINOPHEN	4,006	NA
FLUTICASONE FUROATE-VILANTEROL	889	NA
SOMATROPIN	42	NA
BUPRENORPHINE HCL-NALOXONE HCL	868	NA
ICATIBANT ACETATE	3	NA
EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	157	NA
DULAGLUTIDE	352	NA
EFAVIRENZ-EMTRICITABINE-TENOFOVIR	92	NA
APIXABAN	614	NA
RIVAROXABAN	582	NA
INSULIN ASPART	417	NA
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	80	NA
CERTOLIZUMAB PEGOL	53	NA
EMPAGLIFLOZIN	479	NA
DARUNAVIR-COBICISTAT	120	NA
DULAGLUTIDE	293	NA
HYDROCODONE-ACETAMINOPHEN	9,156	NA
OSELTAMIVIR PHOSPHATE	1137	NA
GLATIRAMER ACETATE	32	NA
ADALIMUMAB	39	NA
SECUKINUMAB	23	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q4 2017	
Drug Name	Count of Claims	Pharmacy Paid
NILOTINIB	17	NA
INSULIN LISPRO	157	NA
INSULIN DETEMIR	357	NA
USTEKINUMAB	8	NA
CANAGLIFLOZIN	355	NA
UMECLIDINIUM-VILANTEROL	406	NA
MOMETASONE FUROATE	652	NA
AMBRISENTAN	16	NA
EPINEPHRINE SOLUTION	490	NA
TERIFLUNOMIDE	23	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q1 2018	
Drug Name	Count of Claims	Pharmacy Paid
ADALIMUMAB	351	NA
GLECAPREVIR-PIBRENTASVIR	89	NA
ALBUTEROL SULFATE	19,302	NA
ELBASVIR-GRAZOPREVIR	56	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOV	344	NA
GLUCOSE BLOOD	9,334	NA
ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	329	NA
INSULIN GLARGINE	2,068	NA
SOFOSBUVIR-VELPATASVIR	34	NA
INSULIN GLARGINE	2,239	NA
EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	435	NA
INSULIN LISPRO	1,160	NA
DOLUTEGRAVIR SODIUM	302	NA
DIMETHYL FUMARATE	66	NA
INSULIN LISPRO	896	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOVDF	144	NA
OSELTAMIVIR PHOSPHATE	2,652	NA
ETANERCEPT	77	NA
INSULIN ASPART	682	NA
FLUTICASONE FUROATE-VILANTEROL	1,058	NA
EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	201	NA
DULAGLUTIDE	469	NA
BUPRENORPHINE HCL-NALOXONE HCL	954	NA
SOMATROPIN	38	NA
FLUTICASONE FUROATE-VILANTEROL	814	NA
OXYCODONE W/ ACETAMINOPHEN	3,550	NA
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	100	NA
APIXABAN	645	NA
RIVAROXABAN	616	NA
EFAVIRENZ-EMTRICITABINE-TENOFOVIR	93	NA
INSULIN ASPART	477	NA
DARUNAVIR-COBICISTAT	130	NA
EMPAGLIFLOZIN	516	NA
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	86	NA
OSELTAMIVIR PHOSPHATE	2,290	NA
NILOTINIB	20	NA
DULAGLUTIDE	326	NA
USTEKINUMAB	10	NA
UMECLIDINIUM-VILANTEROL	497	NA
ICATIBANT ACETATE	2	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q1 2018	
Drug Name	Count of Claims	Pharmacy Paid
TERIFLUNOMIDE	28	NA
AMBRISENTAN	19	NA
CERTOLIZUMAB PEGOL	44	NA
HYDROCODONE-ACETAMINOPHEN	8,164	NA
CANAGLIFLOZIN	355	NA
EPINEPHRINE SOLUTION	558	NA
INSULIN DETEMIR	351	NA
LURASIDONE HCL	111	NA
LEDIPASVIR-SOFOSBUVIR	5	NA
EMPAGLIFLOZIN TAB 10 MG	336	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q2 2018	
Drug Name	Count of Claims	Pharmacy Paid
ADALIMUMAB	345	NA
GLECAPREVIR-PIBRENTASVIR	103	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOV	348	NA
ALBUTEROL SULFATE	16,419	NA
GLUCOSE BLOOD	9,270	NA
INSULIN GLARGINE	2,028	NA
ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	297	NA
INSULIN GLARGINE	2,449	NA
INSULIN LISPRO	1,229	NA
EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	429	NA
DOLUTEGRAVIR SODIUM	347	NA
INSULIN LISPRO	962	NA
DIMETHYL FUMARATE	60	NA
EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	262	NA
DULAGLUTIDE	575	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOVDF	128	NA
ETANERCEPT	73	NA
INSULIN ASPART	628	NA
BUPRENORPHINE HCL-NALOXONE HCL	943	NA
FLUTICASONE FUROATE-VILANTEROL	915	NA
APIXABAN	707	NA
EMPAGLIFLOZIN	604	NA
CORTICOTROPIN	6	NA
FLUTICASONE FUROATE-VILANTEROL	776	NA
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	98	NA
OXYCODONE W/ ACETAMINOPHEN	3,395	NA
DULAGLUTIDE	346	NA
INSULIN ASPART	508	NA
DARUNAVIR-COBICISTAT	136	NA
RIVAROXABAN	566	NA
EFAVIRENZ-EMTRICITABINE-TENOFOVIR	84	NA
NILOTINIB	20	NA
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	80	NA
AMBRISENTAN	20	NA
CERTOLIZUMAB PEGOL	47	NA
BICTEGRAVIR-EMTRICITABINE-TENOFOVIR	62	NA
TERIFLUNOMIDE	27	NA
LURASIDONE HCL	111	NA
LENALIDOMIDE	15	NA
EPINEPHRINE SOLUTION	563	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q2 2018	
Drug Name	Count of Claims	Pharmacy Paid
USTEKINUMAB	8	NA
EMPAGLIFLOZIN TAB 10 MG	343	NA
GLATIRAMER ACETATE	37	NA
INSULIN LISPRO	169	NA
ADALIMUMAB	35	NA
ETANERCEPT	30	NA
HYDROCODONE-ACETAMINOPHEN	7,362	NA
CANAGLIFLOZIN	307	NA
LURASIDONE HCL	123	NA
INSULIN DETEMIR	338	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q3 2018	
Drug Name	Count of Claims	Pharmacy Paid
ADALIMUMAB	343	NA
GLECAPREVIR-PIBRENTASVIR	87	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOV	330	NA
ALBUTEROL SULFATE	15,623	NA
GLUCOSE BLOOD	9,051	NA
INSULIN GLARGINE	1,969	NA
ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	286	NA
INSULIN GLARGINE	2,615	NA
EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	409	NA
INSULIN LISPRO	1,211	NA
DOLUTEGRAVIR SODIUM	335	NA
DULAGLUTIDE	662	NA
EMTRICITABINE-TENOFOVIR ALAFENAMIDE FUMARATE	282	NA
INSULIN LISPRO	937	NA
BUPRENORPHINE HCL-NALOXONE HCL	1,030	NA
DIMETHYL FUMARATE	46	NA
DULAGLUTIDE	447	NA
BICTEGRAVIR-EMTRICITABINE-TENOFOVIR	110	NA
APIXABAN	734	NA
ELVITEGRAV-COBIC-EMTRICITAB-TENOFOVDF	96	NA
ETANERCEPT	61	NA
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	111	NA
FLUTICASONE FUROATE-VILANTEROL	843	NA
FLUTICASONE FUROATE-VILANTEROL	761	NA
RIVAROXABAN	601	NA
USTEKINUMAB	12	NA
NILOTINIB	21	NA
CERTOLIZUMAB PEGOL	57	NA
ADALIMUMAB	40	NA
OXYCODONE W/ ACETAMINOPHEN	3,266	NA
DARUNAVIR-COBICISTAT	105	NA
LENALIDOMIDE	12	NA
LURASIDONE HCL	123	NA
LURASIDONE HCL	146	NA
EFAVIRENZ-EMTRICITABINE-TENOFOVIR	66	NA
MACITENTAN	19	NA
AMBRISENTAN	18	NA
TERIFLUNOMIDE	24	NA
EPINEPHRINE SOLUTION	569	NA
INSULIN ASPART	275	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Paid Amount	Q3 2018	
Drug Name	Count of Claims	Pharmacy Paid
EMTRICITABINE-RILPIVIRINE-TENOFOVIR	59	NA
CORTICOTROPIN	3	NA
INSULIN DETEMIR	331	NA
ARIPIPRAZOLE IM FOR ER SUSP PREFILLED SYRINGE 400 MG	73	NA
GLATIRAMER ACETATE	35	NA
INSULIN LISPRO	146	NA
SECUKINUMAB	24	NA
ETANERCEPT	29	NA
UMECLIDINIUM	390	NA
ETONOGESTREL-ETHINYL ESTRADIOL	794	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q4 2017	
Drug Name	Count of Claims	Pharmacy Paid
ALBUTEROL SULFATE	18,401	NA
IBUPROFEN	14,225	NA
FLUTICASONE PROPIONATE	11,646	NA
GLUCOSE BLOOD	9,668	NA
HYDROCODONE-ACETAMINOPHEN	9,156	NA
GABAPENTIN	7,218	NA
HYDROCODONE-ACETAMINOPHEN	7,102	NA
AMOXICILLIN	6,801	NA
ALBUTEROL SULFATE	6,467	NA
METFORMIN HCL	6,096	NA
AMOXICILLIN (TRIHYDRATE)	6,071	NA
AMLODIPINE BESYLATE	6,034	NA
AZITHROMYCIN	5,825	NA
ONDANSETRON	5,385	NA
METFORMIN HCL	5,353	NA
MONTELUKAST SODIUM	5,307	NA
LORATADINE	5,248	NA
OMEPRAZOLE	5,199	NA
TRAMADOL HCL	5,188	NA
OMEPRAZOLE	5,058	NA
ATORVASTATIN CALCIUM	4,948	NA
ATORVASTATIN CALCIUM	4,854	NA
NAPROXEN	4,722	NA
LANCETS	4,687	NA
CYCLOBENZAPRINE HCL	4,635	NA
LISINOPRIL	4,564	NA
IBUPROFEN	4,533	NA
AMLODIPINE BESYLATE	4,225	NA
LISINOPRIL	4,028	NA
PREDNISONE	4,024	NA
OXYCODONE W/ ACETAMINOPHEN	4,006	NA
PSEUDOEPHED-BROMPHEN-DM	3,969	NA
HYDROCODONE-ACETAMINOPHEN	3,969	NA
PANTOPRAZOLE SODIUM EC	3,863	NA
TIZANIDINE HCL	3,775	NA
HYDROCHLOROTHIAZIDE	3,722	NA
IBUPROFEN SUSP	3,643	NA
MELOXICAM	3,638	NA
ALPRAZOLAM	3,536	NA
CETIRIZINE HCL	3,530	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q4 2017	
Drug Name	Count of Claims	Pharmacy Paid
AMOXICILLIN & K CLAVULANATE	3,423	NA
ERGOCALCIFEROL	3,422	NA
ASPIRIN	3,378	NA
MONTELUKAST SODIUM	3,359	NA
FLUCONAZOLE	3,350	NA
METRONIDAZOLE	3,300	NA
SERTRALINE HCL	3,236	NA
ZOLPIDEM TARTRATE	3,176	NA
CEPHALEXIN	3,086	NA
OXYCODONE W/ ACETAMINOPHEN	3,072	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q1 2018	
Drug Name	Count of Claims	Pharmacy Paid
ALBUTEROL SULFATE	19,302	NA
IBUPROFEN	14,260	NA
FLUTICASONE PROPIONATE	12,288	NA
GLUCOSE BLOOD	9,334	NA
HYDROCODONE-ACETAMINOPHEN	8,164	NA
ALBUTEROL SULFATE	7,802	NA
AMOXICILLIN (TRIHYDRATE)	7,507	NA
GABAPENTIN	7,143	NA
AMOXICILLIN	6,845	NA
AZITHROMYCIN	6,814	NA
METFORMIN HCL	5,876	NA
LORATADINE	5,505	NA
AMLODIPINE BESYLATE	5,423	NA
MONTELUKAST SODIUM	5,359	NA
ONDANSETRON	5,245	NA
PSEUDOEPHED-BROMPHEN-DM	5,120	NA
OMEPRAZOLE	5,080	NA
ATORVASTATIN CALCIUM	5,067	NA
METFORMIN HCL	5,034	NA
NAPROXEN	4,904	NA
ATORVASTATIN CALCIUM	4,887	NA
OMEPRAZOLE	4,830	NA
IBUPROFEN	4,658	NA
HYDROCODONE-ACETAMINOPHEN	4,560	NA
CYCLOBENZAPRINE HCL	4,534	NA
LANCETS	4,508	NA
LISINOPRIL	4,407	NA
PREDNISONE	4,389	NA
IBUPROFEN SUSP	3,962	NA
LISINOPRIL	3,935	NA
AMLODIPINE BESYLATE	3,871	NA
PANTOPRAZOLE SODIUM EC	3,813	NA
AMOXICILLIN & K CLAVULANATE	3,623	NA
MONTELUKAST SODIUM	3,609	NA
OXYCODONE W/ ACETAMINOPHEN	3,550	NA
CETIRIZINE HCL	3,514	NA
HYDROCHLOROTHIAZIDE	3,513	NA
MELOXICAM	3,498	NA
TIZANIDINE HCL	3,494	NA
TRAMADOL HCL	3,416	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q1 2018	
Drug Name	Count of Claims	Pharmacy Paid
ERGOCALCIFEROL	3,364	NA
FLUCONAZOLE	3,296	NA
SERTRALINE HCL	3,267	NA
METRONIDAZOLE	3,210	NA
PROMETHAZINE-DM	3,209	NA
PREDNISOLONE	3,206	NA
ALPRAZOLAM	3,178	NA
ASPIRIN	3,163	NA
METHYLPREDNISOLONE	2,993	NA
CEPHALEXIN	2,972	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q2 2018	
Drug Name	Count of Claims	Pharmacy Paid
ALBUTEROL SULFATE	16,419	NA
IBUPROFEN	13,477	NA
FLUTICASONE PROPIONATE	12,288	NA
GLUCOSE BLOOD	9,270	NA
HYDROCODONE-ACETAMINOPHEN	7,362	NA
GABAPENTIN	6,961	NA
MONTELUKAST SODIUM	6,019	NA
LORATADINE	5,905	NA
AMLODIPINE BESYLATE (BASE EQUIVALENT)	5,888	NA
METFORMIN HCL	5,813	NA
AMOXICILLIN	5,525	NA
ATORVASTATIN CALCIUM	5,391	NA
OMEPRAZOLE	5,151	NA
ATORVASTATIN CALCIUM	5,060	NA
METFORMIN HCL	4,983	NA
NAPROXEN	4,880	NA
ONDANSETRON	4,763	NA
OMEPRAZOLE	4,711	NA
LANCETS	4,593	NA
ALBUTEROL SULFATE	4,578	NA
CYCLOBENZAPRINE HCL	4,449	NA
AMOXICILLIN (TRIHYDRATE)	4,414	NA
LISINOPRIL	4,325	NA
AMLODIPINE BESYLATE (BASE EQUIVALENT)	4,182	NA
IBUPROFEN	4,148	NA
HYDROCODONE-ACETAMINOPHEN	4,133	NA
CETIRIZINE HCL	4,084	NA
PANTOPRAZOLE SODIUM EC	3,953	NA
AZITHROMYCIN	3,832	NA
LISINOPRIL	3,805	NA
MONTELUKAST SODIUM	3,689	NA
PREDNISONE	3,586	NA
TIZANIDINE HCL	3,522	NA
MELOXICAM	3,451	NA
HYDROCHLOROTHIAZIDE	3,427	NA
OXYCODONE W/ ACETAMINOPHEN	3,395	NA
ERGOCALCIFEROL	3,343	NA
FLUCONAZOLE	3,239	NA
SERTRALINE HCL	3,153	NA
ASPIRIN	3,125	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q2 2018	
Drug Name	Count of Claims	Pharmacy Paid
METRONIDAZOLE	3,113	NA
TRAMADOL HCL	3,065	NA
LISINOPRIL	3,006	NA
CEPHALEXIN	3,004	NA
ALPRAZOLAM	2,991	NA
ATORVASTATIN CALCIUM	2,990	NA
AMOXICILLIN & K CLAVULANATE	2,901	NA
TRAZODONE HCL	2,834	NA
RANITIDINE	2,722	NA
CETIRIZINE HCL	2,686	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q3 2018	
Drug Name	Count of Claims	Pharmacy Paid
ALBUTEROL SULFATE	15,623	NA
IBUPROFEN	13,547	NA
FLUTICASONE PROPIONATE	9,883	NA
GLUCOSE BLOOD	9,051	NA
HYDROCODONE-ACETAMINOPHEN	6,806	NA
GABAPENTIN	6,751	NA
ATORVASTATIN CALCIUM	5,739	NA
METFORMIN HCL	5,704	NA
AMLODIPINE BESYLATE (BASE EQUIVALENT)	5,629	NA
MONTELUKAST SODIUM	5,458	NA
ATORVASTATIN CALCIUM	5,134	NA
OMEPRAZOLE	5,097	NA
AMOXICILLIN	5,095	NA
LORATADINE	4,925	NA
METFORMIN HCL	4,785	NA
NAPROXEN	4,743	NA
OMEPRAZOLE	4,677	NA
LANCETS	4,552	NA
CYCLOBENZAPRINE HCL	4,476	NA
HYDROCODONE-ACETAMINOPHEN	4,192	NA
LISINOPRIL	4,134	NA
IBUPROFEN	4,035	NA
AMLODIPINE BESYLATE (BASE EQUIVALENT)	3,998	NA
ALBUTEROL SULFATE	3,872	NA
ONDANSETRON	3,870	NA
PANTOPRAZOLE SODIUM EC	3,806	NA
LISINOPRIL	3,716	NA
TIZANIDINE HCL	3,618	NA
CETIRIZINE HCL	3,578	NA
FLUCONAZOLE	3,313	NA
OXYCODONE W/ ACETAMINOPHEN	3,266	NA
CEPHALEXIN	3,209	NA
MELOXICAM	3,205	NA
ERGOCALCIFEROL	3,195	NA
AZITHROMYCIN	3,181	NA
HYDROCHLOROTHIAZIDE	3,178	NA
METRONIDAZOLE	3,146	NA
MONTELUKAST SODIUM	3,132	NA
AMOXICILLIN (TRIHYDRATE)	3,124	NA
ASPIRIN	3,107	NA

Program Trends HPN Top 50 Drugs

October 1, 2017 - September 30, 2018

Health Plan of Nevada

Top 50 Drugs by Count of Claims	Q3 2018	
Drug Name	Count of Claims	Pharmacy Paid
SERTRALINE HCL	3,051	NA
PREDNISONE	3,051	NA
ATORVASTATIN CALCIUM	2,949	NA
TRAMADOL HCL	2,925	NA
TRAZODONE HCL	2,902	NA
LISINOPRIL	2,887	NA
INFLUENZA VIRUS VAC SPLIT QUADRIVALENT SUSP	2,836	NA
RANITIDINE	2,806	NA
ALPRAZOLAM	2,793	NA
LOSARTAN POTASSIUM	2,635	NA

Top 50 Drugs By Claim Volume- Q4 2017–Q3 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBER	RANK NAME	CLAIM COUNT	UTILIZER COUNT
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	1	VENTOLIN HFA AER	7,272	3,540
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	2	IBU TAB 800MG	4,891	3,303
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	3	FLUTICASONE SPR 50MCG	3,969	2,244
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	4	GABAPENTIN CAP 300MG	3,770	1,277
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	5	AMOXICILLIN CAP 500MG	3,598	2,945
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	6	IBUPROFEN TAB 800MG	3,110	2,095
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	7	ATORVASTATIN TAB 20MG	2,976	768
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	8	HYDROCO/APAP TAB 10-	2,938	862
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	9	CYCLOBENZAPR TAB 10MG	2,932	1,444
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	10	NAPROXEN TAB 500MG	2,891	1,830
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	11	HYDROCO/APAP TAB 5-	2,804	2,072
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	12	AZITHROMYCIN TAB 250MG	2,797	2,406
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	13	MONTELUKAST TAB 10MG	2,705	889
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	14	AMLODIPINE TAB 10MG	2,617	756
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	15	ONDANSETRON TAB 4MG	2,535	2,031
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	16	METFORMIN TAB 500MG	2,535	820
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	17	METFORMIN TAB 1000MG	2,496	671
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	18	LORATADINE TAB 10MG	2,468	1,171
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	19	ATORVASTATIN TAB 40MG	2,413	667
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	20	VITAMIN D CAP 50000UNT	2,372	779
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	21	TIZANIDINE TAB 4MG	2,304	697
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	22	SERTRALINE TAB 100MG	2,202	570
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	23	ALBUTEROL NEB 0.083%	2,199	1,449
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	24	OXYCOD/APAP TAB 10-	2,196	525
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	25	LISINOPRIL TAB 20MG	2,123	685
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	26	LISINOPRIL TAB 10MG	2,117	694

Top 50 Drugs By Claim Volume- Q4 2017–Q3 2018

SilverSummith Healthplan

Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	27	OMEPRAZOLE CAP 20MG	2,083	804
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	28	CEPHALEXIN CAP 500MG	2,028	1,803
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	29	PANTOPRAZOLE TAB 40MG	1,984	730
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	30	TRAZODONE TAB 50MG	1,950	774
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	31	AMOX/K CLAV TAB 875-125	1,949	1,701
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	32	METRONIDAZOL TAB 500MG	1,948	1,644
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	33	SERTRALINE TAB 50MG	1,935	813
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	34	TRUE METRIX TES	1,921	785
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	35	OMEPRAZOLE CAP 40MG	1,856	588
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	36	AMOXICILLIN SUS 400/5ML	1,815	1,561
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	37	PREDNISONE TAB 20MG	1,809	1,480
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	38	AMLODIPINE TAB 5MG	1,799	637
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	39	TRAZODONE TAB 100MG	1,778	582
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	40	ALPRAZOLAM TAB 1MG	1,745	428
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	41	FLUCONAZOLE TAB 150MG	1,721	1,138
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	42	MELOXICAM TAB 15MG	1,698	701
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	43	HYDROCO/APAP TAB 7.5-	1,669	924
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	44	METHYLPRED TAB 4MG	1,607	1,372
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	45	SMZ/TMP DS TAB 800-160	1,570	1,303
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	46	HYDROCHLOROT TAB 25MG	1,528	500
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	47	TRAMADOL HCL TAB 50MG	1,525	977
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	48	IBU TAB 600MG	1,501	1,224
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	49	GABAPENTIN TAB 600MG	1,493	405
Top Drugs By Claim Volume	10/01/2017 - 09/30/2018	50	SUBOXONE MIS 8-2MG	1,479	205

Top 50 Drugs By Spend- Q4 2017–Q3 2018

SilverSummith Healthplan

REPORT TYPE	REPORT DATE RANGE	RANK NUMBER	RANK NAME	CLAIM COUNT	UTILIZER COUNT
Top Drugs By Spend	10/01/2017 - 09/30/2018	1	GENVOYA TAB	426	83
Top Drugs By Spend	10/01/2017 - 09/30/2018	2	MAVYRET TAB 100-40MG	74	36
Top Drugs By Spend	10/01/2017 - 09/30/2018	3	TRUVADA TAB 200-300	436	98
Top Drugs By Spend	10/01/2017 - 09/30/2018	4	TIVICAY TAB 50MG	391	74
Top Drugs By Spend	10/01/2017 - 09/30/2018	5	TRIUMEQ TAB	216	46
Top Drugs By Spend	10/01/2017 - 09/30/2018	6	DESCOVY TAB 200/25	321	67
Top Drugs By Spend	10/01/2017 - 09/30/2018	7	EPCLUSA TAB 400-100	17	6
Top Drugs By Spend	10/01/2017 - 09/30/2018	8	SUBOXONE MIS 8-2MG	1,479	205
Top Drugs By Spend	10/01/2017 - 09/30/2018	9	VENTOLIN HFA AER	7,272	3,540
Top Drugs By Spend	10/01/2017 - 09/30/2018	10	STRIBILD TAB	98	24
Top Drugs By Spend	10/01/2017 - 09/30/2018	11	TECFIDERA CAP 240MG	36	7
Top Drugs By Spend	10/01/2017 - 09/30/2018	12	VICTOZA INJ 18MG/3ML	370	88
Top Drugs By Spend	10/01/2017 - 09/30/2018	13	HUMIRA PEN INJ 40MG/0.8	53	12
Top Drugs By Spend	10/01/2017 - 09/30/2018	14	SYMBICORT AER 160-4.5	801	266
Top Drugs By Spend	10/01/2017 - 09/30/2018	15	LANTUS INJ SOLOSTAR	600	217
Top Drugs By Spend	10/01/2017 - 09/30/2018	16	OXYCOD/APAP TAB 10-	2,196	525
Top Drugs By Spend	10/01/2017 - 09/30/2018	17	HUMALOG KWIK INJ 100/ML	380	125
Top Drugs By Spend	10/01/2017 - 09/30/2018	18	LATUDA TAB 40MG	166	75
Top Drugs By Spend	10/01/2017 - 09/30/2018	19	PREZCOBIX TAB 800-150	111	23
Top Drugs By Spend	10/01/2017 - 09/30/2018	20	JANUVIA TAB 100MG	374	95
Top Drugs By Spend	10/01/2017 - 09/30/2018	21	BASAGLAR INJ 100UNIT	566	165
Top Drugs By Spend	10/01/2017 - 09/30/2018	22	COMPLERA TAB	69	15
Top Drugs By Spend	10/01/2017 - 09/30/2018	23	ELIQUIS TAB 5MG	451	134
Top Drugs By Spend	10/01/2017 - 09/30/2018	24	PRIVIGEN INJ 20GRAMS	12	1
Top Drugs By Spend	10/01/2017 - 09/30/2018	25	REVLIMID CAP 25MG	16	3
Top Drugs By Spend	10/01/2017 - 09/30/2018	26	SUBOXONE MIS 12-3MG	235	31

Top 50 Drugs By Spend- Q4 2017–Q3 2018

SilverSummith Healthplan

Top Drugs By Spend	10/01/2017 - 09/30/2018	27	NOVOLOG INJ FLEXPEN	300	98
Top Drugs By Spend	10/01/2017 - 09/30/2018	28	XARELTO TAB 20MG	379	83
Top Drugs By Spend	10/01/2017 - 09/30/2018	29	ODEFSEY TAB	54	13
Top Drugs By Spend	10/01/2017 - 09/30/2018	30	HUMALOG INJ 100/ML	303	100
Top Drugs By Spend	10/01/2017 - 09/30/2018	31	TECFIDERA CAP 120MG	11	3
Top Drugs By Spend	10/01/2017 - 09/30/2018	32	TRULICITY INJ 1.5/0.5	169	39
Top Drugs By Spend	10/01/2017 - 09/30/2018	33	ATRIPLA TAB	49	11
Top Drugs By Spend	10/01/2017 - 09/30/2018	34	TAGRISSO TAB 80MG	9	1
Top Drugs By Spend	10/01/2017 - 09/30/2018	35	ENBREL SRCLK INJ 50MG/ML	24	5
Top Drugs By Spend	10/01/2017 - 09/30/2018	36	ZEPATIER TAB 50-100MG	7	3
Top Drugs By Spend	10/01/2017 - 09/30/2018	37	AUBAGIO TAB 14MG	19	2
Top Drugs By Spend	10/01/2017 - 09/30/2018	38	ABILIFY MAIN INJ 400MG	58	17
Top Drugs By Spend	10/01/2017 - 09/30/2018	39	ZYTIGA TAB 250MG	12	3
Top Drugs By Spend	10/01/2017 - 09/30/2018	40	LATUDA TAB 80MG	90	34
Top Drugs By Spend	10/01/2017 - 09/30/2018	41	LEVEMIR INJ FLEXTOUC	285	94
Top Drugs By Spend	10/01/2017 - 09/30/2018	42	NUTROPIN AQ INJ	9	1
Top Drugs By Spend	10/01/2017 - 09/30/2018	43	LEMTRADA INJ 12/1.2ML	1	1
Top Drugs By Spend	10/01/2017 - 09/30/2018	44	LANTUS INJ 100/ML	274	112
Top Drugs By Spend	10/01/2017 - 09/30/2018	45	LATUDA TAB 20MG	87	38
Top Drugs By Spend	10/01/2017 - 09/30/2018	46	TRULICITY INJ 0.75/0.5	130	29
Top Drugs By Spend	10/01/2017 - 09/30/2018	47	PENNSAID SOL 2%	40	18
Top Drugs By Spend	10/01/2017 - 09/30/2018	48	LYRICA CAP 150MG	188	46
Top Drugs By Spend	10/01/2017 - 09/30/2018	49	GILENYA CAP 0.5MG	12	2
Top Drugs By Spend	10/01/2017 - 09/30/2018	50	TRADJENTA TAB 5MG	217	65

Prospective Drug Utilization Review System Edits

July 1, 2018 - September 30, 2018 (Q3)

Fee for Service Medicaid

Prospective DUR							
What percentage of claims denied at Point of Sale for the following DUR edits? (# denials for each edit/total # of denials)	**Total Alerts**	**Total Alert Overrides**	**% Alert Overrides**	**Total Alert Cancels**	**% Alert Cancels**	**Total Alerts not adjudicated**	**% Alerts not adjudicated**
Early Refill (ER)							
Therapeutic duplication (TD)	56,289	39,341	69.89	9,436	16.76	7,512	13.35
Ingredient duplication (ID)	49,587	14,816	29.88	4,544	9.16	30,227	60.96
Late Refill (LR)	39,898	34,845	87.34	5,053	12.66	-	0
Total High Dose (HD)	54,282	44,102	81.25	10,061	18.53	119	0.22
Drug-Pregnancy (PG)							
Total Low Dose (LD)							
Drug-Drug (DD)	147,623	127,215	86.18	17,272	11.7	3,136	2.12
Drug-Disease (MC)							
Drug-Allergy (DA)							
Drug-Age (PA)	21	16	76.19	5	23.81	-	0

Top 10 Drugs by Therapeutic Problem Type - Overutilization										
ER	**TD**	**ID**	**LR**	**HD**	**PG**	**LD**	**DD**	**MC**	**DA**	**PA**
	Morphine Sulfate	Hydrocodone/APAP	Gabapentin	Cyclobenzaprine			Alprazolam			Promethazine-DM
	Ketorolac Tromethamine	Amlodipine Besylate	Proventil HFA	Ondasetron ODT			Atorvastatin Calcium			Nitrofurantoin
	Quetiapine Fumarate	Atorvastatin Calcium	Proventil HFA	Sensipar			Alprazolam			Promethazine HCL
	Risperidone	Proventil HFA	Proventil HFA	Famotidine			Hydrocodone/APAP			Acetaminophen/Cod
	Hydrocodone/APAP	Sodium Chloride	Gabapentin	Ipratropium/Albut			Gabapentin			Promethazine/Cod
	Lorazepam	Gabapentin	Proventil HFA	Ipratropium/Albut			Trazodone Hydrchloride			Promethazine/DM
	Gabapentin	Ondansetron HCL	Proventil HFA	Heparin Sodium			Hydrocodone/APAP			Promethegan
	Hydromorphone HCL	Sertraline HCL	Proventil HFA	Pantoprazole			Ondansetron HCL			Guaifenesin AC
	Oxycodone/APAP	Montelukast Sodium	Montelukast Sodium	Amlodipine Besylate			Hydrocodone/APAP			Promethazine/DM
	Gabapentin	Fluticasone Propionate	Montelukast Sodium	Lisinopril			Ondansetron HCL			Nitrofurantoin

Anthem CDUR data from PBM

Q4 2017

Rule DSC	Total CDUR Alerts	Total CDUR Successes (Rejects+Reverals)
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**

Q1 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 CDUR data from PBM continued

Q2 2018

Rule DSC	Total CDUR Alerts	Total CDUR Successes (Rejects+Reverals)
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**

Q3 2018

Rule Category DSC	Total CDUR Alerts	Total CDUR Successes (Rejects+Reverals)
Adverse Drug Risk	44,968	44,673
Adverse Drug Risk	65,974	34,601
Adverse Drug Risk	18,707	18,613
Adverse Drug Risk	22,326	10,424
Omission of Essential Care	21,329	3,251
Adverse Drug Risk	8,934	2,079
Omission of Essential Care	6,836	1,506
Adverse Drug Risk	7,603	1,112
Adverse Drug Risk	472	125
Adverse Drug Risk	472	85
Adverse Drug Risk	225	60
Adverse Drug Risk	71	57
Adverse Drug Risk	126	18
	198,043	**116,604**

Nevada Medicaid

Quarterly cDUR Report

Health Plan Name: Sierra Medicaid (ACUOFNV)
Health Plan Contact: Ryan K. Bitton, PharmD, MBA
Contact Email: Ryan.Bitton@uhc.com
Report Period Start Date: 7/1/2018
Report Period End Date: 9/30/2018
Submission Date of Report: 12/3/2018

Prospective DUR

What percentage of claims denied at Point of Sale for the following DUR edits? (# denials for each edit/total # of denials)	Total Alerts	Total Alert Overrides	% Alert Overrides	Total Alert Cancels	% Alert Cancels	Total Alerts not adjudicated	% Alerts not adjudicated
Early Refill (ER)	17,386	N/A	N/A	N/A	N/A	17,386	100.00%
Therapeutic duplication (TD)	66,726	46,995	70.40%	13,008	19.50%	6,723	10.10%
Ingredient duplication (ID)	42,694	45	0.10%	46	0.10%	42,603	99.80%
Late Refill (LR)	Covered by Dose Duration services below.						
Total High Dose (HD)	Covered by Therapeutic Dose services below.						
Drug-Pregnancy (PG)	Covered by Drug-Disease Services below.						
Total Low Dose (LD)	Covered by Dose Duration services below.						
Drug-Drug (DD)	104,149	71,397	68.60%	21,387	20.50%	11,365	10.90%
Drug-Disease (MC)	185,553	155,251	83.67%	30302	16.33%	N/A	N/A
Drug-Allergy (DA)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Drug-Age (PA)	26,097	19,404	74.40%	6,693	25.60%	N/A	N/A
Therapeutic Dose Limits Screening	3,659	354	9.70%	244	6.70%	3,061	83.70%
Dose Duration	29,799	19,283	64.70%	10,516	35.30%	N/A	N/A

Top 10 Drugs by Therapeutic Problem Type - Overutilization

ER	TD	ID	LR	HD	PG	LD	DD	MC	DA	PA
ONETOUCH ULTRA BLUE	AMLODIPINE BESYLATE	ONETOUCH ULTRA BLUE	ATORVASTATIN CALCIUM	OMEPRAZOLE	BUSPIRONE HCL	COMPOUND CLAIM	ATORVASTATIN CALCIUM	GABAPENTIN	N/A	MONTELUKAST SODIUM
GABAPENTIN	LOSARTAN POTASSIUM	GABAPENTIN	METFORMIN HCL	ADDERALL XR	OXYCODONE HCL	FLUCONAZOLE	LISINOPRIL	HYDROCODONE/ACETAMINOPHEN	N/A	CLINDAMYCIN PHOSPHATE
VENTOLIN HFA	LISINOPRIL	VENTOLIN HFA	OMEPRAZOLE	DULOXETINE HCL	METRONIDAZOLE	NYSTATIN	HYDROCHLOROTHIAZIDE	ZOLPIDEM TARTRATE	N/A	IBUPROFEN
MONTELUKAST SODIUM	ALBUTEROL SULFATE	MONTELUKAST SODIUM	LISINOPRIL	ACETAMINOPHEN/CODEINE	NUVARING	ALBUTEROL SULFATE	TRAZODONE HYDROCHLORIDE	ALPRAZOLAM	N/A	CETIRIZINE HCL
HYDROCHLOROTHIAZIDE	VENTOLIN HFA	HYDROCHLOROTHIAZIDE	LEVOTHYROXINE SODIUM	AMPHETAMINE/DEXTROAMPHETAMINE	TOPIRAMATE	XULANE	FOLIC ACID	ATORVASTATIN CALCIUM	N/A	LORATADINE CHILDRENS
LISINOPRIL	HYDROCHLOROTHIAZIDE	LISINOPRIL	MONTELUKAST SODIUM	SUBOXONE	NORTRIPTYLINE HCL	NORETHINDRONE ACETATE/ETHINYL ESTRADIOL	GABAPENTIN	VENTOLIN HFA	N/A	RANITIDINE HCL
DULOXETINE HCL	METOPROLOL TARTRATE	DULOXETINE HCL	PANTOPRAZOLE SODIUM	OXYCODONE/ACETAMINOPHEN	GABAPENTIN	VITAMIN D3	AMLODIPINE BESYLATE	FLUTICASONE PROPIONATE	N/A	ONDANSETRON ODT
OXYCODONE/ACETAMINOPHEN	GABAPENTIN	OXYCODONE/ACETAMINOPHEN	GABAPENTIN	ESOMEPRAZOLE MAGNESIUM	ZIPRASIDONE HCL	ONDANSETRON ODT	BUSPIRONE HCL	PREDNISONE	N/A	AZITHROMYCIN
AMLODIPINE BESYLATE	CARVEDILOL	METFORMIN HCL	AMLODIPINE BESYLATE	PANTOPRAZOLE SODIUM	BUTALBITAL/ACETAMINOPHEN/CAFFEINE	PHENAZOPYRIDINE HCL	SIMVASTATIN	MONTELUKAST SODIUM	N/A	POLYMYXIN B SULFATE/TRIMETHOPRIM SULFATE
METFORMIN HCL	LEVOTHYROXINE SODIUM	ATORVASTATIN CALCIUM	LOSARTAN POTASSIUM	METHYLPHENIDATE HYDROCHLORIDE	BUPROPION HCL XL	MONTELUKAST SODIUM	LEVOTHYROXINE SODIUM	LEVOTHYROXINE SODIUM	N/A	BUDESONIDE

C-DUR Q3 2018

Silversummit Healthplan

Count of CLAIM PAID/REJECTED	July	August	September	Grand Total
Apparent Drug Misuse	**867**	**823**	**761**	**2,451**
Paid	736	696	636	2,068
Rejected	66	51	47	164
Reversal	65	76	78	219
Buprenorphine with Opioid	**5**	**9**	**9**	**23**
Rejected	5	9	9	23
Cumulative APAP Check	**11**	**9**	**14**	**34**
Paid	3	2	4	9
Rejected	183	6	10	199
Cumulative Morphine Equivalent Dose	**186**	**179**	**143**	**508**
Paid	3	4	7	14
Rejected	183	175	136	494
Reversal	0	0	0	0
Drug-Age Precaution	**1**	**4**	**4**	**9**
Paid	1	4	4	9
Rejected	0	0	0	0
Reversal	0	0	0	0
Drug-Disease Precaution	**673**	**642**	**750**	**2,065**
Paid	478	484	611	1,573
Rejected	104	97	65	266
Reversal	91	61	74	226
Drug-Drug Interaction	**1,709**	**1,726**	**1,736**	**5,171**
Paid	1,227	1,238	1,274	3,739
Rejected	254	283	278	815
Reversal	228	205	184	617
Drug-Gender Alert	0	0	**0**	**0**
Rejected	0	0	0	0
Drug-Pregnancy Alert	**34**	**34**	**44**	**112**
Paid	26	25	27	78
Rejected	3	2	5	10
Reversal	5	7	12	24
Excessive Duration Alert	**621**	**687**	**614**	**1,922**
Paid	453	485	439	1,377
Rejected	80	97	61	238
Reversal	88	105	84	277
High Dose Alert	**419**	**526**	**525**	**1,470**
Paid	252	346	325	923
Rejected	89	64	56	209

Reversal	78	116	144	338
Ingredient Duplication	**2,731**	**2,991**	**2,880**	**8,602**
Paid	0	0	0	0
Rejected	2,731	2,991	2,880	8,602
Reversal	0	0	0	0
Low Dose Alert	**1,460**	**1,497**	**1,381**	**4,338**
Paid	1,029	1,033	984	3,046
Rejected	200	209	183	592
Reversal	231	255	214	700
Refill too Soon	**4,060**	**4,344**	**4,127**	**12,531**
Rejected	4,060	4,344	4,127	12,531
Therapeutic Duplication	**4,650**	**5,018**	**4,809**	**14,477**
Paid	1,508	1,598	1,474	4,580
Rejected	2,777	3,047	2,972	8,796
Reversal	365	373	363	1,101
Underuse Precaution	**2,954**	**3,110**	**3,130**	**9,194**
Paid	2,254	2,411	2,466	7,131
Rejected	258	215	214	687
Reversal	442	484	450	1,376
(blank)				
(blank)				
Grand Total	**13,209**	**13,885**	**13,501**	**40,595**

Retro-Drug Utilization Review

July 1, 2018 - September 30, 2018 (Q3)

Fee for Service Medicaid

Retrospective DUR								
MONTH	**TOPIC**	**DESCRIPTION OF INTERVENTION**	**TYPE OF CONTACT (MEDIA)**	**NUMBER OF CONTACTS**	**NUMBER OF RESPONSES**	**RESPONSE RATE**	**PROVIDER TARGETED (e.g. PHYSICIAN, PHARMACIST)**	**PERFORMED BY (e.g. SUBCONTRACTOR NAME)**
JULY								
AUGUST	Hepatitis C Tx Follow-up	Physician Letter	Letter	28	5	18%	Physician	OptumRx
SEPTEMBER	Buprenorphine/Opioid Combo	Physician Letter	Letter	0*	0	0	Physician	OptumRx
OCTOBER	COPD Compliance	Physician Letter	Letter	15	Pending Responses		Physician	OptumRx
NOVEMBER								
DECEMBER								
JANUARY								
FEBRUARY								
MARCH								
APRIL								
MAY								
JUNE								

* September's initiative - 68 member profiles were reviewed as having Suboxone or Zubsolv in addtion to opioid(s). Two members were identified as meeting the overlap criteria.

Anthem Nevada

July 1, 2018-Sept 30, 2018

Retrospective DUR 3 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	15	TBD	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	TBD	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	3	TBD	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	112	TBD	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	73	TBD	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	1368	TBD	Physician	Internal (Member Management Analytics/RHI)
Oral Diabetes	Identifies members on oral diabetes medications with an MPR of less than 80%	Fax/Mailing	595	TBD	Physician	Internal (Member Management Analytics/RHI)
Statins	Identifies members on Statin medication with an MPR of less than 80%	Fax/mailing	611	TBD	Physician	Internal (Member Management Analytics/RHI)
Asthma	Identifies members on asthma controller medications with an MPR less than 75%	Fax/mailing	615	TBD	Physician	Internal (Member Management Analytics/RHI)
COPD	Identifies members on a COPD medication with an MPR of less than 80%.	Fax/Mailing	23	TBD	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	121	TBD	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	672	TBD	Physician	Internal (Member Management Analytics/RHI)

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)**

Anthem Nevada Jan 1, 2018 to March 31, 2018

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**	**37**	**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**	**9**	**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**	**15**	**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**	**0**	**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**	**16**	**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**	**56**	**Physician**	**Internal (Member Management Analytics/RHI)**

**Some Programs were turned off due to NV rebranding and program maintenance*

Updates were supplied to the Positive Outcomes for Q 1 2018 on 12/12/2018.

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)

Nevada Medicaid

Quarterly Retro - DUR Report

Health Plan Name: Sierra Medicaid (ACUOFNV)
Health Plan Contact: Ryan K. Bitton, PharmD, MBA
Contact Email: Ryan.Bitton@uhc.com
Report Period Start Date: 7/1/2018
Report Period End Date: 9/30/2018
Submission Date of Report: 12/3/2018

Retrospective DUR

PERIOD	TOPIC	DESCRIPTION OF INTERVENTION	TYPE OF CONTACT (MEDIA)	NUMBER OF CONTACTS (Number of Contacts Evaluated YTD)	NUMBER OF RESPONSES (From Contacts Evaluated YTD)	RESPONSE RATE	PROVIDER TARGETED (e.g. PHYSICIAN, PHARMACIST)	PERFORMED BY (e.g. SUBCONTRACTOR NAME)
1/1/18 to 9/30/18	Dose Per Day	This is a provider-targeted program designed to enhance provider awareness of appropriate medication dose and duration use based on approved prescribing information.	Fax/Mail	8 (1)	1	100.00%	Prescriber	OptumRx
1/1/18 to 9/30/18	Drug-Age Interaction	This is a provider-targeted program designed to minimize the occurrence of potentially inappropriate medications (PIMs) in the geriatric (65 years and older) and pediatric (less than 18 years) population.	Fax/Mail	109 (44)	11	25.00%	Prescriber	OptumRx
1/1/18 to 9/30/18	Drug-Disease Interaction	This is a provider-targeted program designed to minimize the occurrence of clinically significant, patient-specific drug-disease interactions.	Fax/Mail	961 (561)	77	13.73%	Prescriber	OptumRx

Nevada Medicaid

Quarterly Retro - DUR Report

Health Plan Name: Sierra Medicaid (ACUOFNV)
Health Plan Contact: Ryan K. Bitton, PharmD, MBA
Contact Email: Ryan.Bitton@uhc.com
Report Period Start Date: 7/1/2018
Report Period End Date: 9/30/2018
Submission Date of Report: 12/3/2018

Retrospective DUR

PERIOD	TOPIC	DESCRIPTION OF INTERVENTION	TYPE OF CONTACT (MEDIA)	NUMBER OF CONTACTS (Number of Contacts Evaluated YTD)	NUMBER OF RESPONSES (From Contacts Evaluated YTD)	RESPONSE RATE	PROVIDER TARGETED (e.g. PHYSICIAN, PHARMACIST)	PERFORMED BY (e.g. SUBCONTRACTOR NAME)
1/1/18 to 9/30/18	Drug-Drug Interaction	This is a provider-targeted program designed to minimize the occurrence of clinically significant, patient-specific drug-drug interactions.	Fax/Mail	6686 (3676)	935	25.44%	Prescriber	OptumRx
1/1/18 to 9/30/18	Duplicate Therapy	This is a provider-targeted program designed to promote awareness of Therapeutic duplication concerns.	Fax/Mail	4108 (2428)	461	18.99%	Prescriber	OptumRx
1/1/18 to 9/30/18	Gaps in Care Asthma	To optimize the use of long-term controller medications (LTCMs) as recommended by current guidelines, promote the appropriate use of short-acting beta-agonists (SABAs), and provide asthma management education to members and their providers.	Fax/Mail	6863 (3689)	336	9.11%	Prescriber	OptumRx

Nevada Medicaid

Quarterly Retro - DUR Report

Health Plan Name: Sierra Medicaid (ACUOFNV)
Health Plan Contact: Ryan K. Bitton, PharmD, MBA
Contact Email: Ryan.Bitton@uhc.com
Report Period Start Date: 7/1/2018
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Retrospective DUR

PERIOD	TOPIC	DESCRIPTION OF INTERVENTION	TYPE OF CONTACT (MEDIA)	NUMBER OF CONTACTS (Number of Contacts Evaluated YTD)	NUMBER OF RESPONSES (From Contacts Evaluated YTD)	RESPONSE RATE	PROVIDER TARGETED (e.g. PHYSICIAN, PHARMACIST)	PERFORMED BY (e.g. SUBCONTRACTOR NAME)
1/1/18 to 9/30/18	Overutilization_Days Supply	This is a provider-targeted program designed to enhance provider awareness of appropriate medication dose and duration use based on approved prescribing information.	Fax/Mail	2203 (1298)	82	6.32%	Prescriber	OptumRx
1/1/18 to 9/30/18	Narcotic Drug Utilization Program	This is a provider-targeted program designed to minimize the occurrence of drug abuse, diversion, and inappropriate use in members utilizing high-risk medications.	Fax/Mail	1214 (1255)	752	59.92%	Prescriber	OptumRx

Retro DUR Q3- 2018

Silversummit Healthplan

	Jul-18	Aug-18	Sep-18
Retrospective Drug Utilization Review (Retro DUR)			
Drug-Use Reports			
Report Name	**Members Identified**	**Members Identified**	**Members Identified**
Therapeutic Duplication	20	20	23
Medication Dose In Elderly	0	0	0
Medication Duration In Elderly	0	0	1
Drug Drug Interaction	504	540	519