Nevada Medicaid Drug Use Review Board Meeting

April 25, 2019

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STEVE SISOLAK
Governor

RICHARD WHITLEY, MS
Director

SUZANNE BIERMAN, JD, MPH
Administrator

DEPARTMENT OF HEALTH AND HUMAN SERVICES
DIVISION OF HEALTH CARE FINANCING AND POLICY
1100 East William Street, Suite 101
Carson City, Nevada 89701
Telephone (775) 684-3676 • Fax (775) 687-3893
http://dhcfp.nv.gov

REVISED NOTICE OF PUBLIC MEETING – DRUG USE REVIEW BOARD

Date of Posting:	March 12, 2019
Date of Revision:	**March 12, 2019**
Date of Meeting:	April 25 ~~28~~, 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:	Grand Sierra Resort and Casino 2500 E. Second Street Reno, Nevada 89595 Phone: (775) 789-2000
Webinar Registration	https://optum.webex.com/optum/onstage/g.php?MTID= e424661217ffff414c07466690b559cbb 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:	643 317 038 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.

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For Audio Only:

Phone: (763) 957-6300
Event: 643 317 038

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 January 24, 2019

b. Status Update by the DHCFP

4. Clinical Presentations

a. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for Substance Abuse 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 updated prior authorization criteria and/or quantity limits for agents used for the treatment of Attention Deficit Disorder (ADD)/Attention Deficit Hyperactivity Disorder (ADHD)

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 Androgen/Testosterone replacement 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.

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

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. 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.

b. Top claims for member under 18 years-old

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 Q3 2018 and Q4 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 Q4 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.

Summary of the DUR Board

Drug Use Review Board

The Drug Use Review Board (DUR) is a requirement of the Social Security Act, Section 1927 and operates in accordance with Nevada Medicaid Services Manual, Chapter 1200 – Prescribed Drugs and Nevada Medicaid Operations Manual Chapter 200.

The DUR Board consists of no less than five members and no more than ten members appointed by the State Director of Health and Human Resources. Members must be licensed to practice in the State of Nevada and either an actively practicing physician or an actively practicing pharmacist.

The DUR Board meets quarterly to monitor drugs for:

- therapeutic appropriateness,
- over or under-utilization,
- therapeutic duplications,
- drug-disease contraindications
- quality care

The DUR Board does this by establishing prior authorization and quantity limits to certain drugs/drug classes based on utilization data, experience, and testimony presented at the DUR Board meetings. This includes retrospective evaluation of interventions, and prospective drug review that is done electronically for each prescription filled at the Point of Sale (POS).

Meetings are held quarterly and are open to the public. Anyone wishing to address the DUR Board may do so. Public comment is limited to five minutes per speaker/organization (due to time constraints). Anyone presenting documents for consideration must provide sufficient copies for each board member and a copy (electronic preferred) for the official record.

The mission of the Nevada DUR Board is to work with the agency to improve medication utilization in patients covered by Medicaid. The primary goal of drug utilization review is to enhance and improve the quality of pharmaceutical care and patient outcomes by encouraging optimal drug use.

Current Board Members:

Paul Oesterman, Pharm D, Chair

Dave England, Pharm D

James Marx, MD

Michael Owens, MD

Marta Bunuel, MD

Jennifer Wheeler, PharmD

Netochi Adeolokun, PharmD

Drug Use Review (DUR) Board Meeting Schedule for 2019

Date	Time	Location
April 25, 2019	5:15 PM	Grand Sierra Resort, Reno, NV
July 25, 2019	1:00 PM	Hyatt Place, Reno, NV
October 17, 2019	1:00 PM	Hyatt Place, Reno, NV

Web References

Medicaid Services Manual (MSM) Chapter 1200:

http://dhcfp.nv.gov/Resources/AdminSupport/Manuals/MSM/C1200/Chapter1200/

Drug Use Review Board Bylaws:

http://dhcfp.nv.gov/uploadedFiles/dhcfpnvgov/content/Boards/CPT/DUR_Bylaws_draft.pdf

Drug Use Review Board Meeting Material:

https://www.medicaid.nv.gov/providers/rx/dur/DURBoard.aspx

Social Security Act, 1927:

https://www.ssa.gov/OP_Home/ssact/title19/1927.htm

Meeting Minutes

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DRUG USE REVIEW BOARD

Meeting Minutes

Date of Meeting: **Thursday, 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

ATTENDEES

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

Board Member Absent
Marta Bunuel, MD
Yvette Kaunismaki, MD

DHCFP
Holly Long, Social Services Program Specialist
Beth Slamowitz, Pharm.D.
Andolyn Johnson, Deputy Attorney General

OptumRx
Carl Jeffery, Pharm.D.

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

Public
Bob Belaski, Actelion
Larry Hurst, Ferrari PA
Sandy Sierawski, Pfizer
Jennifer Lauper, BMS
Kevin Schreur, United Therapeutics
Amy Rodenburg, Allergan
Karen Einbinder
Kelly Hollenack
Kirsten Coulombe, DHCFP

Public Online:
Tony Wang, BMS
Lori Howarth, Bayer
Melissa Sommers, Novartis
Ashley Cruz
Jennifer Solis

AGENDA

1. Call to Order and Roll Call

Meeting called to order.
Roll Call
Holly Long
Beth Slamowitz
Camilla Hauck
David England
Carl Jeffery
James Marx
Paul Oesterman
Andolyn Johnson
Netochi Adeolokun
Jennifer Wheeler
Ryan Bitton
Thomas Beranek
Jeannine Murray
Lisa Todd

2. Public Comment on Any Matter on the Agenda

Kevin Murphy: I am Kevin Murphy, an infectious disease physician here in Reno and also a medical consultant in Washoe County Rehab Health District and (indiscernible) of the Public Commission of Washoe County Medical Society. Catherine O'Mara, the Executive Director of Nevada State Medical Association, has asked me to speak today to our opposition to the proposed antibiotic authorization plan that has been put out by the Department of Health and Human Services. We agree strongly, in fact, that the rising rates of carbipenem resistant enterobacterial, beta-lactamase producers, EFC organisms, multidrug resistant, acenitobacter, pseudomonas and MRSA, VRA and so on are important and need to be addressed in ways much more comprehensive and effective than they have been to date. We believe that the requirement for outpatient antibiotic preauthorization does not achieve that goal and is likely to be very disruptive of patient care. We do believe in antibiotic stewardship, but a comprehensive program of antibiotics stewardship. At the end of my comments I'd like to suggest some things that might be more appropriate. We are concerned that requiring preauthorization does not take into account the clinical challenges the physicians face in seeing the patient in the outpatient arena, or having to distinguish between viral infections and bacterial infections, syndromes that have no clarity that require a decision and perhaps things that are not infections at all. So, the policy of preauthorization, it seems to us, fails that test. I gather that in part the authorization is intended to be culture-based but most of the time at first meeting, we don't have a culture and in fact won't have a culture for 48 or, in an outpatient arena, maybe 72 hours. If your patients are sick enough, they require treatment especially in the case of pneumonia, urinary tract infections, cellulitis and the objective of the outpatient physician or nurse practitioner or P.A. need to keep this patient out of the hospital to prevent the hospitalizations to prevent sepsis and I think we all realize the importance of fighting sepsis, preventing sepsis, I think, is even more important. The antibiotic choice is to be staged; an antibiotic now that bests fits the clinical syndrome and a change in antibiotic in 48-72 hours based on culture if the culture is helpful and of course often times in cases of pneumonia, the culture is either not obtainable or not helpful. On the respiratory (indiscernible). As I understand it, the department has indicated their goal is to have a four hour turnaround time on authorization or denial 24/7. We're a little skeptical that that is possible; that's going to be very extensive first of all, it's going to require money, and we've heard nothing about funding it in order to support such a program and if such funding were available, there are some other ways that the money might be better spent. We're concerned about the delay that that's going to cause. Where is the patient supposed to be while waiting this four hours and if the clinic closes at 8:00, obviously we're talking about a delay of a day, not just four hours. Now, the other thing is it compromises the ability of the physician to see the next patient it potentially decreases efficiency of the (indiscernible) has been waiting around for authorizations. It also adds to the other risk burden physicians already carry of administrative requirements of taking them away from face-to-face with the patient. We should not be providing physicians additional reasons to avoid taking care of Medicaid patients. I think that's a very bad idea and a very perverse incentive. Furthermore, there is a problem that physicians are going to know that emergency room physicians are exempted. Infectious

disease physicians, like me, are exempted and they're going to be tempted to send infected patients to the emergency room which is a much less efficient, much more expensive way to take care of infections. We should be able to treat in such a way we're keeping patients out of the hospital and, in fact, out of the emergency room. I think that's another perverse incentive of this proposal that has to be taken into account. A much more effective approach would be to, that is, first of all, provide physicians the tools that they need for distinguishing between viral and bacterial infections and non-infections and for dealing with those infections that have clinical priority as we have mentioned before, and by that I mean a system insurgent campaign of education through CME, Grand Rounds, and other venues. Help physicians know how to make decisions in a more cost effective way that avoids undue use of the oxazolidinones and then cephalosporins (indiscernible) comprehensive diagnosis by diagnosis. How do you make them? How do you make decisions for each of the kinds of infections or apparent infections that present in the outpatient arena? That comprehensive approach is in state Nevada CMA that I'm aware of. That should be followed, then, by surveillance for how physicians prescribe for each of those diagnosis. That information can be fed back to physicians so that they know what their way of prescribing each of several drugs or was given the diagnosis is as compared to their colleagues. We know from randomized control studies that that kind of approach changes physician behavior. For example, it can be used to reduce surgical infection rates, very, very successful. The other things that ought to be considered are that 80% of the antibiotics used in this country are for agricultural purposes, for animal growth. That's the vast majority. That should be stopped. When I see a patient with a CRE or an ESBL in the hospital, they almost inevitably have a roommate that has now been exposed. Why in the 21st century do we still have semi-private rooms? That should be penalty, and the state has, it seems to me, the power to begin a change. It might take several years of transfer but if that can be done then I think it must be done.

Paul Oesterman: I'm going to interrupt you for just a moment. I apologize, but I forgot to say we try to limit speakers to five minutes. A couple of the things you're talking about are definitely beyond the purview of this committee so if you could focus back on that, that would help.

Kevin Murphy: I think you know that the Nevada State Medical Association is firmly opposed to requiring preauthorization for outpatient antibiotics. On the other hand, we would like to be helpful in designing an alternative with review of reducing CREs, ESBLs and so on. One approach might be to form a task force of infectious disease physicians, surgeons, hospitalists, public health professionals, to take a look at how antibiotic stewardship could be practiced on state wide basis.

Paul Oesterman: Just as a side note, we do have an opening for a physician on this committee. Thank you, Dr. Murphy. For the record, Dr. Owens is with us now.

3. Administrative

a. **For Possible Action:** Review and Approve Meeting Minutes from October 18, 2018.

Motion to approve as presented. Second. Voting: Ayes across the board, the motion carries.

b. Status Update by DHCFP

Holly Long: Hi, I'm Holly Long. I am the program specialist for pharmacy with DHCFP. I do have a couple of updates. I'm going to give a quick antibiotic policy update. I do want to announce that we have been able to appoint Suzanne Bierman, she's our new administrator with DHCFP. She started on January 14th, I apologize she's not here, we invited her but she was not able to make it; she had a prior obligation. Her main office is in Las Vegas. A little background on Suzanne, she was previously at the Guinn Center in Las Vegas. She has also served as assistant director for Medicaid services for the Arkansas Department of Human Services. She has her doctorate and Masters of Public Health degrees from the University of Arkansas while working as a legislative analyst and law clerk for the University of Arkansas for medical sciences. We are all very excited for her to be joining our team and hopefully in the future she will be able to attend a DUR meeting. Just some general Medicaid policy updates that have happened recently: Revisions were made for the Chapter 900 which is over a private duty nursing. These changes will now provide private duty nursing services to be provided in the recipient's home or any setting where normal life activities occur. The requirement for medical necessity has been clarified and prior authorization requirements have been added. Revisions have also been made to Chapter 400 which is mental health, alcohol and substance abuse services. These were made to combine the treatment plan and rehabilitation treatment plan into one. There is comprehensive individualized treatment plans. Proposed policy revisions also include modifications to the treatment plan, reevaluation, progress notes and discharge planning. To provide a quick update on the antibiotic policy implementation, we do have a public workshop that is scheduled for Wednesday, January 30th, this next Thursday, at 3:00. We have the three main location meeting areas which will be Carson, Vegas and Elko and video or call conferencing between the three. All of the information including the agenda, the PowerPoint presentation, an article related to it and an antibiotic fact sheet has all been posted on the DHCFP website under public notices. If anybody needs further information on how to find that or where that is or if you need the pdf, sent by email and just let me know and I'm happy to provide that. We are still planning on going to public hearing with that policy on February 26th to read that policy in and the implementation date for that is currently scheduled for March 4th. We will see how we do with this public workshop. If any other provider communication is needed, we will still have some web announcements that will go out and I'll touch base with Dr. Murphy.

Paul Oesterman: I work with Dr. Murphy and his group quite a bit actually and I find it interesting that they are the most expansive prescribers of antimicrobial therapy.

4. Clinical Presentations

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

Carl Jeffery: There are four different guidelines in your binders. The first one is just general. It covers all oral oncology medications and then there are three that we focused

on. These are just the highest cost, so there's the Sprycel, Afinitor and Ibrance. So, they are all unique, different PA criteria. They basically all follow the same thing whereas the three specifics have all the FDA approved indications listed out and so the call center and the providers know exactly what they're looking for so they can identify those, whereas the general criteria, PA criteria, just has FDA-approved indications. That would make it the responsibility of the caller and the call center to realize that they need to look at those FDA indications themselves. Somebody raised their hand, let's see if there's a comment. Tony, did you have your hand raised? I'm sorry, can you hang on just a second? I need to adjust your volume. Okay, go ahead Tony.

Tony Wang: Hi everybody, my name is Tony Wang. Hopefully you can hear me okay. I'm with Bristol Myers Squibb. I'm one of the field medical science liaisons and part of my territory is of course Nevada. I wish I could be there in person and look forward to being there in person in the future. I just wanted to give an update. I know that one of the kinase inhibitors oncology medications in terms of the oral oncology medications, the Sprycel was mentioned and so in terms of the prior authorization, just want to make sure that all of the FDA indications were updated in terms of the documentation. It is a medication that's been around for a little bit, it is used of course in treatment of CML and probably in the documentation you have that this is indicated for newly diagnosed adults with Philadelphia chromosome-positive CML or chronic myeloid-leukemia in chronic phase, so newly diagnosed patients with chronic (indiscernible) lymphoid lasting so that there's chromosome-positive CML with resistance or intolerance to prior therapy including (indiscernible) and also quality indication of Philadelphia chromosome-positive CML with resistance or intolerance to prior therapy and then two new indications which I wanted to make sure that was on everybody's radar was that there are two newer pediatric indications and hopefully that will be in the documentation in terms of the FDA approved indications so it is approved for pediatric patients one year of age and older with Philadelphia chromosome-positive CML in chronic phase and then the newest indication for pediatric patients one year of age and older with newly diagnosed Philadelphia chromosome-positive ALL in combination with (indiscernible) So, those are all the indications that I just wanted to make sure that the two newer pediatric indications which are from the last year, year and a half.

Carl Jeffery: The Sprycel that he's referring to starts on Page 51 in your binder.

David England: If that's an FDA indication, why do we need to have a specific other discussion about that?

Carl Jeffery: Tony, I will unmute you. I guess there's a question. Did you get a chance to review the criteria that was presented in the binder?

Tony Wang: This is Tony, I'm sorry. That's the criteria we see right now.

Carl Jeffery: Yeah, so it starts on Page 52 of the binder that was available.

Tony Wang: I'm looking at it right now.

Beth Slamowitz: David, are you asking specifically on the Sprycel or are you asking why we have criteria for oral oncology if FDA approved indications. And then we have three items that are pulled out.

Holly Long: So Carl, I think that question is for you.

Carl Jeffery: So you want to know why we have the separate criteria for the three?

David England: I mean, I can see why but as I was reading his question, he was talking about something specifically, but if we are already saying we are covered for FDA indications and that's an FDA indication. That kind of answers the question, it appears to me.

Paul Oesterman: I think it is more difficult for me, too.

Carl Jeffery: There was some initial direction to have the specific criteria established for these and then I think it just makes it easier when you get into these specific agents, they are so defined on what they are approved for. The indications on here are three sentences long so it just makes that easier for the call center and for the providers to know what exactly is on there. They just make it for simplicity sake but I see your point, too. It's like, why not just have the one all oral oncology drug form and use that one.

David England: Some of those there are some specifics you have to deal with as far as if there are other alternatives, the alternatives have to be used before we go to this first line but if we're following those guidelines, it kind of covers it anyway.

Carl Jeffery: Right.

Jeannine Murray: I know that sometimes the reason why there's special specificity in the criteria is because when the reviewer is reviewing it and you do have maybe nuances between the drugs, it helps to prompt the prescriber to submit that information so that that review can be a little bit faster instead of having to reach back out to the prescriber for more information it can delay PA approval. I think sometimes there's a reason why there's more.

James Marx: Prior authorization criteria is just becoming a major, major bottleneck in practice and I wonder if it isn't more practical just to say please limit these particular drugs to a board-certified oncologist and just let it go at that and let them be on the hook for it. It's easy to say, well, I'll just do a prior authorization. That's just a couple hours so I mean we are really, really under the gun right now and I'm working harder now than I was 20 years ago because I'm spending time doing – sometimes two days a week, I spend three days a week on prior authorization, pharmacy benefit managers and insurance companies. It's really becoming an issue and I think there's going to be some legislative action at least proposed for this for the state of Nevada. I think that limit to accredited providers is all you need to do and let them be on the hook for it.

Carl Jeffery: I think what's commonly seen, especially when you get into the oncology realm, is that if you're not limiting the use to only FDA approved indications, there are a lot of oncologists who, I think they are making some educated guesses saying this will probably work on this. So, they're using agents that are not FDA approved indications and they're not shown to be safe and effective in their literature.

James Marx: So they're really engaging in malpractice and there are ways of dealing with malpractice that are outside judicial but I think you have to give them some sort of leeway. It's becoming very, very obtrusive.

David England: Especially in a chemo realm. In some places I've worked at, I've had arguments with the oncologist, in fact, who say we're trying to distinguish between the art of medicine and the practice of medicine. In some cases, there is an art to it but at the same time, there is also best practices with a pathway you need to go down and once you've exhausted those, then you're into research and that's a whole other ballgame unless you have peer-reviewed journals that allow such things. Therefore, that's where it's a gray area. If its FDA approved and it's the oncologist prescribing it, what do we need a P.A. for? It's when they start getting more into the art rather than the best practices, there's going to be trouble with that.

James Marx: So much of the research is pharma-driven biased. I think we can already see many, many instances of this evidence-based medicine being heavily tilted in the directions that really aren't evidence-based and they are really financially based and based upon the tremendous amount of cost and developing these drugs, getting them to NDA's and so forth. I'm not so sure that we're really doing such a good job and maybe putting more responsibility on the physicians who may have more skin to game than pharma who really, their only option is to sell the drug.

Beth Slamowitz: I think some of the concern too from Medicaid standpoint is that a lot of these oncology drugs that are coming out in a fast and furious rate that the FDA is fast-tracking on studies that have minimal evidence of effectiveness and when you are taking somebody who has cancer, especially when you're talking a pediatric population and a lot of these drugs have specific biomarkers and they're very specific for treatment and for what they're FDA approved for. What we're seeing is that at times, it's a bit of a hail Mary, sometimes by these oncologists and trying to treat the patient with whatever they can possibly do to be effective. From a utilization standpoint and yes, of course, there is a cost issue involved because as these drugs are fast-tracked and hitting the market, they are not cheap, especially the ones that are some of the gene therapies and some of the things that have the biomarkers. There are the tests that are involved on top of the treatment to make sure that they're appropriate. So, I think it's more a concern of appropriateness of use and effectiveness.

Paul Oesterman: If physicians wish to use a product beyond the FDA or recognized compendia of medically accepted indications, they can always do a compassionate care

program as an investigation file and then it should be provided by the drug manufacturers to the provider and/or patient as new drugs.

Beth Slamowitz: Especially for Medicaid since we are held to the social security act and we are required to only be paying for those medications that are FDA approved, we have certain restrictions that perhaps other payers don't.

Paul Oesterman: I would like to propose that maybe simplify this process and go with what I'm hearing and that with prior authorization guidelines for the blanket for oral oncology medications that the patient have the diagnosis, that's indicated by #1 in the bullet point and that is prescribed by or in consultation with an oncologist or hematologist and limit it to those two, that's it. Make it easy and try and not put up barriers for the practitioners and make it easier for the call center.

A motion is made to accept and seconded.

Ryan Bitton: So basically appropriate indication for FDA and by an appropriate prescriber. I think for the most part under care criteria oncology is based on that. FDA and then appropriate prescribers so I think that the beginning of it was a lot of these may look like that but we're just building them out, because it's difficult to go to NCCN every time.

Carl Jeffery: Right. Our criteria that we put together for the other three specific agents is just FDA approved indications and oncologist or hematologists.

Jeannine Murray: We don't have an overall policy. We have individual drug policies that we then label so we'll still maintain those but they may need the NCCN diagnosis and everything they ask for.

Paul Oesterman: All those in favor of the simplified prior authorization guidelines for oral oncology medications, please indicate by saying Aye. All opposed say nay. Motion carried.

Motion approved.

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

Carl Jeffery: This is something we've been talking about for years. On page 86, the P.A. criteria starts and it's a short-acting bronchodilators we're starting with and so that's your Proventil, the ProAir and the Ventolin. There's a couple new dosage forms that are coming out in the future but basically just limit it to 2 units per month. Anything that exceeds that would require prior authorization. So, there would be the diagnosis of asthma, they would have to have what's causing the asthma through external causes. They've been trained on the appropriate use of their inhaler and they're receiving either maximally tolerated long-acting treatment or is contraindicated for some reason. There is an exception in there for if they're under 18 and you need a second one for school.

Paul Oesterman: Just to clarify, the one for the exception for school would be a third one, correct? They can get two but –

Carl Jeffery: It would be for a third one, right. Yeah.

Paul Oesterman: Our managed care organizations have mixed comments on this. We'll start off with Anthem.

Jeannine Murray: I have a problem with the policy comment about it, which is that we have preferred products in there so our policy would be the same but it would say this drug is preferred before this drug. That was the only thing I was commenting on.

Carl Jeffery: That brings up a good point, fee-for service has prior authorization for non-preferred as well that would be separate.

Jeannine Murray: I just wanted to call that out.

Paul Oesterman: SilverSummit is okay with this and HPN.

Ryan Bitton: I have the same feelings. We have preferred products as well so we have the same comment. My comment here was we have a formulary too. I think the quantity limit is appropriate.

Paul Oesterman: This prior authorization guideline is for the short-acting bronchodilators and in essence is a quantity limit. Is there a motion and a second to approve the criteria as presented?

Jennifer Wheeler: Can I ask a question? Is that per 28 days or 30 days? I only ask that because I recently got an audit. I ran it for 30 days instead of the 28.

Beth Slamowitz: I believe Medicaid's maximums are 31 days or 5, or something like that.

Carl Jeffery: It says 34 days.

Beth Slamowitz: I think it would depend on the inhaler and how many metered doses it is and what advisors, how much would even do it.

Jennifer Wheeler: So would you fill it in, if it were a 24 day supply, would you bump it out to a 30 or 34?

Beth Slamowitz: I would fill it for exactly what it is so that way if they need it more often, they'll be able to get it within that timeframe.

Carl Jeffery: So, if they're getting two inhalers and they're blowing through two inhalers in 24 days, that's going to stop for PA.

James Marx: Why does it say for 30 days?

Carl Jeffery: It just says per month and so I think she just wanted to clarify it because all we have is the criteria that says per month, so clarification on there. Because there are some months that are –

James Marx: Are you using 24 days in a month?

Carl Jeffery: Yeah.

Paul Oesterman: We have a motion and a second to approve.

Motion to accept the criteria as presented. Seconded.

Paul Oesterman: Any further question or discussion? All those in favor, please indicate so by saying Aye to approve the guideline that's presented. All opposed say Nay.

Motion carried.

James Marx: When did these stop being $5 drugs? I remember back in the day, these were like $4 a piece. Now they're $50 or something like that?

Carl Jeffery: Montreal protocol.

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

Paul Oesterman: We have some utilization and clinical information. Carl, do you want to go ahead.

Holly Long: I just wanted remind everyone too that this was just approved, was this the July meeting?

Carl Jeffery: The board discussed this and approved the initial criteria in July and it is set to be implemented the 4th of February. We're bringing it back to the board because as you may recall, the board decided on a $200 limit so anything that exceeds $200 would require prior authorization. So, we're bringing it back to the board to have you discuss no limit so they would all, regardless of the cost – so if it's $3 it's going to require prior authorization. That's the proposal of the board to require prior authorization on all of them and I think there's some concern and I'll let Beth give more detail. She went to a conference about it but I think there was some concern that these aren't FDA approved. They're mimicking some commercial products that probably are borderline legal and I'm sure I'm missing something.

Beth Slamowitz: No, you're right on point. I went to a conference in Washington D.C. at the FDA and the conference was in regards to guidance that the FDA is putting out and has

put out. They finalized their guidance less than a month ago regarding compounds and compounding pharmacies and compounding medications. There is a lot of concern about safety and quality with these products and also a lot of fraud and abuse within the same area. So the original request and with the $200 limit, I think part of what we noticed, too, was that the majority of our compounding claims are less than $200 so really nothing is going to hit that prior auth. If anything, for us this is more of a safety concern than anything. They are not FDA approved, so that in itself is an issue for us and a lot of other states that were there and a few Medicaid programs some of them don't even cover compounds because of that particular point. There was a lot of discussion around some of the hormone compounds that occur and how they'll change them by a $1/10^{th}$ of a percent so that it can be considered a compound even though there's commercially available product. There is some concern from the FDA perspective that it does hinder production and research of new drugs and so more or less from a safety perspective, it just felt more appropriate to require prior auth on any compound to make sure that they are, one, coming from a compounding pharmacy and appropriate place and that the products that are being used in the compound are FDA approved and that it is something that the patient could be getting from a commercial perspective rather than having the risk of it being compounded into a product but at the same time not wanting to restrict access to care and to those patients that definitely need it. Make sure that that's part of our criteria as well that if it's a certain dosage for them or if it's a child who needs a liquid or an ointment or something along those lines, to make sure that we're allowing that access as well.

Paul Oesterman: I guess from a (indiscernible) perspective, are we finding some of the issues with the cosmetic type products more than the, say something like magic mouthwash which is a compound but has a medical indication.

Beth Slamowitz: Yeah, some of the topical pain ointments. I'll say that a lot of what we see are the hormones, the ointments and creams and things like that that are kind of skirted around. Some of the concerns that were brought up at the conference as well were doctors who are compounding within their office and, again, not having either sterile procedures or using appropriate products or FDA approved products or trying to have some type of cosmetic type of business on the side and then charging Medicaid or the plans for those types of things. I think it's kind of just a stop-gap or a way for us to make sure that these are being given to patients in a safe manner.

Carl Jeffery: You can see on page 128, there's our utilization numbers and we have the top 3 are the Diclofenac is commercially available, the Doxapin is FDA approved for topical cream and I'm not sure why they're covering that and then there's lidocaine powder. All of those top… We get a little bit of a pass because the manufacturers who make a lot of the compounding ingredients like PCCA, Letco, they don't participate in federal drug rebate programs so Medicaid doesn't reimburse for those so we get a little bit of pass. There's a lot of other ones in here that they do use.

James Marx: I'm really concerned about these compounded drugs. This is getting to be really ridiculous. I think gabapentin, Diclofenac gel you can buy on Amazon Europe 3 ounces for 30 bucks, so here it's 3800 so I mean, there's a lot of room for abuse. I mean,

I'm constantly barraged by people promoting all kinds of Gabapentin. It's pretty much everything else compounded. We don't know about safety, but we don't even have any idea about efficacy and we're approving all these things just smeared on and I think probably most of them are just very expensive placebos. If there's anything to do to kind of temper this I think would be positive until there's some sort of logical or rational way of evaluating these things.

Holly Long: Originally when I had brought this up in July, I had offered all that information with the dollar amount trying to find some way that we could look at it to be able to put the PA on it, and I provided the information to other states that they were doing, but they were doing the 500-dollar limit and they were gradually having to decrease it because the fraudulent activities, and this has definitely been the way since July, the other states are getting rid of the price, they're getting rid of the threshold for the amount, and they're just putting a PA on everything or they're making the decision that they're not going to be going with them. Hopefully the PA on all of them requiring that medical necessity again, safety for the recipients, would be helpful.

James Marx: This is one area where we need to do more prior authorization, not less, because I think it's really airing some potential abuse fraud and anything else you can imagine to that.

David England: And states where the compound is built, a lot of times the law will make the distinction between sterile compounds and non-sterile compounds, and even though these are nonsterile compounds, I've had some requests sometimes to put some real strange concoctions together and we've gone to try to do alerts, are these compatible? You can't find it. So how can we do this; how can we justify 2, 3, or 4 ingredients if there isn't a standard to go back to the pair. I mean I have to get out my organic chemistry and other handbooks. I mean, are these compatible? Are these isotonic? I mean, what is the deal with this. It's just too much of a hassle to go through. The discussion we had earlier where we wanted to decrease the use of the PAs, my thought would be to put all these on a PA, but the only PA that we approved was something that there's some therapeutic purpose for and there's an official compendium recipe that you can use in NF or USP somewhere, that's acceptable but these other concoctions, there's nothing to support them other than I tried it and it worked.

Paul Oesterman: And if there's something already commercially available, why is there a need compound.

David England: Take the commercial and dilute it with whatever compound. I think I agree with Dr. Marx on this. Put the PA on everything and then it's going to have to come down to there has to be a compendium mark somehow; how to compound it, not just we can and therefore we did kind of thing.

Paul Oesterman: We have a number of criteria here. One of the things that was in here, bullet point number 8 on page 114, that's a pharmacy compounding medication has

received the appropriate certification for the dosage form being compound. What about those physicians who are running a dermatology mill or hormone replacement therapy.

Carl Jeffery: Number 9 applies, compounding will not be done in a physician's office.

Lisa Todd: Another thing to consider also when I was looking at the ingredients for like the top 25 ingredients, a lot of those were powders and those are not considered drugs; they are covered outpatient drugs. So you could also help just take those off the formulary and make those NDC not covered because they're not rebatable, the powders aren't, so you can do that. The only other consideration, maybe like the captopril suspensions and I don't remember what that criteria was like in age, but drive it through the formulary, don't cover some powders. If they're going to make something out of gabapentin, they could use the capsule right? They can filter it out.

David England: There's recipes for those and concoctions for peds and neonates. Some of this other stuff is like…

Lisa Todd: So that's what I'm concerned about.

Carl Jeffery: We have to make it for ease of administration right now.

Beth Slamowitz: I think my only concern with that, while I agree we don't want to limit access for the kids but from a safety perspective, if that's why we're truly looking at this, that would be a population I would be most concerned about, is making from the pharmacy something that's appropriate and not something that's just being concocted, mixed randomly, or used products that aren't FDA approved. We do have some criteria for different dosage forms, it's something that they require in a liquid versus a powder.

Lisa Todd: I was just thinking that there was, if you wanted to work about not stopping for children, so we want to discharge the baby from the hospital, going home, they need that solution specially made. It's just a thought. I'm not arguing it.

Beth Slamowitz: I mean, if it's a matter of crushing a pill and giving some way to give to the child….

Jeannine Murray: First omeprazole, or first whatever, that's not FDA approved right? So we would reject if it's not covered and then try to instruct mom on how to get that down a G-tube or whatever she needs to do with that.

Beth Slamowitz: From a retail perspective, I don't know how many have those conversations.

Beth Slamowitz: As an alternative, it does take some education for mom and dad. There's more options than there have been in the past as far as dosage forms and availability for children.

James Marx: If the compound is for ease of administration, that's different than some sort of new application like topicals so I think if it's indications for infant administration purposes, that should be a buy, that should pass right through. If it's for applying to somebody's heel, it's a totally different deal.

David England: Nine times out of ten, there is a recipe how to do that somehow, Micromedex or NF, there's always something available to do it on as opposed to I'm just going to wing it.

Lisa Todd: Can you check the pH balance on that nasal spray?

Paul Oesterman: So we have this criteria in front of us and sounds to me from what I'm hearing is we are waiving the need for prior authorization for orally administered medications for kiddos with age cut off to be determined and then prior authorization would be required for everything else.

Holly Long: Carl, would there be a way to look at the utilization, what age would be good, that we could stick in there.

Carl Jeffery: I could certainly pull that for the next meeting.

Beth Slamowitz: I think it would be cautious as far as putting an age limit on it as there are other reasons besides age, it has to be something in a different dosage form or (multiple speakers).

Paul Oesterman: But then they can get the prior authorization if needed.

Holly Long: We can look at that as more of a case-by-case basis. That would be the question and between Carl and I being involved in hearing prep meetings and with monitoring prior authorizations, if that seems to be an issue that we are limiting in any way of specific authorization, then we can bring it back to the board to change that.

Paul Oesterman: Can we pick an age at this point to….

David England: Since it's administration only…it could be elderly, do we really want to do that?

Paul Oesterman: Let's go through each of these 9 points on this proposed prior authorization criteria and see if we're okay with what is here. So bullet point number one, there's each active ingredient in the compounded drug, it's FDA approved or compendia supported for the condition being treated. Two, the therapeutic amounts are supported by national compendia or peer reviewed literature from the condition being treated in the requested route or delivery. I guess for me, the only thing here is a therapeutic amount could be very close to what's commercially available and that's where we're running into the issue somebody's compounding this and it really isn't necessary. I don't know how we get around concentration with the active ingredient.

James Marx: If you put in, and/or/if a commercially available product is available, rationale for providing commercially available concentrating being provided.

Beth Slamowitz: Number 5 being, like that.

Paul Oesterman: Four, the compounded drug is not including ingredient that has been withdrawn or removed from the market due to safety reasons and any questions there? Number five, the patient has tried and failed therapy or have an intolerance to two FDA-approved commercially-available prescription therapeutic alternatives, one of which is the same route of administration as the requested amount unless one of the following criteria are met. The patient has a contraindication to the commercially available product, one or no other therapeutic alternatives are commercially available, preparing the strength not commercially available or currently in short supply, prepared in a different dosage form for patients who are unable to take the commercially available product, mixing or reconstituting commercially available products based on the manufacturer's instructions or the products approved, labeling, does not meet this criteria. And if the patient has an allergy or sensitivity to inactive ingredients, for example dyes, preservatives, sugars, etc., that are found in commercially available products. Six, the compounded drug has not been used for a cosmetic purpose. If the compound is subject to the drug-specific targeted compound program, then meets all the applicable drug-specific criteria for all of the targeted ingredients used in the request of compound products, and eight, the pharmacy compounded the medication and has received the appropriate certification for the dosage form being compounded. How is that verified?

Carl Jeffery: That would be just like a lot of other PA criteria, because it would be the physician that's calling this in, so they would have to have the trust that the pharmacy is accredited, and it's subject to audit.

David England: Also, we have to go by what the regs say, you know, as far as what they allow. If they allow that to be compounded having the PCCA license of approval and needs to be compounded, I think that's kind of superfluous. A lot of places are doing that because it's a little more consistent in how they do it but as long as you have a formula or compendia that's here how to do it and you're following that and get audited, you can show I made this under these guidelines and this is what we followed rather than I just pulled this off the shelf and slapped it together kind of thing, but you have to show that you used that guideline and that would be a Board of Pharmacy. If it was an issue, it would be a Board of Pharmacy issue, they would have to deal with that pharmacy compounding in accordance with regs and staff.

Paul Oesterman: I know the Board does not like compounding pharmacies. The last point, compounding will not be done in a physician's office. I think this covers most of everything that we talked about. Do we have anything that we wish to amend to what we have here?

Ryan Bitton: Our criteria just listed a bunch of products that the FDA says cannot be compounded or not for topical use.

Carl Jeffery: You mean the utilization? Is that what you're referring to?

Ryan Bitton: Refer to table 1. What page is table 1? It talks about patients who withdrawn or removed for safety reasons. The list of the HPN protocols, so that's the one comment that we had and then the whole cost item, I guess we had proceeded with a 200-dollar… I think of other people trying to get a compounded medication, the things cost 6 bucks, is there really a safety concern, but are there actual things that have happened from this perspective?

Beth Slamowitz: When I went to the FDA conference, I can tell you I don't ever want a compounded prescription in my life, from you or anyone right now.

Holly Long: Regardless of cost, there is a big potential for fraud. Abuse and safety problems.

Holly Long: So I'm sorry, I missed the table 1 thing. Can you show me what you are referring to?

Carl Jeffery: It's not included in the criteria. It's what is in the HPN criteria as far as what is excluded and what products are not allowed.

Holly Long: So, if we were to accept everything, you would want that table included within the policy? Okay.

Carl Jeffery: Yeah.

Paul Oesterman: So, it sounds like general consent is for this coverage criteria as well ask for a motion and a second.

Motion to accept the criteria as presented. Second. Voting Ayes across the board, the motion carries.

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

Carl Jeffery: We have a new medication here. It's similar to the Tamiflu for influenza to treat the signs and symptoms and shorten the duration of the influenza symptoms. Very similar results as Tamiflu. It's kind of an advantage where it's a one-time dose so it's just a single dose but it needs to be caught within the 48 hours. I think that's one of our concerns here is that it won't be started timely and after it's not shown to be effective after that 48 hours so that's the main crux of the added criteria; page 143.

Paul Oesterman: One question, is there a preferred?

Carl Jeffery: There is and they do have it on the preferred drug list and it's on the agenda to talk about.

Paul Oesterman: So if it's pending, it may not be a first-line agent and the Tamiflu product is the preferred list. You can go beyond that 48 hours and how do you see when flu symptoms started?

James Marx: There's a drug combination out that's a combination of Zyrtec and Singulair, and it's as effective as Tamiflu and it's about a two dollars treatment.

Jeannine Murray: At the time when I had to submit it, they didn't, but I thought Tamiflu also had to be started within 24 to 48 hours onset, so they made them clinically similar so then that would go to our cost committee. The reason normally expect a generic Tamiflu then would be preferred and the Xofluza would be not preferred, but we ended up preferring Xofluza only because in discussion with Medicaid because you have to allow 72 hours supply, it's a one-day treatment. I don't think you're going to be able to stop it with a PA so why incur the cost of the PA admin. So that was I think some of the rationale, so the Xofluza is the preferred PA now or as of the 15th of this month.

David England: There really is any clinical criteria out there; the IDSA said anything use this versus that first or something like that? Do we have any protocol for proposed because it's new? Otherwise, I could go either way on this one.

Paul Oesterman: I know the CDC was going to revise their guidelines, have they done that yet?

David England: I did a Google search on it and I didn't see anything out there so. I did the Google for Tamiflu versus this and it's kind of, it's all mostly lay press comments rather than anything literature.

Holly Long: Carl, I thought I had in my notes that we just discussed this at P&T or is it coming up? I thought we had Tamiflu as preferred and this is non-preferred unless I was mistaken? Currently fee-for service Tamiflu is on the preferred list. I don't know that we have the updated one. I did not find in my research any other states that currently have PA on this, although everybody's talking about it.

Paul Oesterman: Page 160, I had a question on the Xofluza product where is says no dosage adjustments recommended for creatinine clearance for greater than 50 ml/min. That would be less than…

Carl Jeffery: I'd have to check with the team. But it's a good catch.

Paul Oesterman: I know it's a new product, but there is any information available that somebody may have been given, and I know this is supposed to be given within 48 hours,

but they've been given Tamiflu and it didn't work and they've had a recurrence of the flu and now they're going to try Xofluza?

Jeannine Murray: I read on the manufacture's website it was supposed to have some efficacy against certain H1N1 strains that Tamiflu had some resistance to. That is all I have heard.

Carl Jeffery: So I just checked. It is on the agenda for the March PT meeting so the PT will discuss it in March.

David England: Do we want to postpone it?

Paul Oesterman: That might be wise to defer until our next meeting?

David England: We're getting close to the end of the flu season anyway.

Paul Oesterman: But if we defer and we start to get prescriptions for it, they are going to be covered, so… Have we had any usage yet?

Carl Jeffery: No, well…

Beth Slamowitz: I think from what I've heard, too, the pharmacies are still having a hard time getting it. I may be wrong, it's what I've heard.

Jennifer Wheeler: At the beginning of the flu season I was, and the second quarter…

Beth Slamowitz: Yeah, I think the last one that I got from the manufacturer was that it was delayed to getting out to the pharmacies.

Paul Oesterman: It's not currently available and it might be wisest to defer for our next meeting.

Carl Jeffery: Is that per pill? I thought it was two pills there?

Jennifer Wheeler: No, it's for two pills, one package two pills. So, per package.

Paul Oesterman: Per treatment.

Paul Oesterman: I would error on the side of caution that if we fall on my thinking is to go ahead and put the prior authorization criteria in now. How long would it take to implement that?

Holly Long: I was just about to comment on that. The implementation, it's really backed up because of the modernization product and that could mean going into legislation, the ones that are for July, is what we are implementing now and then October is backed up, as well, over 6 months.

Paul Oesterman: Flu season will be over, I say defer until the last PT.

Motion to defer. Second.

Thomas Beranek: Will that push it past the fall/winter when we start to see it again?

Beth Slamowitz: If we defer it to the April meeting, and we figure by that time, the new system should be so much stabilized so we have six months, and then it would be in by October just before the next flu season.

Holly Long: Is there anything different that you want us to bring, or for Carl to bring, as far as information to that meeting?

Carl Jeffery: For the comments for the greater than or equal, that's what it says on the package insert so there's no dosage adjustment necessary for down, so if they are 50 or over, there is no dose adjustment, but there's no data for below that.

Paul Oesterman: We have a motion and second to defer the discussion for the prior authorization criteria for the April meeting?

Voting, Ayes across the board, the motion carries.

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

Melissa Summers: This is Melissa Summers with Novartis, I would like to make a brief statement if I can? I see that Optum made a recommendation to remove the prior authorization criteria. I did, though, want to comment because I do see that the three managed Medicaid plans do not agree with this, so I just did want to make a quick point obviously that I know it's been a while since you all had discussed Entresto; however, since that time, the American College of Cardiology, American Heart Association, Heart Failure Society of America did update their guidelines. Entresto does have a class-I recommendation to reduce morbidity and mortality in patients with reduced ejection fraction heart failure and the guidelines to go on to further say that patients who can tolerate an ACE or ARB but remain symptomatic should actually switch to Entresto. I know that you all talked about guidelines already earlier this evening and talked about simplicity. The fact of the matter is, some of the suggestions being brought up by like Anthem for example brought up reducing the ejection fraction to 35% which even HPN removed that requirement a couple years ago, so I really just wanted to point out the guidelines, be here to answer any questions if you guys have any but obviously, I really think in the best interest of patients, especially to the majority of heart failure patients, are seen outside of Cardiology that it makes the most sense to remove this PA.

Paul Oesterman: This is Paul, I do have one question, one of the components of Entresto is valsartan. It seems that almost every product that contains valsartan has been withdrawn from the market due to possibility of contamination. Is Entresto impacted by this?

Melissa Summers: It is not nor is Diovan, which is also ours.

Carl Jeffery: This was a recommendation to have the PA criteria removed from the guy that does our stuff for the P&T meetings so it's impacting our deals we make with the manufacturer so that kind of what drives it, but we're certainly open.

Jeannine Murray: Earlier we talked about how if it was a specialist that that should be kind of a good go-to and then I think the person on the phone was just saying how the majority of these are not prescribed necessarily by a cardiologist. I think for Anthem it will come up again in P&T review and probably mention of elements that the person on the phone was speaking to, meets the criteria but for right now, we would still prefer to have criteria placed. The criteria that we have in place is national across all of our plans so obviously not specific to one another so it's a little more difficult for us to make that change without going to our plans and process.

Ryan Bitton: We have criteria on Entresto and all those things, and initially there was a lot of people with financial concerns about overuse so we're in support of that prior authorization. It's evolved over the years so ours requires beta-blockers and appropriate diagnosis, so this feels like the prior authorization works, for appropriate use, our recommendation is to not remove it.

Thomas Beranek: For SilverSummit, we agree with leaving the criteria in place.

Paul Oesterman: So we have the proposal to remove the prior authorization criteria but our 3 MCOs are all on requesting to keep the criteria. Would you have any changes in the existing criteria that you want to put in place if we don't remove?

Jeannine Murray: I think there are a couple of things that we called out. I think with the ejection fraction, but it sounds like maybe that would be something that we would be removing in the P&T review based on the clinical information, that the person on the phone speaking to but the other information that I had spoke to, I think in there, had to do with some of the black box warning on the drug.

Melissa Summers: Yeah, it's not a black box.

Jeannine Murray: Not for pregnancy or anything?

Melissa Summers: No, you guys are really, it's really hard to hear you guys.

Jeannine Murray: Is there not a black box for pregnancy? I don't have your PA open so I don't know. I'm just going from our reference on our document.

Carl Jeffery: The question was, is there a black box related to pregnancy?

Melissa Summers: No there's not. Sorry, yes, there is.

Carl Jeffery: Yeah, we can touch on utilization real fast.

James Marx: There is an objective requirement for a 35 or 40% ejection fraction so I mean that's really a low ejection fraction. I mean you're really incapacitated at a 35% ejection fraction if you've ever seen anybody. They're not walking around and having a good time….

Carl Jeffery: Is that something that can only be measured really in a cardiologists or specialist office?

James Marx: Anybody can do with echo.

Paul Oesterman: Carl I had one question, who requested the removal and what potential impact is with removal of the prior authorization criteria?

Andolyn Johnson: It was a request from somebody…

Carl Jeffery: It was. It was with our group that works with manufacturers. I don't know where it originated from, but it came from that group.

Jeannine Murray: I tried to open up our stats but it took me too long to pull it open, because I am curious to see the approved and denied numbers.

Carl Jeffery: I don't have those readily available, but you can see the utilizations on the page 170, so this is fee for service. Combined all of them we're seeing maybe 30 claims a month on average would be my…

David England: There needs to be some criteria from a PA/cardiology, guidelines that we have.

Jeannine Murray: I'd like to just stick with the guidelines we have, but I'm just offering this.

Paul Oesterman: I'm sensing the feeling of the DUR Board and I think at this point, do we have a motion and a second to remove the prior authorization criteria for this product? Prior authorization will remain in place as they are right now.

Carl Jeffery: Any modifications we want to make from the Board? There are some differences with the MCO.

Jennifer Wheeler: They changed to class-1 so shouldn't we update that?

Holly Long: On A?

Jennifer Wheeler: Yeah.

James Marx: I really like to keep this intact. I have no patients with this; my heart failure patients have 60% ejection fractions.

Michael Owens: I mean, most of the patients, they're being followed by a cardiologist and typically the only thing, just because you have an ejection fraction of 40% one day doesn't mean that you're not going to get some remodeling and some improved ejection fractions which I've seen more often than I was expecting, especially the younger population. I've seen people with an ejection fraction coming out of the hospital 30% and remodeling EF is 45%. The only thing that I can see is if sometimes we'll get our patients coming in with prescriptions to fill in our pharmacy from a specialist, and so then I just reorder it but I think our pharmacy is a pretty big pharmacy.

Paul Oesterman: Is it the New York classification one now? Melissa are you still on the phone?

Melissa Summers: Sorry, it's 2 through 4.

James Marx: So as it stands, the prior authorization guidelines stay as they were prior to this meeting; no changes.

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

Kelly Hollenack: Good afternoon. My name is Kelly Hollenack and I'm the associate director for Clinics Biosciences, the manufacturer for Epidiolex. As you all are aware, Epidiolex is kind of a hot topic in the press and all around and I can give you guys some information and background and be available if you have any questions or issues that you'd like to have me address. It's the first that has been FDA approved. It's indicated for patients two years of age and older that have seizures associated with LGS, Lennox-Gastaut syndrome, and Dravet syndrome. Dravet and Lennox-Gastaut are very rare intractable epilepsies that typically are childhood onset but do go on lifetime so that's I'm asked is if they outgrow these types of seizures but it's something that they have for life. They are very severe forms of epilepsy. They often have high-frequency seizures, hundreds a day, often times. They also have developmental and physical disabilities and high morbidity and mortality, and it's this mortality issue why it's really important that these patients get treated early on. Again, we'll try to get this as soon as possible. The current guidelines were just in general for epilepsy. So cannabidiol, the active ingredient in Epidiolex, is a highly purified and structurally distinct from other antiepileptic drugs, although the PI states the exact mechanism of action is unknown, there's several that are thought to be the actual Mechanism of action. However, it does not interfere or work on cannabidiol receptors so THC does so that's the big difference between CBD or cannabidiol and THC is that there's no interaction with those CB receptors that cause the

euphoria and psychoactive properties. We did have FDA-prepared abuse potential studies so this is another important aspect and it's clearly defined in the PI, as well. So, the administration of Epidiolex shows low abuse potential. Acute administration of cannabidiol to nondependent adult recreational drug users, at therapeutic and super-therapeutic doses, produce responses on positive subjective measures such as drug liking and taking the drug again which are very common indices for abuse potential, that were in acceptable range and were not different than placebo. Because of that we are schedule-5 so that's important to note, too. There were some really large randomized trials that took place, the largest to date and this patient population, nearly 700 patients in these trials. The efficacy and safety of Epidiolex for the treatment of seizures associated with LGS and Dravet were demonstrated in these trials, 3 of them that were submitted to the FDA but the fourth one that's been published. These were double blind placebo-controlled trials where Epidiolex or placebo were added to patients current and antiepileptic drug therapy, and as stated, these were the largest. They were also the longest so we have 96 weeks so we extension to address safety data after the 14-week trials. We did achieve the primary endpoint of significant percentage change in convulsive and/or dropped seizures; the frequency from baseline, all studies versus placebo and the treatment that was first established during the first four weeks of therapy and was maintained throughout the duration of the trials and again was also seen in the open label extension. The results show the 39 to 44% reduction in median convulsive and/or drop frequency over baseline across all of these trials. Just want to note, too, that the drop seizures sometimes there's some confusion that we see out there with what a drop seizure is and these trials it was defined as atonic-tonic or tonic-clonic seizures that could have related to a fall and safety concern. Another important aspect of this, I think there's the secondary endpoint which is looking at 50% responders which in clinical classes is something that is really important not only to those who are providing the care but also to the direct therapy they were seeing the patient, so we did see that there was 50% responder rate was greater in patients taking Epidiolex than placebo and across all 3 of those trials. I think what's really important since we are dealing with treating children in a safety profile, the safety profile of Epidiolex was consistent across not like all 3 of these trials but also in the open label studies, as well. The most common adverse events that we saw at least 10% or greater was somnolence, decreased appetite, diarrhea, transaminase elevation, feelings of malaise and rash. There were some sleep disorders as well. Most of the side effects were seen early on and sort of dissipated by the end of the trial so most patients experienced those side effects when they got to the end. In summary, Epidiolex has been demonstrated as effective for the treatment of seizures associated with Lennox-Gastaut and Dravet syndrome with a well characterized safety profile, with that, expect to improve with time and safety.

Netochi Adeolokun: Were there any studies that compared it to other available products?

Kelly Hollenack: No, there's been no head-to-head trials. We were just approved this summer, and got the DEA to schedule us 90 days after that so it just went on the market in the last few months so there's no head-to-head trials but the patients were already taking a lot of different antiepileptic drugs and have therefore poorly controlled seizures by the time they got to our therapy. One other thing that I wanted to state, too, is that it is a specialty product. This isn't something that you can go to CVS or Walgreens will even have on their

shelves so we have five national specialty distributors for the product and we recently opened it up to some of the institutions like Children's in Columbus and Alabama that specialize in treating these patients so they can also distribute it, but we really kept the distribution to a limited number.

Holly Long: Looking at some of the criteria that other states have, one of the things that stood out, that they were asking for written attestation that the patient, or if they had a caregiver, that it's not currently used recreational or medicinal cannabis along with this drug. Is there anything that you have that would make that necessary?

Kelly Hollenack: So that was one of the inclusion criteria for our trial and part of that is, when you're doing a clinical trial, you want to make sure that you're really looking at what you're looking at not sort of bringing in another substance that may sort of address that you're trying to address or you get them to say well these patients could have been on medicinal or medical marijuana versus your product. It was inclusion criteria. Some states have adopted some plans and have also adopted some of our inclusion criteria which we're working with them on, because we really don't think a lot of them are appropriate for patients.

David England: As far as my understanding with respect of the pharmacies would be, so the specialty pharmacists I've dealt with in this past, they've had specific criteria, like they have specific education per the patient and doing special…there has to be some specific education that the patient can use this drug and possibly another drug. What is it with this product that has to be coming from a specialty pharmacy since medicinal marijuana is available all over the place. Why is it that this needs to be specialized and if your pharmacy provides this, are they requiring the patient not having been on any other cannabinoid?

Kelly Hollenack: Well, the criteria for prior cannabinoid use is really based on what various plans have put in their policies, not what the specialty would recommend or state, again, some of those plans are based on the inclusion criteria I think I've only seen maybe 3 based on that. We wanted specialty we are plant-based, grown in the UK, so because of the supply potential issue, we're fine with it but we wanted to make sure that it wasn't something that was cost to us and might have a supply issue because it's got a year shelf life so it's not something that you want to sit around on the shelves. We also wanted specialty because we wanted high touch on that education purposes and send out initially a travel kit; it's in a glass bottle and there's education on how to dose, how to use the syringe. They also distribute out this kit where they can take sort of a lunchbox that's padded so they can take it on outings. We really try to pick some of the specialty distributers that really like to provide that and we do a lot of education with them to help them with education.

Paul Oesterman: Has this gone to P&T?

Holly Long: Yes, I was just about to add that. Kelly joined us at P&T last time and it was voted as preferred.

Carl Jeffery: Epidiolex is very limited indication at this time to LGS and the Dravet syndromes, which are very severe forms of epilepsy and it's shown to be effective; it's a very promising medication and that's why the P&T Board made it preferred but because it's getting so much press and because there's so much misinformation, I think a lot of unknowns about cannabidiol in general, that I think people are going to see this and think it's a cure-all and it can be used now with various disorders but again, no indications, I think we wanted to get on top of this as quickly as possible to cover it for the kids who need it and as indications come out or other information comes out, then we can address those, but right now I just wanted to limit just really to the LGS and Dravet syndrome.

David England: Do we want to deal with anything as far as other cannabinoid use? If they're using this, the other cannabinoids not supposed to be on board because it would how would you know which one's doing the job?

Holly Long: How can you monitor that because the other states asking for a written attestation. It would be hard to…

Beth Slamowitz: You could do the same type of thing, just like with the opioids where you have to ask that they're not on another opioid.

David England: Is there a test, if there's any way to differentiate?

Paul Oesterman: Measure their THC level.

David England: It's hard to differentiate this from other cannabinoids.

Kelly Hollenack: Some labs can; it's not always easy. There's no discernable amount of THC in our product when you're talking about medicinal products there could be. It's kind of few and far between with the labs really do a good job of sort of looking after. There is not a contraindication in the label, as well, to again some of what we found were using inclusion criteria. The inclusion criteria for some studies are pretty lengthy and why they pick out some of the things that they want to pick out and not others is not a question I can answer.

James Marx: It's actually not that hard to detect other than mass spec but most labs don't look for that particular spot in the spectroscopy but about 800 so the THC is really easy and they're not going to be looking for, again, either cannabidiol metabolites but they're there and they can be detected very easily if you're looking for them but I don't know what the point would be.

Lisa Todd: I think it's more diversion, that the parent might take the kids drug. I think the one criteria was the caregiver…

Holly Long: Other states have an attestation by the patient or the caregiver, the patient is not currently using recreational or cannabis along with the product.

James Marx: So you're saying we're drug testing the caregivers for?

Holly Long: No. Because it's directed at children, I think they're allowing that written attestation by either the patient or the parent or a caregiver. The other thing that I found. There's a couple of other States that have currently put out criteria right away, they have more specific on the dosage that's allowed. I don't know how necessary that is. I know that you have that the total dose will not exceed. They also had to provide the information on the things necessary. Where doses allowed, the recommended starting dosage is 2.5 mg taken twice daily. After 1 week, the dosage can be increased to maintenance dosage with the 5 mg twice daily. Individual clinical responses, can be increased up to a maximum recommended maintenance dosage of the 10 mg/kg twice daily and that's where the dose comes in. See drug package insert particulars. I don't know how necessary that is. The same states also had reauthorization for criteria. They're a little more specific. I like that we have the members responding positively to therapy, they're just a little bit more specific in it and they provide the chart notes have been provided and so the member has decreased in frequency and the member does not have elevations of transaminase levels greater than 3 times upper limit of normal and bilirubin levels greater than two times the upper limit of normal.

Paul Oesterman: Question, you had indicated, if I heard correctly, the transaminases are elevated initially and then…

Kelly Hollenack: The transaminases, we had used them up to 18 months but we saw that very few patients, it's usually something that does occur sooner. Almost all the patients with concomitant valproic acid and up to 20 mg/kg per day so there are risk factors. The PI recommends baseline before you start and then after clinically appropriate. You have to manage that and it's something that you've had to ask for.

Paul Oesterman: We have the proposed authorization guidelines for the initial PA being for 3 months with diagnosis of LGS or DS and the patient must be at least 2 years old and serum transaminase and total bilirubin levels are obtained and within normal limits and it's prescribed by or in consultation with a neurologist and the total dose will not exceed 20 mg/kg per day and use in adjunctive therapy in patients taking one more antiepileptic drugs and has chart notes confirming the presence of at least 4 convulsive seizures per month. The reauthorization criteria would require that the members responding positively to the therapy as evidenced by increasing frequency of seizures and would be good for 12 months.

Carl Jeffery: The initial on it is 3 months.

Holly Long: The other states that have it, is that they took it 3 months initially and there is 12 months after.

Ryan Bitton: HPN has 12 months for the initial length. We also did not have the AST/ALT requirements. We just recommend removing that. And failure of two agents rather than one.

Carl Jeffery: You mean like number 6 would require 2 agents? Is that because they're preferred criteria or is that for therapeutic or kind of a?

Ryan Bitton: That was for therapeutic, not necessarily for non-formulary

David England: Yeah, it really doesn't say how many other medications they could be on and they can be adding to it because this adjunctive.

Carl Jeffery: The indication is written such that it's not indicated for adjunctive therapy but it's not indicated for monotherapy, either, so, all the studies were done, as Kelly said, they had multiple other medications.

Motion to approve the criteria as presented.

Second

James Marx: I want to be clear on what the transaminases we're monitoring for elevation of transaminase 2 or 3 times or we're not?

Paul Oesterman: The criteria just says that a recent one is obtained and is within normal limits.

James Marx: In other words, for the people on valproic acid anyway, for them it looked like it had normal so I mean, that eliminates almost everybody.

David England: Maybe I want to add that, 3 times the normal limit has that on there because I agree with Dr. Marx, some of it doesn't matter, they're all going to elevate it and even 3 times normal limits still within normal range, this doesn't include it and the person so be excluded if their AST/ALT is normally elevated.

James Marx: That's a lot. Really, I can tell you, I've had two times that I can tell you, you're really sick at two times so it's whatever there's not much I can tell you having had it, it's not nothing. You're sick with that elevated.

David England: Then I make a motion of the amendment to be on number 3 that the recent serum transaminase and total bilirubin are not anymore than two times normal limit.

James Marx: I just think a notation needs to be made of it. It's not insignificant. I see it all the time, two or three times transaminases are wow, I don't ever want to be there.

Paul Oesterman: We had a motion and a second, lets backtrack. We will withdraw your second and motion. We present the revised criteria to include bullet point number three to indicate the transaminase and total bilirubin have been obtained and are within two times normal limit.

Kelly Hollenack: The label says to discontinue if the transaminase is great than three times for AST and ALT or greater than two for bilirubin. There were people in the trail had elevations, they watched and they decreased over time or they decreased the valproic acid.

Carl Jeffery: You're looking at pre-treatment values.

Paul Oesterman: Do we want followup transaminases added to the reauthorization criteria?

James Marx: I think they should be checked every 90 days.

Paul Oesterman: Do we want the initial criteria to say a baseline transaminase and total bilirubin have been obtained and rechecked every 3 months.

Beth Slamowitz: Do you want that under the reauthorization?

Paul Oesterman: For the reauthorization criteria, we should have another baseline, because that would be 90 days out. Would you want it continuously every 90 days? So my understanding the proposed prior authorization guidelines are they stand for the initial authorization, for the reauthorization a second bullet point for transaminase and bilirubin will be checked every 90 days.

Beth Slamowitz: You have it for the first three months, after the reauthorization it will be approved for 12 months, so you won't see that lab value again. Do you want a attestation that the lab values will be done.

Paul Oesterman: Bullet point number two will be an affidavit that the transaminase and bilirubin will be checked every 90 days.

Lisa Todd: Would these kids get labs every 90 days?

Beth Slamowitz: You could put monitored per guidelines.

Paul Oesterman: Does the package insert have any guidelines?

Kelly Hollenack: Yes, the PI is baseline, one month, three months, six months and then clinically appropriate afterwards.

Paul Oesterman: So the proposal is the initial criteria is as presented. The reauthorization criteria is bullet point number two is the serum transaminase and bilirubin will be checked per package insert.

Motion to accept.
Second

Voting: Ayes across the board, the motion carries.

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

Kevin Schreur: Good evening, Kevin Schreur with United Therapeutics. Are there any changes that you are recommending related Orenitram or oral prostinoids?

Carl Jeffery: Everything we are looking at today is the nitric oxide.

Kevin Schreur: Then I won't waste your time. Thank you.

Carl Jeffery: our P&T Committee who was looking at utilization and saw that there was some potentiation that there could be some misuse like tadalafil and sildenafil prompted this. The guidelines look different. The proposed criteria in the binder are broken in to two sections. The first page on page 223 is the indications. I put two alternative criteria for the board to consider. The first is the most simple and requires the pharmacy submit a diagnosis on the claim of pulmonary hypertension. Or if they don't submit it the prescriber would call for an approval and the one criteria would be if they have pulmonary hypertension. The other proposed criteria is more similar to our commercial criteria. It is much more involved and gets into the symptoms, how the diagnosis was made. And prescribed by cardiologist or pulmonologist. On page 226 has the ejection fraction differences. All of these would require calls to the PA call center.

David England: I think we should stick with criteria A.

James Marx: Do patients have to promise they are not using for ED?

David England: I move we accept criteria A on page 224.

Holly Long: Do any of the MCO have comments?

Lisa Todd: This is similar to the other criteria. Our specific PA criteria we have meets the spirit of the rule, we would keep those.

Ryan Bitton: If we are going with option A, we would support this.

Paul Oesterman: We have a motion to approve proposed criteria A.

Second

Voting: Ayes across the board, the motion carries.

5. DUR Board Requested Reports

a. Prior Authorizations on High Dollar Claims

Carl Jeffery: So, if the board remembers – I don't remember what meeting it was actually voted on, it was back in 2017, but the beginning of August 2018 is when we implemented the criteria of any medication that was over $10,000 would stop for P.A. So, this is just a summary of those P.A.s. So, you can see which ones were approved, which ones were denied and it's broken down by month so August – sorry, I'm on Page 275 if you're trying to catch up to me. So, you can see that the numbers went to only September. Not very many are denied but still it's enough to be worthwhile of maybe they not being used for the – the only criteria that we have on there pretty much is the FDA approved indication or it's in a common compendia.

Jeannine Murray: What would be interesting is how many rejected at the point of service versus actually came in because I think when we talked about that at the time it was about fat finger or coding, you know, people enter and that's why we put it in was to stop that from happening. So it would be interesting to look at if we stop claim.

Carl Jeffery: Right, yeah and I have looked at that. There were quite a few claims that came in that were denied at the point of sale and I don't the exact numbers but there were a significant number of claims that we received that were rejected because they hit the $10,000 but no P.A. was ever submitted. It's either fat finger or the prescriber says, it was worth a shot and they didn't get a P.A.

Beth Slamowitz: And unfortunately, too, there's no way to measure how many P.A.s were never submitted. Like, never even initiated.

Jeannine Murray: That's how you look at your rejects at point of service, right? So, that's what you're saying is there were a lot but then no P.A. submitted.

Beth Slamowitz: But there's also a number there, you know, however, those P.A.s that were never submitted because this is in place.

Jeannine Murray: Oh, I see what you're saying. This changes behavior.

Beth Slamowitz: Right.

Holly Long: So, the total there is 42?

Carl Jeffery: Yeah, it's hard to read on that one but 42 approved in August and a lot of those would have been – we went through and kind of grandfathered a lot of people in that were on and entered P.A. so some of those would be included in there.

Holly Long: Where the denials are?

Carl Jeffery: The denials are down below. So, just underneath there's seven denials.

Ryan Bitton: There's a policy, HPNs report. So, we looked at rejects and everything that we had was over $2000 rejected for prior authorization and non-formularies. It was

reviewed by those criteria. Nothing – they were rejected because it was just affecting this PA, so we had 734 claims to process for $10,000 but they were all reviewed and the non's just $10,000.

Jeannine Murray: I can definitely see the Sprycel in there on the fee for service when you require P.A. I think that's what – one thing I know that that's Anthem with we get the request for this data and say well, we already reject all the hep C drugs and they reject for P.A. so we don't have a P.A. that comes in because of drug-rejected just at point of service. They usually have to adjust.

Lisa Todd: You don't want to stop it twice.

Holly Long: Tom, Can you explain a little bit, you have 42 approval there. Do you know anything about the 56 denials?

Thomas Beranek: They're all hep C drugs so physicians are – most of them are submitting for Zepatier or Epclusa and so we're not denying them flat out, we're just saying hey, we prefer Mavyret. Can you tell me, is there a reason why you can't use Mavyret and they go, no we can use Mavyret. Okay, it's fine.

Holly Long: Okay.

Thomas Beranek: So, we're not flat out denying anybody. We do pay for – I don't have to provide something clinically that says this is why I need this, basically I need to stay on this drug or why I need to continue. They're almost all related to those two drugs.

Paul Oesterman: Is there anything that the DUR board wishes to do in terms of follow-up on this?

b. Opioid Utilization – top prescribers and members

Carl Jeffery: So, Page 283 – catch up to where we are. So, again, the same story we've been seeing in the past which I think is a good story – a decline in the count of claims and opioids. I added in there that claims per member, you can see that's decreasing. So, October 2017 we went from 13 claims per member down to 1.24 so I don't know how statistically significant that is but then also the quantity per member is slowly decreasing so we're looking at 102 units per member down to 100.

James Marx: Is that amortized over all the members?

Carl Jeffery: Right. You're just taking the total quantity, the total sum of the quantities divided by the number of members.

James Marx: Yeah, but all those members aren't getting that opioid so it's like how many per people in the United States.

Carl Jeffery: It's a metric that you're comparing consistently throughout the month so even though it may include some liquid in there, you can't take that 100 and draw that back to something else because there may be some other dosage forms in there but I think as far as when you're looking at a trend, it's useful.

James Marx: Then, as your membership grows then it gives you more allowance for – it keeps the ratio the same.

Carl Jeffery: Well, we're not looking at the – so the members that utilize it. So that's the number of utilizers. Those are the people who – the total number of people I've got, so not the total Medicaid memberships. And continuing on Page 284, again this is kind of a standard report, utilizers by members. Then, we also matched back the NPIs so you can see they're blue highlighted C and a D. I think there's one on the next page A. It's also on here so you can see – I think last time the board asked if there was some match back to those providers so that carries over to the next chart that's on Page 286 of the top ten prescribers by count. So, those correspond to those numbers. I think before I included some of the detail about which medications these members were on and I didn't have – it would have been way too long here to see the metrics that each of those members is on.

Paul Oesterman: Looking at Page 286, I did have a concern that shows up with prescriber E, maxillofacial surgery, P.A. It just seems like that's an awful lot of opiates to be prescribed by this kind of practitioner and I'm wondering if it wouldn't be beneficial to send out another letter, just making you aware that your usage seems to be somewhat out of the norm.

Carl Jeffery: Yeah, right, and that letter we sent to the nurse practitioner that was #1 on our list, it dropped. So, I don't know if they stopped seeing Medicaid patients or if they actually adjusted their prescribing habits.

Paul Oesterman: Well, that would be my recommendation at this point. It lets these practitioners and make them aware with a letter that they would rather or not. Just that they are –

Carl Jeffery: And I think our last letter was very appropriate and respectful and say we understand every practice is different and it may be totally justified but we just want to know where you are.

Paul Oesterman: Yeah.

Carl Jeffery: We can certainly do that.

David England: I guess on the other hand, this has always been the bane of this project, even in the past. We send these letters out; do we really get a response? And if we don't get a response, are we going to do any follow-up? I mean, if we've requested why, why, why several times and we get nothing, what are we going to do after that? Otherwise, it's like –

Holly Long: Well, we weren't really saying why, right? We were just providing information – in a nice way saying we're watching you. We see that this is going on and but we could take it a step further if we want if we didn't see changes.

David England: Right, I'm saying in the event we see an increase or they stay consistent where they are, I guess that's the question. Do we have the authority to ask a justification why it's consistently like this? If that's their practice, that's their practice but if they stand out from the crowd, maybe –

Holly Long: Yeah, we could include some statement like that within the letter asking them if they would like to speak to it and get back to us. Is there a way we can present that to the board? Sure.

James Marx: Otherwise, there's no special investment that happens. Does it carry over from the previous listed specialty?

Carl Jeffery: No, the specialty was is it known or it's not in our system or I try to Google these prescribers, too, and it's like you never know.

David England: I think some of these changed, but most of these are P.A.s or NP's.

Carl Jeffery: My theory with that is that the N.P.s and the P.A.s are the ones who handle most of the refills so they're the ones who see the follow-up and they're the ones who probably to continue to prescribe.

Jeannine Murray: It's looks what you're saying that it would almost be interesting on the Letter E to – I'd be curious to know how many of those are the short-term that they can get versus how many are long-term chronic utilizers and know who really is the problem that has everybody chronically on them versus somebody who has a practice where whatever surgery they're doing, everybody leaves with a script for an opioid for a week. I don't know.

James Marx: I agree. I think somehow you need to get some ICD trends that sort of correlate with these different specialists because if the maxillofacial is for TMJ or something like that, that's one thing versus if they're all doing complex maxillofacial surgery, you know, like sagittal splits and surgery and stuff like that. That's a totally different deal than somebody that's doing TMJ prosthesis and things like that.

Paul Oesterman: Aren't all prescriptions for controlled substance now requiring ICD-10 codes on them? So it should have that information.

Holly Long: So, I can request that.

James Marx: The problem with that though, there's a big problem and it was one of my concerns initially. The problem is all the systems only allow – the pharmacy board only

collects one ICD-10 and sometimes there's a whole slew of them and like you're electronic prescribing system, which mine only allows – well, actually I have to put them in as pharmacy notes if I have any more than one and then I don't even know what the pharmacy does. Some of the pharmacies maybe committed to those other ICD-10 and others may not. The pharmacy board only gets one and their response is, well, if we're really concerned we ask for the prescription. Well, maybe it's only got one on the prescription so it's really kind of not adequate and I think that the e-prescribing people need to maybe step up to the plate and help us here.

Holly Long: I can try. I can take it to our data analytics team and see what information they can pull related to the diagnosis and talk to them about that concern and see if there's any kind of reassurance that they can provide around accuracy. I can see what we can do.

Beth Slamowitz: Well, isn't that something since they're inputting in at the point of sale?

Carl Jeffery: Are they required to put it in at point of sale? We don't have to have it.

James Marx: I thought they require more than once. I don't know if they require more than… The pharmacy board only collects one, so I mean –

Michael Owens: Yeah, but if you're going to have one, it's probably going to be the one that matters the most.

James Marx: Sometimes though, the even when I'm…the way your system, it makes it look and say, well that's not really relevant and I see there's three others that are listed there but they aren't the ones that are going to the pharmacy board. That's the problem.

Holly Long: So, you want to look at that tentatively and see if I can get back some information for the next meeting? Is that specific to prescriber E or is that specific to that utilization list?

Paul Oesterman: The list I think would be beneficial.

Holly Long: And when you were talking about the letter, did you want a letter sent out to just E or to everyone on the list?

Paul Oesterman: I don't think it hurts to send it to everyone. I know pain management; it's not surprising that they're on the list there.

Beth Slamowitz: They might need that information unless it's down to the member ID level.

Jeannine Murray: Oh, you mean the ICD-10 stuff? Is that what you're talking about?

Beth Slamowitz: Right, I mean, if you want diagnosis information based on these providers, it wouldn't be based on the prescriptions they wrote. So, it would be for that

member and that member ID based on visit. So, it would be difficult to get that data without – I mean, I guess you could look at a timeframe and – it would be pretty in depth data pull .

James Marx: Doesn't the NPI also do some sort of medical specialty? I don't know what the case is for P.A.s but I think for at least for physician providers I think the NPI has to take some sort of medical specialty.

Jeannine Murray: Yeah, the specialty list first is like what it will be. So, if you list surgery first, it may be pediatrics next.

Paul Oesterman: Pediatric oncology may show up as a pediatrician.

Jeannine Murray: Yeah, that's how I understand it. I'm not a doctor but I just understand it that way.

Lisa Todd: It's how they filled out the form.

James Marx: I guess my point is, I think we should really get a handle on what these specialties are and just having a blank there leaves me kind of empty. I really think we need to have a better handle on what those people are and if it's just a letter, Dear Doctor or whoever you are, I think that somewhere that should get listed and get it in the system so we can monitor that. I don't think it would be too difficult to do that because obviously we know and we can pick it up for some of them.

Lisa Todd: Is it possible – you know when we have the PreDUR meeting that's a private meeting, not public, maybe to share some of those NPIs to see if we don't all have E. I mean we all label them because it's a public meeting.

James Marx: I don't think we can do that.

Lisa Todd: Okay, I was just curious in a private meeting we can say –

Andolyn Johnson: It's a good idea but the privateness would be problematic.

Holly Long: However, the other thing that we can do is what I suggested last time was to ask is that you do the same letter.

Jeannine Murray: Whoever my E is.

Holly Long: Okay. So, we can't require you to do that but it was suggested for you to way back and limit that and I can draft a letter and say what we're doing if you want to try to do something similar but then if it came from all of us it might be more impactful.

Andolyn Johnson: The letter, how we phrase the request for records, is what we talked about that before because the authority is what I wonder about.

Holly Long: The request for records?

Andolyn Johnson: Or not records, but the request for response.

Holly Long: Okay.

James Marx: We're just asking for specialization and I think in a case of P.A., I don't know if there really are any board certifications for a subspecialty or specialty certifications in P.A.s. So, it would be a self proclaimed sort of specialization.

Holly Long: Yeah.

Beth Slamowitz: I think what we can look at to because in the Medicaid management in the information system, you can pull place of service. So, we can look at the NPI for that provider and then see what their place of service is. It could be very generalized and it might not help but it could be specific to the emergency room or to whatever in that may help. So, we can certainly look at that as well.

Paul Oesterman: Opioid utilization covered by provider. Now we have by member.

Carl Jeffery: I'm looking for – which one are you looking at that?

Paul Oesterman: It's 299.

Carl Jeffery: Do you want to hear about Anthem's?

Jeannine Murray: I already said that I thought it was crazy that the P.A. and the M.D.'s is where I don't have what their specialty is it's because it wasn't listed when I tried to Google and find them or they were just general practitioners.

Carl Jeffery: That's right. It's the same thing.

Jeannine Murray: But I have a couple rehab guys and internal medicine and then the rest would be the surgeons and anesthesiologists.

Holly Long: So, just to clarify, would all of you like to participate in collaborating with that letter and sending that out to those top prescribers or are you not interested?

Jeannine Murray: Me? I think we can do that. We would take the letter and send it through our process and review so, sure. It might get tweaked a little bit but the intent is still the same.

James Marx: I think it would be considered to be like discriminatory if you just pick on the high prescribers, I think that might be considered to be discriminatory. I think you need to ask everybody, hopefully you can cast some light of the pick by prescribers and if you

don't you can go back to them but I think really, obviously, I know you got this just dying with that but…So, I think we should collect all that information. I don't this we should be discriminatory and if we don't pick up the high prescribers then you go back and come back and say, hey, I guess you didn't open your mail or it got tossed or whatever but I think really we should be collecting that information just in general, at least at call center level so the people at the call center will know, hey I'm dealing with a pediatric P.A. versus a neurosurgical P.A. or something like that.

Beth Slamowitz: I think it's helpful to recognize, too, that besides the data the board of pharmacy collects and reviews and does whatever they do with it. HHS has their own analytics group that does a lot of in depth stuff with substance abuse and opioids so Medicaid is not the only one in the arena that is doing a lot of this data, kind of deep-dives and stuff like that. So, just because it's not necessarily being presented here doesn't mean it's not being looked at and that these providers aren't being addressed in some manner.

Paul Oesterman: I think if we understand correctly, you're proposing that the letter kind of go out to every provider. I don't think it would hold as much weight with those that are in this report if they talk to their peers and go, oh, yeah we all got the letter.

James Marx: Nobody talks to anybody anymore. That's not going to happen.

Paul Oesterman: So, I guess the question is are we sending the letters – is every provider who takes Medicaid patients going to receive four letters, one from you and one from each of you – every single provider is going to get four letters? I don't think it would hold any value.

Beth Slamowitz: That's a lot of paper.

Carl Jeffery: The letters we sent out previously just had was to the top 10 prescribers and we said, you know, you're number three on the list here and just to let you know where you stand compared to your peers.

Paul Oesterman: In a prior life when I was a drug indication coordinator at Kaiser in California, that's kind of what we did and providers were interested in how they compared to their peers and it did impact behavior. I lean towards, for now, is to try just the top 10 and revisit those at the next meeting after they have received the letters.

James Marx: The other thing that's really sort of a hot button for me is that I know if you just look at dosages, and I'm guilty of this particularly, I use lower dosages and higher quantities. So, when you look at my dosages you say, Dr. Marx writes 10,000 pills a year but at 15 mg not 100.

Paul Oesterman: So, if that's your response that's okay. That's fine. That makes sense.

James Marx: But I think that just for the survey I think we need to look at MMEs or something like that rather than just total dosages. I don't see that on paper or show up here.

David England: Maybe they haven't reported morphine equivalence as opposed to total dosages, well morphine equivalence. That might be a better measure.

James Marx: Slice and dice now.

Paul Oesterman: I think what we've got is a big pie in front of us and this is just one slice. We'll start with a slice and see where it takes us and decide how big our next piece of pie will be.

Holly Long: I apologize, Ryan, I didn't hear what you said. So, Tom said he already had a letter written up. Do you have one as well or would you like to see the one we draft?

Ryan Bitton: I'll see what you draft.

Holly Long: Okay.

Ryan Bitton: You've got other programs in place. This letter is going out but we would like to align.

Holly Long: Okay.

Thomas Beranek: I have the letter. I'm not saying I'm sending it to these top 10 right now. I will, now that we've had this conversation.

Paul Oesterman: Okay, very good. Time is ticking, so opioid utilization by member – any input on this?

Carl Jeffery: You're looking at 299? Tom, you want to comment on that?

Paul Oesterman: Page 299, any comments on the top 25 members for opioid utilization?

Thomas Beranek: No. Unless you have questions for me.

Paul Oesterman: It seems like there's very consistent NPI that ends at 686.

James Marx: Just for the record, I'm not on it.

Paul Oesterman: Okay, so I assume that each of our managed care organizations is looking at the high users anyhow.

c. Antibiotic Utilization

Carl Jeffery: So this is Page 300. These are the medications; they include fluoroquinolone, third generation cephalosporins and then oxazolidinone, I can't say it either, Holly. So you can see the number of claims per month I've got in the graph down there for this. There's

a fee for service and the top five I just have listed on the graph because it gets busy otherwise. A lot of cefdinir and ciprofloxacin seems to be kind of cyclical around flu season probably and then cough and cold season.

James Marx: Which ones of those are the third generation?

Carl Jeffery: The top five is cefdinir, but the cefpodixime the cefixime, Suprax.

David England: With the fluoroquinolones, again, I don't recall, are we getting a diagnosis for when these are being prescribed, too? An indication? The reason I'm asking is because are we certain that the fluoroquinolones aren't being utilized for what the FDA said not to utilizing them for like 2017 I think where, you know, I don't want to see them for upper respiratory tract infections and that kind of hub-bub. Do we know that they're not being used for that or we're just seeing them across?

Carl Jeffery: No, that's one of the reasons that we're talking about putting the P.A. criteria on them because we don't – they could be used for colds and viruses. We don't know.

David England: I think just with an ICD-9 code, would that resolve it or is that supposed to tie them and include an ICD-9 in the order. I mean, all of the hospitals now when we get antibiotics, an indication has to go with it.

Paul Oesterman: Indication and duration.

David England: And if it doesn't, it's either reject it or there's a call. And, do that rather than P.A. it so to speak.

Beth Slamowitz: The only way that we can do that is if we had a list of acceptable diagnosis codes and we would have to program the system to reject if any code but those were included and that would be a monumental task on our part – an manual task at that.

David England: I'm just saying, because in some cases if that's taking place, our numbers may be bad to begin with. There's no indications.

Carl Jeffery: I think some of the issues with the antibiotics though is that I think there's a lot of prescribing for viral infections and a lot of empiric therapy that started before they know what the bacteria is or what bug it is or if it's even susceptible.

Beth Slamowitz: I think that's kind of what Dr. Murphy eluded to was that until they know, they give an antibiotic and then wait for the susceptibility testing to come back and then 24 to 48 to 72 – however many hours it is, then they go and re-prescribe a new antibiotic that's more appropriate. Where, I think, and I'm not an ID doc, but probably within that 48 to 72 hours the majority of thing that they're prescribing antibiotics for are not going to progress or get worse or to the point where they're going to end up in a hospital or a ER situation.

David England: I was thinking about asking when I was here earlier, are we going to do that task force on…Wasn't there a task force we're going to be doing on antibiotics?

Holly Long: He's recommending a task force. No, we're not.

David England: If they don't want a P.A. – if they think it could be a viral infection, why don't we just give a 72 hour supply rather than a 10 day supply and after that 72 hours they have got their numbers back, then they could call in for the specific antibiotics and then no P.A. is indicated needed. It's just that it's going to take 2 visits.

Carl Jeffery: I still think within that 72 hours though, if you get 72 hours worth of antibiotics you still run the risk of creating resistant bacteria.

David England: It's not like they're giving a 10 day supply.

Beth Slamowitz: Some of what we had talked about, too, I think is we're trying to pull some data to see how long after either a hospital stay or if there is any antibiotic is filled is if that antibiotic is not filled within a certain day of when it's written that perhaps the prior auth comes into play at that point where if the pharmacy receives it seven days after the prescription is written, at that point did they really need it? Should we be dispensing it? Should we be giving it? Are we creating more of a problem? I think that's some of the conversation that we'll have at the workshop and we'll see what kind of things that the provider community brings forward.

Holly Long: Finding the most appropriate monitoring tool or tools has been our greatest challenge at this and trying to find with system challenges and other challenges what would be the best monitoring tools in trying to see what's going on with this and making sure that we're making the right decisions for the P.A.

David England: When I was in the retail world if I had an antibiotic come in dated seven days later, I'd call the doctor.

Holly Long: Right and that was one of the suggestions made actually for legislation as well, let alone with a P.A. that we should not be allowed to – it should have an expiration date, if you will, the prescription would have an expiration date.

Beth Slamowitz: So they aren't banking them for the next time they go back which my parents do, so.

David England: There's got to be something for us to know what it's being used for and if would save the call if you have the ICD-9, that ICD-9 would cut out and then after that 72 hours even though we have the desensitization or sensitivity, or resistance developing or at least cutting down so there's not as much out there and the patient would have to come back twice, the first 72 hours and then you have to come back for the other seven days if that's what it is – or five days. But it would save the phone call to the doctor or the P.A.s if they didn't want to deal with the P.A.s.

Paul Oesterman: So, initial fill of antibiotics in this category would be for a three day supply -

David England: Yeah, 72 hours.

Paul Oesterman: - with no P.A., then anything additional requires a P.A.

Holly Long: I think we're going against guidelines though with that recommendation aren't we? I guess part of what we're proposing is because everyone's been pushing education on us, provide education on P.A. Part of the education is following the guidelines so I want to be consistent.

Beth Slamowitz: I think that would also elicit some feedback from access to care issue is that you have individuals that maybe go to the pharmacy to pickup a three days worth and will never come back because they don't have the transportation to go back and get the rest. That would be an issue.

Jeannine Murray: One thing that you think about with the workshop anyway is regardless they'll only be able to get a 72 hour supply, with anything that requires a P.A. So there won't be a way to really stop that use of it.

Beth Slamowitz: I think it depends on what language you have around that 72 hour and what you could turn is as an emergency and how you have it defined. That's something that we have talked about as well is that that's always an issue.

Jeannine Murray: Oh it's for sure because we do monitor those reports and sometimes you'll see acne medication on your 72 hour supply. Really? Shouldn't we be able to say what is an emergency?

Paul Oesterman: I don't think we're going to resolve that tonight but we'll see what comes out of the workshop. I don't recall his name.

Holly Long: Dr. Wilson.

Paul Oesterman: Dr. Wilson. Hopefully he will be there and he and Dr. Murphy can duke it out.

Holly Long: No, and there was some information that Dr. Murphy spoke to that was obviously mis-communicated so I'll do my best to clarify that at the workshop. Not only will we see what happens at that workshop but after implementation I think is going to be very impactful to see if this is a good – I think that these are baby steps towards figuring out whether it's appropriate or not. Figuring out if we can change it and make it better. If it's required around other antibiotics, if it should be required in the emergency room. So, baby steps until we get it figured out.

6. Public Comment on any Standard DUR Report

7. Standard DUR Reports

a. Review of Prescribing/Program Trends.

Carl Jeffery: It's pretty standard. The top ones are all variable. So, we've got antivirals that include your hep C agents, the anti-hemophilia and you never know those kind of episodic treatments. Those are kind of hard to predict month over month and in the same kind of antipsychotics. They're episodic. Page 308 is where these start if you're catching up and then by count of claim, still the opioids were up at the top. Anticonvulsants have taken over, probably because of Neurontin but you can see the opioids have dropped to number two if we look at Q3 of 2018.

Paul Oesterman: I know this may be opening up a can of worms but for next meeting, can we look at the top ten by claim count for the under 18 population? We did that once before. Just take a look and kind of revisit that.

Holly Long: I'm sorry, the top ten count for under 18 just in the opioid drug class?

Paul Oesterman: Just in general.

Carl Jeffery: Just want to see what the patient is using.

Paul Oesterman: Just see what the kids are using.

Holly Long: Got it.

David England: Our other edits have done any good for that, antipsychotics and neuroleptics and so on that.

Carl Jeffery: That's on our next meeting. ADHD is on our next agenda so we'll bring that back.

Paul Oesterman: Next report.

Carl Jeffery: 312. I'll let Lisa speak.

Jeannine Murray: Those are our top therapeutic classes. Antidepressants, oh that's been a long time always at that time. There really weren't any changes. This is something that we monitor on a quarterly basis in our quality page, but really no changes here. I would expect to see some changes in the next quarter just only with the ebbs and flows of the flu season.

Carl Jeffery: Where are your opioids?

Jeannine Murray: Our opioids fell out of our top ten. They're at the bottom, combination narcotics. There they are. Sometimes some quarters they look at in our meetings and they're number 12 and our medical advisor committee will ask the same thing. So, they kind of bounce between 10 or 12 but it used to be number 2 on there. So, it has really fallen. Yeah, it is. There is one doctor on our MAC and he always asks me how the legalization of marijuana is impacting my reduction in opioids and I told him we don't get a claim for that. It's not covered. So, that's where your hydrocodones are, down there.

Paul Oesterman: HPN on Page 313.

Ryan Bitton: We have by paid amount and claim count. I don't see any huge changes. Antivirals are on there.

Carl Jeffery: Do you have – I was just wondering if you have them broken down by hep C versus influenza, or?

Ryan Bitton: The drug class behind this and so there's the other subclass that's different. We're talking about…so I apologize for that. Going down, you can see the opioids for us. It's like number four for us, from the count perspective, and it's the same thing. It used to be one or two and now it's decreasing.

Paul Oesterman: It looks like Silver Summit, down at number five for opioid combination.

Thomas Beranek: Yeah, so I'll go to Page 315 so on drug classes by spend, so it's pretty much the same ones we've had up there. I would say opioids are moving down. It used to be in the three or four range and it's down to eight now but anti retrovirals and insulin are always in our top two for quite a while and that's for hepatitis usually in third but some of those others bounce around a little bit so nothing grossly unusual or anything to call out there. Pretty standard, as well.

James Marx: Something to wet your enthusiasm is and you know this is really a lot of anticonvulsants are abusable and it is growing appreciation of that so it may not be – maybe we should not get too giddy about the anticonvulsives coming up and the opioids going down. It's another aside, a recent malpractice lawsuit in Las Vegas for a hospital and their enthusiasm to get the patient off opioids because the patient was admitted for sickle cell crisis and some prescriber decided that they were going to be opioid prior experience so they used Toradol in patient went into renal failure and died. There's a multi-million dollar lawsuit over that now so we need to rethink this whole opioid thing and really realize that maybe they're not really so bad and maybe somebody should look at the package insert for Toradol and not use it p.r.n. for sickle cell crisis.

Paul Oesterman: Carl, next report.

Carl Jeffery: So, top 50 drugs, each page here, so it's already on Page 316 so that's first quarter 2018 goes to Page 318 is third quarter 2018. So, that's the most recent we have here and this is by claim count – I'm sorry, pharmacy paid amount first. Next report would

go into claim counts. Hemophilia drugs really are number one. That's another one we've got some criteria going in on February 4th so it will be interesting to see how this changes with that new criteria. Then, when you look at the claim count, albuterol which we addressed today so we'll see if that gets implemented, we'll see if we see a drop in those but still, we've got a lot of hydrocodone/acetaminophen still. It's a lot of claims. That's Q1, even in Q3 we're still at 14,000 claims per quarter and then as Dr. Marx eluded, gabapentin I think – and we're seeing the same thing. We've kind of toyed with the idea of doing some RetroDUR activities around the anticonvulsants with opioid use.

James Marx: It looks like our MCO trends are pretty consistent. Let's jump to the c. DUR report, prospective DUR on Page 347.

b. Concurrent Drug Utilization Review (ProDUR)

c. Retrospective Drug Utilization Review (RetroDUR)

Holly Long: We were going to ask the board and you would like us to remove the top 50 report if it's not necessary to have in there anymore since there's a top 10 and a top 25.

Paul Oesterman: Yeah, that's redundant so I would say let's keep the top 25, split the difference.

Carl Jeffery: So, actually, fee for service starts on 344 which is tiny, so we're updating this form to make it a little bit more readable, too, but it's just a new form that I think we'll be using going forward. I think we've made some minor modifications so it will be consistent across the programs so you can easily compare these but nothing really to report. I don't think there's anything that's weird or unusual that I wouldn't expect on these. So, these are the edits that the pharmacy sees when they run a claim through and some of them are messages, some of them are soft responses and some of them are hard stops so they can't bypass without a P.A.

Jeannine Murray: Every PBM is different I think in that they spit out what the language is around the region.

Carl Jeffery: Right. I'm not sure we use that language. I'm trying to think –

Lisa Todd: Refill too soon.

Carl Jeffery: Yeah, and I'm not sure if the DUR has it.

Lisa Todd: Yeah.

Carl Jeffery: I don't think we use that. I think that's why it doesn't.

Holly Long: Are we on a particular topic or are we all just sitting here?

Jeannine Murray: We're just scrolling, right? Aren't we scrolling?

Paul Oesterman: I think we're approaching brain death.

Carl Jeffery: You're going to be all dozed off.

David England: Unless there's something just glaringly and we need to fix it.

Paul Oesterman: One thing I do like is the Anthem reports about controlled substance utilization management. That report –

Jeannine Murray: Oh, are on our RetroDUR program?

Paul Oesterman: On your RetroDUR. Yeah.

Jeannine Murray: So that program looks at all the high flyers and they get the letter.

Paul Oesterman: Does anybody have anything else they wish to add to any of these reports? Hearing none, seeing none – does anybody have anything they want to add to the agenda for next time? Anything specific other than what we'll be getting? Hearing nothing at this point –

James Marx: Something I'd like to, Carl, look at is, we know that the combination of opioids is really common. I'd like to see why the lower dose formulations aren't used more or if they're hardly used at all and I think they should be used a lot more. Actually, I think I brought this up before, like the 2.5 hydrocodone, oxycodone acetaminophen combinations and I think we really should be encouraging people to get into that dose range rather than the 7.5 or 10s. It's a common, I was wondering why we're not really avoiding, or not some way to encourage that because pretty much all initial prescriptions are written for 7.5 and 10 mg and it's really way overkill.

Beth Slamowitz: I think it kind of falls into the same category or issues that we kind of have with the antibiotic and prior auth is that prescribing something that prescribers don't like be told how to prescribe and for the information that you want, we can certainly look at utilization data to see how many scripts we have for those lower doses versus for the higher doses. The only thing we won't know is are they acute, are they chronic, are they initial prescriptions, are they given four prescriptions. I mean, I'm not really sure that the data would really tell you anything -

James Marx: Yeah, it's hard to sort that out.

Beth Slamowitz: - or necessarily encourage providers to go down that path.

James Marx: We need to figure out some way to encourage providers to do that because I don't know if any of you have ever taken opioids, I'm not a big user but I've had some fairly painful things and I took like 1 mg of oxycodone and I was amazed at how well it

worked. It was just incredible so these people are being introduced to much too high a dose and the tolerance involves rapidly, and then we end up with this whole situation. The other thing is that introducing patients to higher doses increases the instance of euphoria and overusing and habituation so by keeping them at a lower dose level, you're really minimizing the opportunity for them to really start liking it and that liking it is what really causes the problem and we're really doing a horrible job. I think I told the story before that I can't get pharmacies to order the 2.5 of anything because nobody else uses it. Patients have to go with 5 and cut them in half.

Holly Long: I'm not really sure. I mean, if you ever have any suggestions for how to encourage that, we would definitely take that to the board.

James Marx: I don't know if there's an echo but maybe there might be some way.

Beth Slamowitz: I would take it to the medical school because that's where it needs to start, education for the providers at the school.

James Marx: They don't get it either so I mean, you really have to put full on somewhere else.

Holly Long: You already have that recommending a lower dose within the prior authorization criteria.

James Marx: Everybody thinks 7.5 is a low dose. That's the problem.

7. Closing Discussion

a. Public comments on any subject.

b. Date and location of the next meeting.

Paul Oesterman: Next meeting is scheduled for April.

i. Discussion of the time of the next meeting.

c. Adjournment.

Substance Abuse Agents

Prior Authorization Guideline

Guideline Name Lucemyra (lofexidine)

1 . Indications

Drug Name: Lucemyra (lofexidine) **Indications** **Opioid withdrawal**: Mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults.

2 . Criteria

Product Name: Lucemyra (lofexidine)

Diagnosis	Opioid Withdrawal
Approval Length	14 days
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of opioid withdrawal with symptoms due to abrupt opioid discontinuation.

   AND

2. The requested quantity does not exceed 2.88mg/day for up to 14 days.

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: April 25, 2019

Prior Authorization Criteria being reviewed: Substance Abuse Agents

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.

Lucemyra is non-preferred. Our quantity limits are the same.

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: _Lisa Todd_____

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: April 25, 2019

Prior Authorization Criteria being reviewed: Substance Abuse Agents

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 suggests the following adjustments to the proposed OptumRx FFS criteria for Lucemyra

- Replace "diagnosis of opioid withdrawal with symptoms to abrupt opioid discontinuation" with:
    - All of the following:
        - For symptoms of abrupt opioid withdrawal AND
        - Opioids have been discontinued AND
        - One of the following:
            - History of failure, contraindication, or intolerance to clonidine OR
            - Lucemyra was initiated in the inpatient setting

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: RK 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: April 25, 2019

Prior Authorization Criteria being reviewed: Substance Abuse Agents - Lucemyra

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.

1. Diagnosis of opioid dependence (may be limited to physiologic dependence/tolerance) or opioid use disorder;
2. Prescribed by or in consultation with a physician specializing in one of the following areas: emergency medicine/inpatient care, pain management, addiction psychiatry;
3. Age ≥ 18 years;
4. Member is currently or will be undergoing abrupt opioid discontinuation within the next seven days and one of the following (a or b):
    a. Has taken one or more opioids for at least the last three weeks;
    b. Has been or will be administered an opioid antagonist (e.g., naltrexone) after a period of opioid use;
5. Medical justification supports why an opioid taper (e.g., with buprenorphine, methadone or other opioid) cannot be used;
6. One of the following (a or b):
    a. Failure of clonidine unless contraindicated or clinically significant adverse effects are experienced;
    b. Lucemyra has already been initiated (e.g., in an inpatient/ER setting);

7. Lucemyra has not been prescribed for a prior opioid withdrawal event within the last 30 days or medical justification supports retreatment;
8. Dose does not exceed 2.88 mg (16 tablets) daily.

Approval duration: 7 days (112 tablets) *Total number of tablets/duration per course of treatment should not exceed 224 tablets/14 days.*

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.

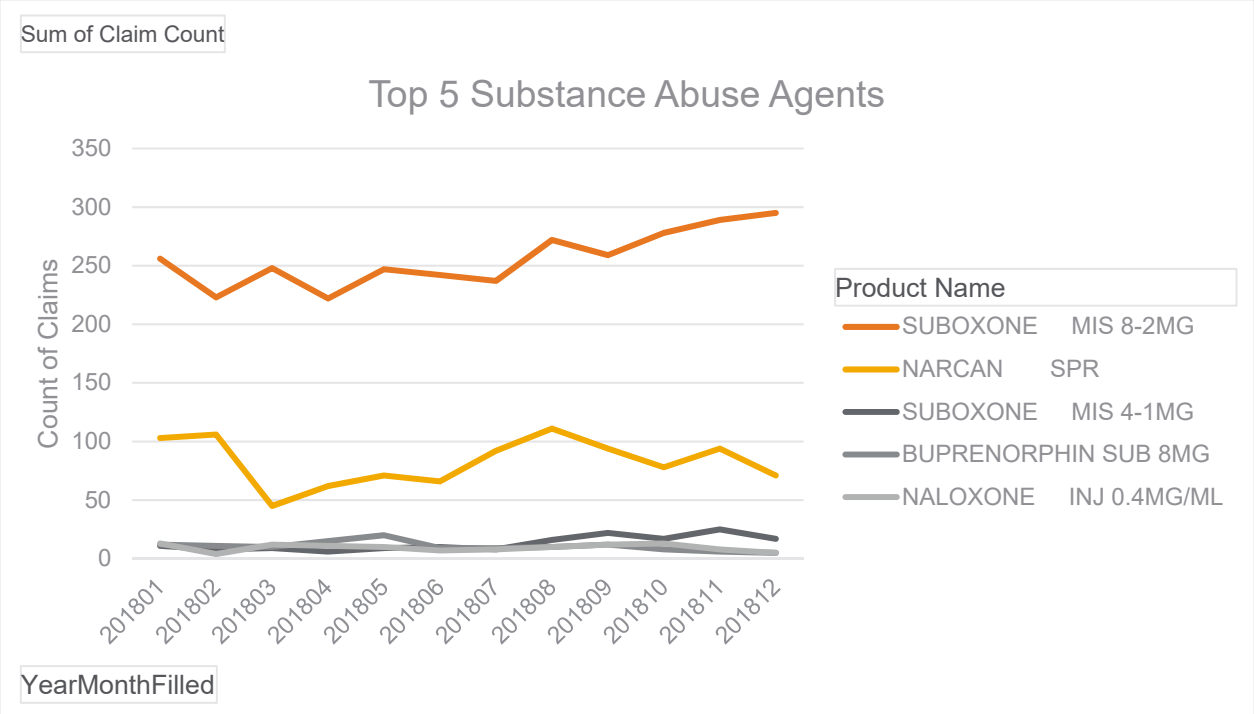
Please print the name of the individual completing this form: _____Tom Beranek_____

Signature of individual completing this form: _____*Tom Beranek*_____

Substance Abuse Agents

Summary of Utilization
January 1, 2018 - December 31, 2018
Fee for Service Medicaid

Product Name	Member Count	Claim Count	Days Supply	Sum of Qty
BUNAVAIL MIS 4.2-0.7	1	11	330	660
BUNAVAIL MIS 6.3-1MG	1	8	240	240
BUPREN/NALOX MIS 8-2MG	6	7	112	141
BUPREN/NALOX SUB 2-0.5MG	2	16	382	774
BUPREN/NALOX SUB 8-2MG	13	34	565	772
BUPRENORPHIN SUB 2MG	11	24	590	1,216
BUPRENORPHIN SUB 8MG	27	127	2,387	5,705
NALOXONE INJ 0.4MG/ML	106	113	206	165
NALOXONE INJ 1MG/ML	68	68	214	198
NARCAN SPR	823	993	15,114	1,993
SUBLOCADE INJ 100/0.5	1	1	28	1
SUBLOCADE INJ 300/1.5	8	8	224	12
SUBOXONE MIS 12-3MG	16	108	1,853	2,482
SUBOXONE MIS 2-0.5MG	30	94	2,312	3,365
SUBOXONE MIS 4-1MG	43	158	3,168	4,815
SUBOXONE MIS 8-2MG	397	3,068	56,540	99,116
ZUBSOLV SUB 1.4-0.36	3	9	250	460
ZUBSOLV SUB 11.4-2.9	1	5	110	300
ZUBSOLV SUB 2.9-0.71	1	7	49	98
ZUBSOLV SUB 5.7-1.4	7	23	382	677
ZUBSOLV SUB 8.6-2.1	4	12	360	1,050



Substance Abuse Agents

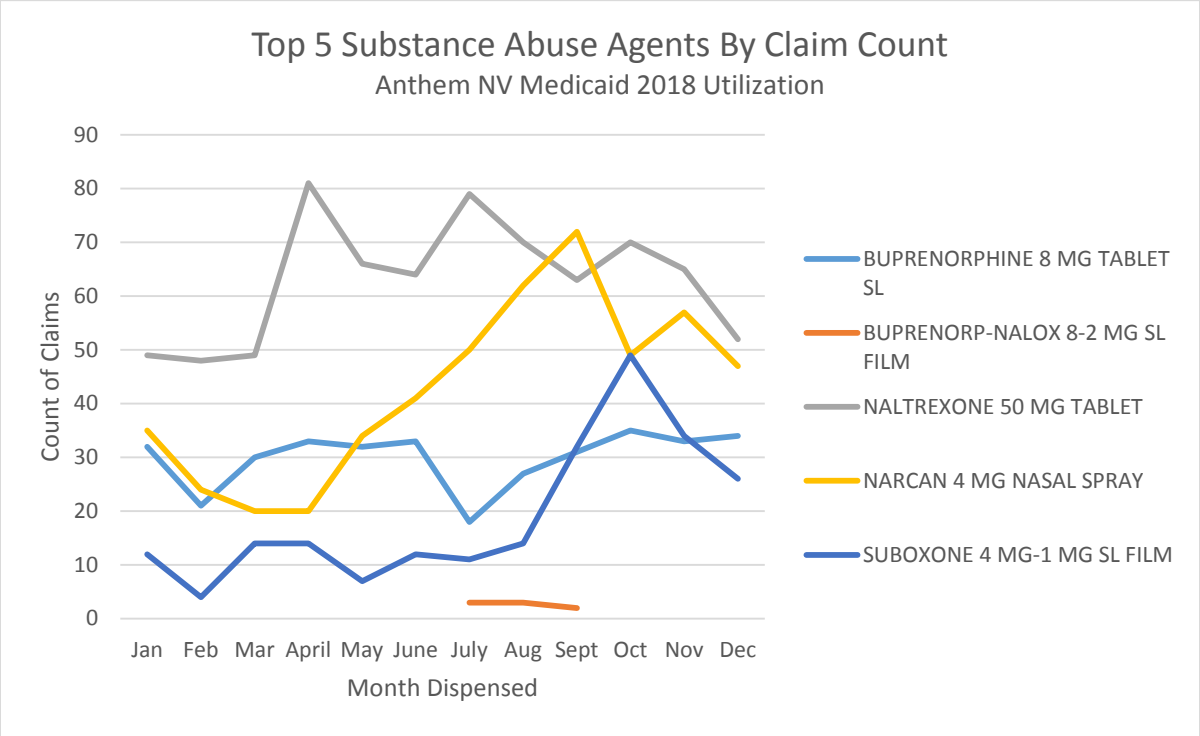
Summary of Utilization

January 1, 2018 - December 31, 2018

Anthem Nevada Medicaid

Drug Names	Count of Members	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
NALTREXONE 50 MG TABLET	756	756	18236	18024
NARCAN 4 MG NASAL SPRAY	511	511	6285	1054
BUPRENORPHIN-NALOXON 8-2 MG SL	426	426	7173	12418
BUPRENORPHINE 8 MG TABLET SL	359	359	6965	14953
SUBOXONE 4 MG-1 MG SL FILM	229	229	3652	6970
VIVITROL 380 MG VIAL + DILUENT	200	200	5645	200
ACAMPROSATE CALC DR 333 MG TAB	139	139	3479	15420
SUBOXONE 2 MG-0.5 MG SL FILM	135	135	2751	3843
BUPRENORPHINE 2 MG TABLET SL	79	79	1361	2790
SUBOXONE 12 MG-3 MG SL FILM	25	25	703	823
BUPRENORPHN-NALOXN 2-0.5 MG SL	24	24	611	879
ZUBSOLV 5.7-1.4 MG TABLET SL	19	19	524	538
BELBUCA 300 MCG FILM	17	17	510	1020
BELBUCA 900 MCG FILM	16	16	480	960
BELBUCA 450 MCG FILM	15	15	434	868
ZUBSOLV 1.4-0.36 MG TABLET SL	13	13	328	321
ZUBSOLV 2.9-0.71 MG TABLET SL	9	9	270	360
PENTAZOCINE-NALOXONE TABLET	8	8	240	1380
BUPRENORP-NALOX 8-2 MG SL FILM	8	8	214	256
NALOXONE 2 MG/2 ML SYRINGE	8	8	154	16

SUBLOCADE 300 MG/1.5 ML SYRING	7	7	210	10.5
NALOXONE 0.4 MG/ML VIAL	7	7	12	18
BELBUCA 75 MCG FILM	6	6	164	314
BELBUCA 150 MCG FILM	6	6	165	330
LUCEMYRA 0.18 MG TABLET	5	5	59	335
ZUBSOLV 8.6-2.1 MG TABLET SL	4	4	120	120
BELBUCA 600 MCG FILM	3	3	90	180
BELBUCA 750 MCG FILM	2	2	60	120
SUBLOCADE 100 MG/0.5 ML SYRING	2	2	60	1
	1	1	117227	182440.5
Grand Total	**5718**	**5718**	**234454**	**364881**



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Substance Abuse Agents Utilization

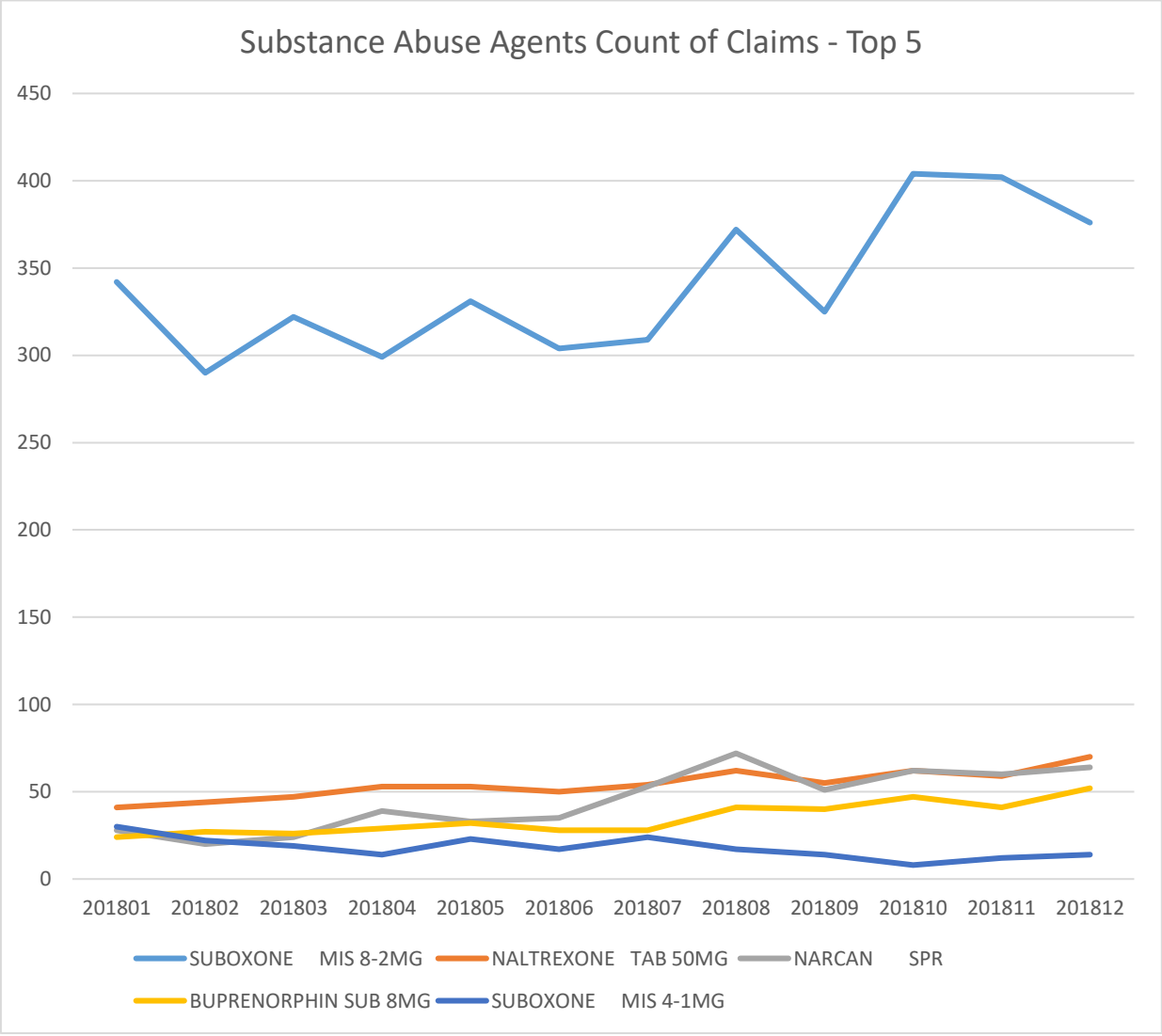
January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
SUBOXONE MIS 8-2MG	671	4,076	88,513	166,770	NA
NALTREXONE TAB 50MG	291	650	18,760	19,003	NA
NARCAN SPR	445	541	6,891	1,076	NA
BUPRENORPHIN SUB 8MG	84	415	9,281	16,486	NA
SUBOXONE MIS 4-1MG	46	214	3,893	5,375	NA
SUBOXONE MIS 2-0.5MG	39	148	3,214	5,064	NA
ACAMPRO CAL TAB 333MG	40	97	2,849	14,814	NA
BUPRENORPHIN SUB 2MG	26	89	1,505	2,451	NA
BUTORPHANOL SOL 10MG/ML	8	83	1,275	240	NA
ZUBSOLV SUB 5.7-1.4	15	79	2,172	3,925	NA
BUPREN/NALOX MIS 8-2MG	19	33	666	1,100	NA
VIVITROL INJ 380MG	12	31	853	31	NA
SUBOXONE MIS 12-3MG	9	21	507	917	NA
ZUBSOLV SUB 2.9-0.71	3	17	433	1,166	NA
BUPREN/NALOX SUB 8-2MG	9	15	178	304	NA
BELBUCA MIS 900MCG	1	12	360	1,080	NA
BUPREN/NALOX SUB 2-0.5MG	3	7	152	364	NA
ZUBSOLV SUB 1.4-0.36	2	7	150	270	NA
NALOXONE INJ 1MG/ML	6	6	36	18	NA
NALOXONE INJ 0.4MG/ML	4	4	33	6	NA
BELBUCA MIS 300MCG	2	3	74	148	NA
BELBUCA MIS 450MCG	2	3	90	180	NA
ZUBSOLV SUB 8.6-2.1	2	2	60	90	NA
ZUBSOLV SUB 0.7-0.18	1	1	30	30	NA
Grand Total	**1,740**	**6,554**	**141,975**	**240,908**	**NA**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Substance Abuse Agents Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada



Substance Abuse Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan

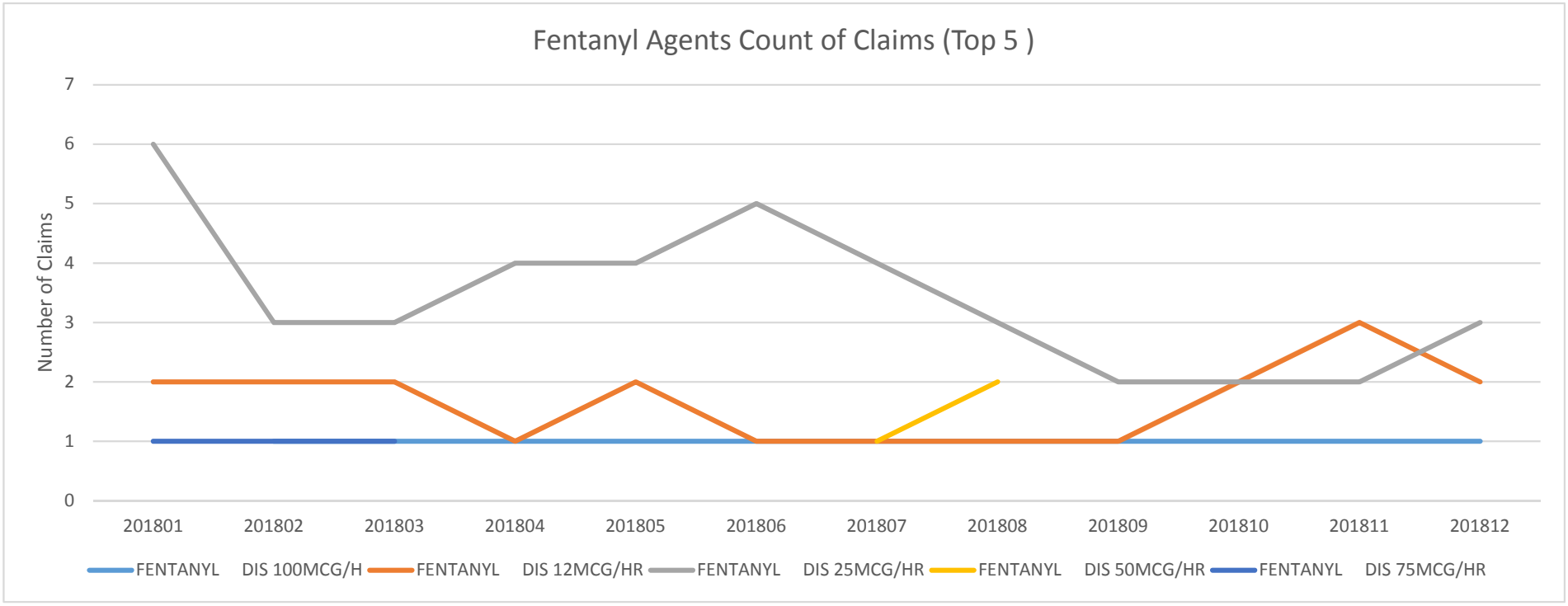
Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
SUBOXONE MIS 8-2MG	497	1,622	30,308	55,061	$ 445,337.84
SUBOXONE MIS 12-3MG	92	273	5,922	11,665	$ 190,815.00
BUPRENORPHIN SUB 8MG	69	229	3,474	7,238	$ 21,323.29
NALTREXONE TAB 50MG	107	153	4,505	4,508	$ 8,347.71
NARCAN SPR	93	98	1,055	202	$ 12,433.77
SUBOXONE MIS 4-1MG	31	57	1,378	2,314	$ 10,331.79
BUPREN/NALOX SUB 8-2MG	16	33	522	1,008	$ 7,563.60
SUBOXONE MIS 2-0.5MG	15	31	600	827	$ 3,873.77
BUPRENORPHIN SUB 2MG	10	20	360	1,090	$ 2,123.27
ACAMPRO CAL TAB 333MG	11	19	438	2,324	$ 2,910.31
VIVITROL INJ 380MG	7	12	336	12	$ 15,927.96
ZUBSOLV SUB 5.7-1.4	4	6	111	147	$ 1,230.56
BUPREN/NALOX SUB 2-0.5MG	2	4	97	97	$ 404.64
NALOXONE INJ 0.4MG/ML	4	4	35	8	$ 130.17
BUPREN/NALOX MIS 8-2MG	2	3	43	58	$ 429.93
ZUBSOLV SUB 8.6-2.1	2	3	90	120	$ 1,501.40
BELBUCA MIS 150MCG	2	2	45	90	$ 458.91
BELBUCA MIS 75MCG	2	2	45	90	$ 458.91
LUCEMYRA TAB 0.18MG	1	1	9	96	$ 25.00
NALOXONE INJ 1MG/ML	1	1	1	2	$ 34.32
Grand Total	**968**	**2,573**	**49,374**	**86,957**	**$ 725,662.15**

Substance Abuse Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan



BB. Buprenorphine/Naloxone

Therapeutic Class: Narcotic Withdrawal Therapy Agents
Last Reviewed by the DUR Board: January 26, 2017
Previously reviewed by the DUR Board: April 28, 2017

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

1. Coverage and Limitations

a. To initiate therapy:

1. Buprenorphine/Naloxone will be covered without Prior Authorization (PA) approval for an initial prescription of seven days or less.

a. An ICD diagnosis related to opioid dependence must be written on the prescription and transmitted on the claim.

b. To re-initiate therapy:

1. Buprenorphine/Naloxone will be covered without PA approval to re-initiate therapy for a prescription of seven days or less for recipients with a gap in treatment.

a. An ICD diagnosis related to opioid dependence must be written on the prescription and transmitted on the claim.

c. Prior authorization approval is required to exceed the seven-day limit.

1. Approval will be given if all of the following criteria are met and documented:

Nevada Medicaid encourages recipients to participate in formal substance abuse counseling and treatment.

a. The recipient is 16 years of age or older; and

b. The recipient has a diagnosis of opioid dependence; and

c. Requests for a diagnosis of chronic pain will not be approved; and

d. There is documentation the recipient has honored all of their office visits; and

e. The medication is being prescribed by a physician with a Drug Addiction Treatment Act (DATA) of 2000 waiver who has a unique "X" DEA number; and

f. All of the following are met:

1. The recipient will not utilize opioids, including tramadol, concurrently with the requested agent; and

2. If the recipient is currently utilizing an opioid, medical documentation must be provided stating the recipient will discontinue the opioid prior to initiation of buprenorphine or buprenorphine/naloxone.

g. Requests for buprenorphine will be approved if one of the following is met:

1. The recipient is a pregnant female;

2. There is documentation that the recipient is breastfeeding an infant who is dependent on methadone or morphine;

3. The recipient has had an allergy to a buprenorphine/naloxone; or

4. The recipient has moderate to severe hepatic impairment (Child-Pugh B to C).

d. Requests that exceed the quantity limit must meet all of the following:

1. There is documentation in the recipient's medical record that the requested dose is the lowest effective dose for the recipient; and

2. The treatment plan has been provided.

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

ZZ. Vivitrol® (naltrexone)

Therapeutic Class: Opioid Dependence Agents
Last Reviewed by DUR Board: January 28, 2016

Vivitrol® (naltrexone®) 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

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

   a. The drug is being used for an FDA approved indication; and

   b. The drug must be delivered directly to the prescriber's office; and

   c. The drug is only to be administered once per month; and

   d. Routine urine screening and monitoring is recommended.

2. Prior Authorization Guidelines

   a. Prior Authorization approvals will be for six months.

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

INTRODUCTION

Products for Treatment of Opioid Dependence

- The American Psychiatric Association (APA) defines opioid use disorder as a syndrome characterized by a problematic pattern of opioid use, leading to clinically significant impairment or distress (*APA 2013*).
  - In 2015, approximately 2 million Americans had a substance use disorder involving prescription pain relievers and 591,000 had a substance use disorder involving heroin (*American Society of Addiction Medicine [ASAM] 2016*).
- Methadone, buprenorphine (with or without naloxone), and naltrexone are Food and Drug Administration (FDA)-approved for the detoxification and maintenance treatment of opioid dependence (*Micromedex 2.0 2018*).
  - Methadone products, when used for the treatment of opioid addiction in detoxification or maintenance programs, may be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs may dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (Code of Federal Regulations, Title 42, Sec 8).
  - The Drug Addiction Treatment Act of 2000 expanded the clinical context of medication-assisted opioid addiction treatment by allowing qualified physicians to dispense or prescribe specifically approved medications, like buprenorphine, for the treatment of opioid addiction in treatment settings other than the traditional Opioid Treatment Program. In addition, DATA reduced the regulatory burden on physicians who choose to practice opioid addiction therapy by permitting qualified physicians to apply for and receive waivers of the special registration requirements defined in the Controlled Substances Act (*Center for Substance Abuse Treatment 2004*).
  - Naltrexone, an opioid antagonist, is only indicated for the prevention of relapse after opioid detoxification; patients must be opioid-free for at least 7 to 10 days prior to initiation of naltrexone therapy in order to avoid precipitation of withdrawal.
- All buprenorphine products are Schedule III controlled substances (*Drugs@FDA 2018*).
- In 2012, Reckitt Benckiser Pharmaceuticals notified the FDA that they were voluntarily discontinuing production of Suboxone (buprenorphine/naloxone) sublingual tablets as a result of increasing concerns over accidental pediatric exposure with the tablets. The unique child-resistant, unit-dose packaging of the film formulation is believed to be a contributing factor to reduce exposure rates in children. Generic formulations of the sublingual tablets remain available.
- In November 2017, the FDA approved Sublocade (buprenorphine ER) subcutaneous injection for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days.
  - Sublocade is injected as a liquid and the subsequent precipitation of the polymer creates a solid depot which contains buprenorphine. Buprenorphine is released via diffusion from, and the biodegradation of, the depot.
- Lofexidine, an oral central alpha-2 agonist, was approved in May 2018 for the mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults. This product is indicated for short-term use, up to 14 days, during the period of peak opioid withdrawal symptoms.
- Included in this review are the products that are FDA-approved to be used in the treatment of opioid dependence; however, methadone products are not included since they must be dispensed in an opioid treatment program when used for the treatment of opioid addiction in detoxification.
- Medispan Class: Opioid Use Disorder Agents

Table 1. Medications for Treatment of Opioid Dependence Included Within Class Review

Drug	Generic Availability
Single Entity Agents	
Lucemyra (lofexidine) tablet	-
naltrexone hydrochloride* tablet	✔

Drug	Generic Availability
Sublocade (buprenorphine) subcutaneous injection	-
Subutex (buprenorphine)* sublingual tablet	✔
Vivitrol (naltrexone) intramuscular injection	-
Combination Products	
Bunavail (buprenorphine/naloxone) buccal film	-
Suboxone‡ (buprenorphine/naloxone) sublingual tablets	✔
Suboxone (buprenorphine/naloxone) sublingual film	✔ †
Zubsolv (buprenorphine/naloxone) sublingual tablets	-

*Brand name product was discontinued; however, generic formulations are available.
‡Suboxone tablets were discontinued; however, generic formulations are available and brand name Suboxone is available as a film.
†Dr. Reddy and Mylan received FDA approval for AB-rated generic versions of the Suboxone sublingual film. Mylan has not yet launched their generic version. The manufacturer (Indivior) of brand Suboxone also announced it will pursue an immediate injunction against Dr. Reddy's "at-risk" launch.

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

Products for Emergency Treatment of Opioid Overdose

- Opiate overdose continues to be a major public health problem in the United States (U.S.). It has contributed significantly to accidental deaths among those who use or abuse illicit and prescription opioids. The number of opioid overdoses has risen in recent years, partly due to a nearly 4-fold increase in the use of prescribed opioids for the treatment of pain. Overdose deaths involving prescription opioid analgesics increased to about 19,000 deaths in 2014, more than 3 times the number in 2001 (*Substance Abuse and Mental Health Services Administration [SAMHSA] 2016)*.
- Death following opioid overdose can be averted by emergency basic life support and/or the timely administration of an opioid antagonist such as naloxone. As a narcotic antagonist, naloxone displaces opiates from receptor sites in the brain and reverses respiratory depression, which usually is the cause of overdose deaths *(SAMHSA 2016, World Health Organization [WHO] 2014)*.
- Naloxone is provided to patients through the regular course of medical care, by pharmacist-initiated collaborative practice agreements, or through community-based opioid overdose prevention programs (*Doe-Simkins 2014*).
- Recognizing the potential value of providing naloxone to laypersons, some states have passed laws and changed regulations authorizing prescribers to provide naloxone through standing orders and/or to potential overdose witnesses as well as protecting those who administer naloxone from penalties for practicing medicine without a license (*MMWR 2012, Coffin 2018*).
- In patients with opioid overdose, naloxone begins to reverse sedation, respiratory depression, and hypotension within 1 to 2 minutes after intravenous (IV) administration, 2 to 5 minutes after intramuscular (IM) or subcutaneous (SC) administration, and 8 to 13 minutes after intranasal (IN) administration. Since the half-life of naloxone is much shorter than that of most opioids, repeated administration may be necessary (*Lexicomp 2018)*.
- Naloxone was first approved by the FDA in 1971. In April 2014, an auto-injector formulation of naloxone was approved (Evzio) which incorporates both audio and visual instructions to guide the person administering the drug during a medical emergency. In November 2015, the FDA approved the first IN formulation of naloxone (Narcan nasal spray). Prior to the approval of these products, naloxone was only available in glass vials and ampules, which were distributed with syringes and needles for manual injection or with syringes and atomizers for off-label IN administration (*Evzio FDA Summary Review 2014*).
- Included in this review are the naloxone products that are FDA-approved for opioid overdose.
- Medispan Class: Opioid Antagonists

Table 2. Medications for Emergency Treatment of Opioid Overdose Included Within Class Review

Drug	Generic Availability
Evzio (naloxone hydrochloride [HCl]) auto-injector	-
Narcan (naloxone HCl)* injection	✔
Narcan (naloxone HCl) nasal spray	-

*Narcan injection was discontinued; however, generic formulations are available

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

INDICATIONS

Table 3. Food and Drug Administration Approved Indications for Buprenorphine and Buprenorphine/Naloxone Products

Indication	Single Entity Agent		Combination Products			
	Sublocade (buprenorphine) subcutaneous injection	Subutex (buprenorphine) sublingual tablets	Bunavail (buprenorphine/ naloxone) film	Suboxone (buprenorphine /naloxone) sublingual tablets	Suboxone (buprenorphine/ naloxone) film	Zubsolv (buprenorphine /naloxone) sublingual tablets
Treatment of opioid dependence			✔		✔	✔
Treatment of opioid dependence and is preferred for induction		✔				
Maintenance treatment of opioid dependence				✔		
Treatment of moderate to severe opioid use disorder†	✔					

†For use in patients who initiated treatment with transmucosal buprenorphine-containing product, followed by dose adjustment for at least 7 days.

(*Prescribing information: buprenorphine sublingual tablets 2018, buprenorphine/naloxone sublingual tablets 2018, Bunavail 2018, Sublocade 2018, Suboxone film 2018, Zubsolv 2018*)

Table 4. Food and Drug Administration Approved Indications for Other Medications Used in Opioid Dependence

Indication	Lucemyra (lofexidine) tablets	naltrexone hydrochloride tablets	Vivitrol (naltrexone HCl) injection
Mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation	✔		
Blockade of the effects of exogenously administered opioids		✔	
Treatment of alcohol dependence		✔	✔
Prevention of relapse to opioid dependence following opioid detoxification			✔

(*Prescribing information: Lucemyra 2018, naltrexone tablets 2017, Vivitrol 2015*)

Table 5. Food and Drug Administration Approved Indications for Naloxone Products

Indication	Evzio (naloxone HCl) auto-injector	Narcan (naloxone HCl) injection	Narcan (naloxone HCl) nasal spray
Emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system (CNS) depression	✔		✔
Complete or partial reversal of opioid depression, including respiratory depression, induced by natural and synthetic opioids, including propoxyphene, methadone, and certain mixed agonist-antagonist analgesics: nalbuphine, pentazocine, butorphanol, and cyclazocine		✔	
Diagnosis of suspected or acute opioid overdosage		✔	
Adjunctive agent to increase blood pressure in the management of septic shock		✔	

(*Prescribing information: Evzio 2016, naloxone injection 2015, Narcan nasal spray 2017*)

Limitations of use

- Prescription of Narcan nasal spray 2 mg should be restricted to opioid-dependent patients expected to be at risk for severe opioid withdrawal in situations where there is a low risk for accidental or intentional opioid exposure by household contacts.

- 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

Products for Treatment of Opioid Dependence

- Clinical trials have demonstrated that buprenorphine/naloxone is practical and safe for use in diverse community treatment settings including primary care offices (*Amass et al 2004, Fiellin et al 2008*).
- Studies have shown that in adult patients with opioid dependence, the percentage of opioid negative urine tests was significantly higher for both buprenorphine and buprenorphine/naloxone compared to placebo, while no significant difference was seen between the 2 active treatment groups (*Daulouede et al 2010, Fudala et al 2003*). In addition, a small randomized controlled trial (N=32) also showed no significant difference in withdrawal symptoms between buprenorphine and buprenorphine/naloxone (*Strain et al 2011*).
- Several studies have compared the effectiveness of short-term detoxification to medium- or long-term maintenance treatment with buprenorphine monotherapy or buprenorphine/naloxone. Three studies have shown higher treatment retention rate or self-reported drug use with longer treatment duration compared to detoxification; however, 1 of the studies showed no significant difference in the percentage of positive urine tests between the 2 treatment groups at 12 weeks (*Kakko et al 2003, Woody et al 2008, Weiss 2011*).
- In a meta-analysis of 21 randomized controlled trials, patients receiving buprenorphine at doses ≥16 mg/day were more likely to continue treatment compared to patients receiving doses <16 mg/day; however, no significant difference was seen in the percentage of opioid positive urine tests between the high- and low-dose groups (*Fareed et al 2012*).

- Studies that compared different dosing regimens of buprenorphine showed no difference in rate of treatment retention, percentage of urine tests positive for opioids, or withdrawal symptoms (*Bickel et al 1999, Gibson et al 2008, Petry et al 1999, Schottenfeld et al 2000*).
- One study found that buprenorphine/naloxone sublingual film was comparable to the sublingual tablet form in dose equivalence and clinical outcomes (*Lintzeris et al 2013*).
- A randomized, parallel-group, noninferiority trial (N=758) found that for the treatment of patients with opioid dependence, Zubsolv (buprenorphine/naloxone) sublingual tablets was noninferior to generic buprenorphine sublingual tablets during induction and was noninferior to buprenorphine/naloxone sublingual film during early stabilization (*Gunderson et al 2015*).
- Buprenorphine has been compared to methadone in several clinical studies and reviewed in multiple meta-analyses. Overall, studies have demonstrated that buprenorphine-based therapy was as effective as methadone in the management of opioid dependence (*Farre et al 2002, Gibson et al 2008, Gowing et al 2017, Johnson et al 1992, Kamien et al 2008, Law et al 2017, Meader et al 2010, Perry et al 2013, Petitjean et al 2001, Soyka et al 2008, Strain et al 2011).* However, when low doses of buprenorphine were studied (≤8 mg/day), high doses of methadone (≥50 mg/day) proved to be more efficacious *(Farre et al 2002, Ling et al 1996, Mattick et al 2014, Schottenfeld et al 1997*).
- In a 24-week, Phase 3, double blind, placebo-controlled, randomized controlled trial (N=504), the efficacy and safety of multiple subcutaneous injections of buprenorphine (100 mg and 300 mg) over 24 weeks were assessed in treatment-seeking patients with opioid use disorder. Buprenorphine injection was shown to be superior vs placebo in achieving more illicit opioid-free weeks ($p < 0.0001$). The proportion of patients achieving treatment success (defined as any patient with at least 80% of urine samples negative for opioids combined with self-reports negative for illicit opioid use from week 5 through week 24) was statistically significantly higher in both groups receiving buprenorphine compared to the placebo group (28.4% [300 mg/100 mg], 29.1% [300 mg/300mg], and 2% [placebo]) ($p < 0.0001$) *(FDA Advisory Committee Briefing Document, Sublocade Prescribing Information)*.
- Extended-release intramuscular naltrexone was compared to buprenorphine/naloxone sublingual film in a 24-week, open-label, randomized controlled trial (N=570). More induction failures were seen with extended-release intramuscular naltrexone; as a result, in the intention-to-treat analysis, relapse-free survival was lower with extended-release intramuscular naltrexone compared to sublingual buprenorphine/naloxone. However, among patients who were able to successfully initiate treatment, extended-release intramuscular naltrexone had similar efficacy to buprenorphine/naloxone in terms of relapse prevention (*Lee et al 2018*). A 12-week, randomized, open-label, noninferiority trial (N=159) similarly found that extended-release intramuscular naltrexone was noninferior to oral buprenorphine/naloxone in terms of negative urine drug tests and days of opioid use (*Tanum et al 2017).*
- In a meta-analysis examining the efficacy of oral naltrexone for maintenance treatment of opioid dependence, oral naltrexone was no better than placebo or no pharmacologic treatment in terms of treatment retention or use of the primary substance of abuse. Based on the results of 1 study, it was also not significantly different from buprenorphine for retention, abstinence, and side effects (*Minozzi et al 2011*).
- The safety and efficacy of lofexidine for inpatient treatment of opioid withdrawal symptoms was examined in an 8-day, randomized, double-blind, placebo-controlled trial (N=264). In this study, patients treated with lofexidine had lower scores on the Short Opioid Withdrawal Scale (SOWS) Gossop scale on day 3 compared to placebo. More patients in the placebo group terminated study participation early (*Gorodetzky et al 2017).* Similar resulted were found in another, unpublished trial *(Lucemyra prescribing information 2018)*. Meta-analyses have found that although lofexidine reduces withdrawal symptoms compared to placebo, it is less effective than buprenorphine for managing opioid withdrawal in terms of withdrawal severity, withdrawal duration, and likelihood of treatment completion *(Gowing et al 2016, Gowing et al 2017)*. It is likely to be less effective than buprenorphine or methadone for opioid detoxification (*Meader 2010*).

Products for Emergency Treatment of Opioid Overdose

- The approval of Evzio auto-injector and Narcan nasal spray were based on pharmacokinetic bioequivalence studies comparing these products to a generic naloxone product, delivered SC or IM. No clinical studies were required by the FDA (*Prescribing information: Evzio 2016, Narcan 2017*).
  - The manufacturers also conducted a human factors validation study in which participants were asked to deliver a simulated dose of the drug to a mannequin without training and most demonstrated appropriate use of the device (*FDA Summary Review: Evzio 2014, Narcan nasal spray 2015*).
- Studies have suggested that IN naloxone is an effective option in the treatment of opioid overdose (*Kelly et al 2005, Kerr et al 2009, Merlin et al 2010, Robertson et al 2009, Sabzghabaee et al 2014*).

- A meta-analysis of naloxone studies found that lay administration of naloxone was associated with significantly increased odds of recovery compared with no naloxone administration (odds ratio: 8.58, 95% confidence interval [CI], 3.90 to 13.25) (*Giglio et al 2015*).
- A 2-year, non-randomized intervention study found that prescription of naloxone to patients who were prescribed long-term opioids for chronic pain was associated with a 47% decrease in opioid-related emergency visits per month after 6 months and a 63% decrease after 1 year compared to those who did not receive naloxone (*Coffin et al 2016*).

CLINICAL GUIDELINES

- The American Academy of Pediatrics (AAP), APA, American Society of Addiction Medicine (ASAM), Center for Substance Abuse Treatment (CSAT)/United States Substance Abuse and Mental Health Services Administration (SAMHSA), and the Veterans Health Administration (VHA) have published guidelines for the treatment of opioid dependence. In general, these guidelines support access to pharmacological therapy for the management of opioid dependence. Buprenorphine/naloxone combination products may be used for induction and maintenance. In pregnant women for whom buprenorphine therapy is selected, buprenorphine alone (ie, without naloxone) is recommended. Naltrexone may be considered for the prevention of relapse, although outcomes with this medication are often adversely affected by poor adherence. Extended-release injectable naltrexone may reduce, but not eliminate, some of the problems with oral naltrexone adherence. The VHA guideline recommends extended-release injectable naltrexone if opioid agonist treatment is not feasible; it does not recommend for or against oral naltrexone (*CSAT 2004, CSUP 2016, Kampman 2015, Kleber et al 2006, Kraus et al 2011, VHA 2015*).
- Clinical practice guidelines from ASAM and VHA recommend against withdrawal management alone due to the high risk of relapse compared with treatment with maintenance therapy. However, opioid withdrawal can be managed with either gradually tapering doses of opioid agonists or use of alpha-2 adrenergic agonists (eg, clonidine) along with other non-narcotic medications *(Kampman 2015, VHA 2015).*
  - Using tapering doses of opioid agonists has been shown to be superior to alpha-2 adrenergic agonists in terms of retention and opioid abstinence. However, the use of non-opioid medications may be the only option available to clinicians in some healthcare settings and may also facilitate the transition of patients to opioid antagonist medications (eg, naltrexone) and help prevent subsequent relapse.
- Various organizations including the World Health Organization (WHO) and the ASAM have endorsed the availability of naloxone for patients, bystanders, and first responders for the emergency management of suspected opioid overdose. It is recommended that people who are likely to witness an overdose should have access to and be trained in the use of naloxone (*WHO 2014, Kampman 2015*).
  - According to the WHO guidelines for community management of opioid overdose, naloxone is effective when delivered by IV, IM, SC, and IN routes of administration. Persons using naloxone should select a route of administration based on the formulation available, their skills in administration, the setting, and local context.

SAFETY SUMMARY

Products for Treatment of Opioid Dependence

- Buprenorphine and buprenorphine/naloxone products are contraindicated in patients with known hypersensitivity to the active ingredients.
- Buprenorphine products have several warnings and precautions, including: Abuse potential; respiratory depression; CNS depression; unintentional pediatric exposure; neonatal opioid withdrawal; adrenal insufficiency; risk of opioid withdrawal with abrupt discontinuation of treatment; hepatitis and hepatic events; hypersensitivity reactions; precipitation of opioid withdrawal signs and symptoms; use in patients with impaired hepatic function; impairment of ability to drive or operate machinery; orthostatic hypotension; elevation of cerebrospinal fluid pressure; elevation of intracholedochal pressure; and effects in acute abdominal conditions
- Concomitant use of buprenorphine and benzodiazepines or other CNS depressants increases the risk for adverse events, including overdose, respiratory depression, and death. Cessation of benzodiazepines or other CNS depressants is preferred in most cases of concomitant use. This additional warning was added to opioid products in February 2018 after data demonstrated an increased risk of mortality in patients receiving benzodiazepines while on opioid maintenance treatment (*Abrahamsson et al 2017, FDA Drug Safety Communication 2017*).

- The buprenorphine subcutaneous injection also has several unique warnings and precautions, including: serious harm or death could result if administered IV (boxed warning); risks associated with treatment of emergent acute pain; use in patients at risk for arrhythmia.
- In the treatment of addiction involving opioid use in pregnant women, the buprenorphine/naloxone combination product is not recommended for use (insufficient evidence); however, the buprenorphine monoproduct is a reasonable and recommended option for use.
- Similar to other opiate products, these products may increase intracholedochal pressure, increase cerebrospinal fluid pressure, and obscure diagnosis or exacerbate acute abdominal symptoms.
- These products should not be used as analgesics.
- The most common adverse reactions observed with buprenorphine and buprenorphine/naloxone products include headache, insomnia, nausea, pain, sweating, and withdrawal syndrome.
- All of the buprenorphine-containing products have an associated risk evaluation and mitigation strategy (REMS) program (*REMS@FDA 2018*).
- Lofexidine has several warnings and precautions, including: risk of hypotension, bradycardia, and syncope; risk of QT prolongation; increased risk of CNS depression with concomitant use of CNS depressant drugs; and increased risk of opioid overdose in patients who complete opioid discontinuation and resume opioid use.
- Sudden discontinuation of lofexidine can cause a marked rise in blood pressure and symptoms that include diarrhea, insomnia, anxiety, chills, hyperhidrosis, and extremity pain. Lofexidine should be discontinued by gradually reducing the dose.
- The most common adverse reactions observed with lofexidine include orthostatic hypotension, bradycardia, hypotension, dizziness, somnolence, sedation, and dry mouth.
- The safety of lofexidine in pregnancy has not been established.
- Naltrexone products are contraindicated in: patients receiving opioid analgesics; patients currently dependent on opioids (including those currently maintained on opioid agonists); patients in acute opioid withdrawal; individuals who have failed a naloxone challenge test or have a positive urine screen for opioids; individuals with a history of sensitivity to naltrexone or other components of the product; and individuals with acute hepatitis or liver failure (oral naltrexone only). Extended-release injectable naltrexone is contraindicated in patients with hypersensitivity to polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other component of the diluent.
- Naltrexone can precipitate withdrawal if given to an opioid-dependent patient. Prior to initiating naltrexone, an opioid-free interval of 7 to 10 days is recommended for patients previously dependent on short-acting opioids; patients transitioning from buprenorphine or methadone may be vulnerable to precipitation of withdrawal symptoms for up to 2 weeks. A naloxone challenge test may be helpful to determine whether or not the patient has had a sufficient opioid-free period prior to initiating naltrexone.
- Patients may be more vulnerable to opioid overdose after discontinuation of naltrexone due to decreased opioid tolerance.
- Monitor patients on naltrexone for the development of depression or suicidality.
- Warnings unique to extended-release intramuscular naltrexone include: injection site reactions, which may be severe; eosinophilic pneumonia; hypersensitivity reactions, including anaphylaxis; use in patients with thrombocytopenia or any coagulation disorder; and interference with certain immunoassay methods of urine opioid detection.
- The most common adverse reactions observed with oral naltrexone include difficulty sleeping, anxiety, nervousness, abdominal pain/cramps, nausea/vomiting, low energy, joint and muscle pain, and headache. The most common adverse reactions observed with extended-release intramuscular naltrexone include hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache.
- There are no adequate and well-controlled studies of naltrexone in pregnant women; it should be used only if the potential benefit justifies the potential risk to the fetus.
- Extended-release intramuscular naltrexone has a REMS program due to the risk of severe injection site reactions (*REMS@FDA 2018*).

Products for Emergency Treatment of Opioid Overdose

- These products are contraindicated in patients with hypersensitivity to naloxone or to any of the other ingredients.
- These products carry warnings and precautions for risks of recurrent respiratory and CNS depression, limited efficacy with partial agonists or mixed agonists/antagonists (eg, buprenorphine, pentazocine), and precipitation of severe opioid withdrawal.

- Naloxone may precipitate acute withdrawal symptoms in opioid-dependent patients including anxiety, tachycardia, sweating, piloerection, yawning, sneezing, rhinorrhea, nausea, vomiting, diarrhea, increased blood pressure, and abdominal or muscle cramps. Opioid withdrawal signs and symptoms in neonates also include convulsions, excessive crying, and hyperactive reflexes.

DOSING AND ADMINISTRATION

Table 6a. Dosing and Administration for Products for Treatment of Opioid Dependence

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Single Entity Agents				
Lucemyra (lofexidine)	Tablet	Oral	4 times daily at 5- to 6-hour intervals	• May be continued for up to 14 days with dosing guided by symptoms • Adjust dose for patients with hepatic or renal impairment
Naltrexone hydrochloride	Tablet	Oral	Single daily dose May also be dosed every other day or every 3 days	• Contraindicated in patients with acute hepatitis or liver failure • Use caution in patients with hepatic or renal impairment
Sublocade (buprenorphine)	Subcutaneous injection	SC	Monthly (minimum 26 days between doses)	• Can only be administered by a healthcare provider • Patients with moderate or severe hepatic impairment are not candidates for this product
Subutex (buprenorphine)	Sublingual tablets	Oral	Single daily dose	• Severe hepatic impairment: Consider reducing the starting and titration incremental dose by half and monitor for signs and symptoms of toxicity or overdose.
Vivitrol (naltrexone extended-release)	Intramuscular injection	IM	Monthly or every 4 weeks	• Can only be administered by a healthcare provider • Use caution in patients with moderate to severe renal impairment
Combination Products				
Bunavail, Suboxone, Zubsolv (buprenorphine/ naloxone)	Buccal film (Bunavail) Sublingual film (Suboxone) Sublingual tablet (Zubsolv; generics equivalent to Suboxone tablet)	Oral	Bunavail: Single daily dose (except day 1 of induction for patients dependent on heroin or other short-acting opioid products: start with an initial dose of 2.1 mg/0.3 mg and repeat at approximately 2 hours, under supervision, to a total dose of 4.2 mg/0.7 mg based on the control of acute withdrawal symptoms) Suboxone: Single daily dose (except day 1 of induction:	• These products should generally be avoided in patients with severe hepatic impairment and may not be appropriate for patients with moderate hepatic impairment.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			titrate in buprenorphine 2 mg to 4 mg increments at approximately 2 hour intervals based on the control of acute symptoms) Sublingual tablet generics (Suboxone): Single daily dose Zubsolv: Single daily dose (except day 1 of induction: divided into 1 to 2 tablets of 1.4 mg/0.36 mg at 1.5 to 2 hour intervals)	

See the current prescribing information for full details

Table 6b. Equivalent Doses of Buprenorphine/Naloxone Combination Products[a]

Bunavail buccal film	buprenorphine/naloxone sublingual tablets and/or Suboxone sublingual film	Zubsolv sublingual tablets
-	2 mg/0.5 mg	1.4 mg/0.36 mg
2.1 mg/ 0.3 mg	4 mg/1 mg	2.9 mg/0.71 mg
4.2 mg/ 0.7 mg	8 mg/2 mg	5.7 mg/1.4 mg
6.3 mg/1 mg	12 mg/3 mg	8.6 mg/2.1 mg
	16 mg/4 mg	11.4 mg/2.9 mg

[a] Systemic exposures of buprenorphine and naloxone may differ when patients are switched from tablets to films or vice versa.

Table 7. Dosing and Administration for Products for Emergency Treatment of Opioid Overdose

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Evzio (naloxone HCl)	Auto-injector	IM/SC	• After initial dose, additional doses should be administered, using a new device, if the patient does not respond or responds and then relapses into respiratory depression. • Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.	• The requirement for repeat doses depends upon the amount, type, and route of administration of the opioid being antagonized.
Naloxone HCl	Vials, prefilled syringe, solution cartridge	IV	*Adults:* • An initial dose may be administered IV. It may be repeated at 2 to 3 minute intervals if the desired degree of counteraction and improvement in respiratory functions are not obtained.	• IM or SC administration may be necessary if the IV route is not available. • The American Academy of Pediatrics, however, does not endorse SC or IM administration in opiate intoxication since absorption may be erratic or delayed.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			Children: • The usual initial dose in children is given IV; a subsequent dose may be administered if the desired degree of clinical improvement is not obtained.	
Narcan (naloxone HCl)	Nasal spray	Intranasal	• A single spray should be administered into 1 nostril. • Additional doses should be administered, using a new nasal spray device in alternating nostrils, if the patient does not respond or responds and then relapses into respiratory depression. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.	

CONCLUSION

Products for Treatment of Opioid Dependence

- Buprenorphine sublingual tablets, buprenorphine/naloxone sublingual tablets, Bunavail (buprenorphine/naloxone) buccal film, Sublocade (buprenorphine) subcutaneous injection, Suboxone (buprenorphine/naloxone) sublingual film, and Zubsolv (buprenorphine/naloxone) sublingual tablets are used for the treatment of opioid dependence. Some products are indicated for maintenance treatment only, while others are indicated for both induction and maintenance.
- Buprenorphine is suggested as a first-line maintenance treatment for opioid use disorder; it may be preferred over methadone because it is safer and does not require clinic-based treatment. Buprenorphine is typically administered in a combination product with naloxone, an opioid antagonist, to discourage abuse. These agents are Schedule III controlled substances (*Strain 2018*).
- Clinical trials have demonstrated that buprenorphine/naloxone is practical and safe for use in diverse community treatment settings including primary care offices (*Amass et al 2004, Fiellin et al 2008*).
- Physicians prescribing buprenorphine for opioid dependency must undergo specialized training due to the potential for abuse and diversion. Because of these risks, buprenorphine monotherapy should be reserved for patients who are pregnant or have a documented allergy to naloxone (*DATA 2000, CSAT 2004*).
- Overall, studies have demonstrated that buprenorphine-based therapy was as effective as methadone in the management of opioid dependence (*Farre et al 2002, Gibson et al 2008, Gowing et al 2017, Johnson et al 1992, Kamien et al 2008, Meader et al 2010, Petitjean et al 2001, Soyka et al 2008, Mattick et al 2014, Strain et al 2011*).
- The most common adverse reactions observed with buprenorphine and buprenorphine/naloxone products include headache, insomnia, nausea, pain, sweating, and withdrawal syndrome. These products also have REMS criteria.
- Lofexidine is an oral central alpha-2 agonist indicated for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation.
- Meta-analyses have found that although lofexidine reduces withdrawal symptoms compared to placebo, it is less effective than buprenorphine for managing opioid withdrawal in terms of withdrawal severity, withdrawal duration, and likelihood of treatment completion *(Gowing et al 2016, Gowing et al 2017)*. It is likely to be less effective than buprenorphine or methadone for opioid detoxification (*Meader 2010*).

- The most common adverse reactions observed with lofexidine include orthostatic hypotension, bradycardia, hypotension, dizziness, somnolence, sedation, and dry mouth.
- Naltrexone is an opioid antagonist. Oral naltrexone is indicated for the treatment of alcohol dependence and blockade of the effects of exogenously administered opioids. Extended-release intramuscular naltrexone is indicated for the treatment of alcohol dependence and the prevention of relapse to opioid dependence following opioid detoxification. In order to initiate naltrexone treatment, patients must be opioid-free for at least 7 to 10 days to avoid precipitation of withdrawal.
- In a meta-analysis examining the efficacy of oral naltrexone for maintenance treatment of opioid dependence, oral naltrexone was no better than placebo or no pharmacologic treatment in terms of treatment retention or use of the primary substance of abuse. Based on the results of 1 study, it was also not significantly different from buprenorphine for retention, abstinence, and side effects (*Minozzi et al 2011*). Extended-release intramuscular naltrexone has been shown to have similar efficacy to oral buprenorphine/naloxone among patients who are able to successfully initiate treatment (*Lee et al 2018, Tanum et al 2017*).
- The most common adverse reactions observed with oral naltrexone include difficulty sleeping, anxiety, nervousness, abdominal pain/cramps, nausea/vomiting, low energy, joint and muscle pain, and headache. The most common adverse reactions observed with extended-release intramuscular naltrexone include hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache. Extended-release intramuscular naltrexone also has a REMS program.
- The AAP, APA, ASAM, CSAT/SAMHSA, and VHA publish guidelines for the treatment of opioid dependence. These guidelines support access to pharmacological therapy for the management of opioid dependence. Buprenorphine/naloxone combination products may be used for induction and maintenance. In pregnant women for whom buprenorphine therapy is selected, buprenorphine alone (ie, without naloxone) is recommended. Naltrexone may be considered for the prevention of relapse, although outcomes with this medication are often adversely affected by poor adherence. Extended-release injectable naltrexone may reduce, but not eliminate, some of the problems with oral naltrexone adherence. The VHA guideline recommends extended-release injectable naltrexone if opioid agonist treatment is not feasible; it does not recommend for or against oral naltrexone (*CSAT 2004, CSUP 2016, Kampman et al 2015, Kleber et al 2006, Kraus et al 2011, VHA 2015).*
- Clinical practice guidelines from ASAM and VHA recommend against withdrawal management alone due to the high risk of relapse compared with treatment with maintenance therapy. However, opioid withdrawal can be managed with either gradually tapering doses of opioid agonists or use of alpha-2 adrenergic agonists (eg, clonidine) along with other non-narcotic medications. Lofexidine has not been added to practice guidelines but it likely has a similar place in therapy as clonidine *(Kampman 2015, VHA 2015).*

Products for Emergency Treatment of Opioid Overdose

- Naloxone is the standard of care to treat opioid overdose. It has been used by medical personnel for over 40 years and its use outside of the medical setting has gained traction through improvements in legislation and community-based opioid overdose prevention programs.
- Evzio (naloxone HCl) auto-injector, naloxone HCl injection, and Narcan (naloxone HCl) nasal spray are approved for treatment of known or suspected opioid overdose. Prior to the approval of Evzio and Narcan nasal spray, naloxone was only available in glass vials and ampules, which were distributed with syringes and needles for manual injection or with syringes and atomizers for off-label IN administration (*Evzio FDA Summary Review 2014*).
- Naloxone can be administered IV, IM, or SC using naloxone vials/syringes as well as IM or SC using an auto-injector device (Evzio). Although Narcan nasal spray is the first IN formulation to be FDA-approved, naloxone has historically been given IN off-label via kits containing a syringe and an atomization device. Potential advantages of IN administration of naloxone include easier disposal, no needle stick risk, and avoidance of needle anxiety. Both Evzio and Narcan nasal spray are designed for use by laypersons.
- The approval of Evzio and Narcan nasal spray were based on pharmacokinetic bioequivalence studies. No new clinical studies were required by the FDA.
- Various organizations including WHO and ASAM have endorsed the availability of naloxone for patients, bystanders, and first responders for the emergency management of suspected opioid overdose. It is recommended that people who are likely to witness an overdose should have access to and be trained in the use of naloxone (*WHO 2014, Kampman 2015*).

- According to the WHO guidelines for community management of opioid overdose, naloxone is effective when delivered by IV, IM, SC, and IN routes of administration. Persons using naloxone should select a route of administration based on the formulation available, their skills in administration, the setting, and local context.

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Publication Date: August 23, 2018

Attention Deficit Disorder (ADD)/Attention Deficit Hyperactivity Disorder (ADHD)

Prior Authorization Guideline

Guideline Name ADD/ADHD Agents

1 . Criteria

Diagnosis	ADD/ADHD
Approval Length	12 Months
Guideline Type	Prior Authorization

Approval Criteria

1. All of the following:

- Patient is between 5 years of age to less than 18 years of age
- Prescriber is a psychiatrist
- Diagnosis documented as one of the following ICD-10 codes: F90.0, F90.1, F90.2, F90.8 or F90.9

OR

2. All of the following:

    a. Diagnosis of ADD/ADHD (i.e. ICD-10 codes: F90.0, F90.1, F90.2, F90.8 or F90.9)

AND

    b. Documentation in the patient's medical record of all of the following:

i. The decision to medicate for ADD or ADHD is based on problems that are persistent and sufficiently severe to cause functional impairment in one or more of the following social environments: school, home, work or with peers

AND

ii. Other treatable causes of ADD or ADHD have been ruled out

AND

c. One of the following:

i. Request is not for a long-acting agent

OR

ii. Request is for a long-acting agent and one of the following:

- Patient is not currently on a different long-acting ADD/ADHD agent
- Patient is currently on a different long-acting ADD/ADHD agent and there is documentation that the patient will be discontinuing the previous long-acting agent within 30 days and switching to the new agent

AND

d. One of the following:

i. All of the following:

1. Patient is less than 18 years of age

AND

2. Patient has had an initial evaluation or regular examination within the past 12 months by the treating physician, pediatrician, psychiatrist, or neurologist that documents all of the following:

- Developmental history
- Physical evaluation
- Any medical or psychological history
- Any primary neurological diagnosis (including any history of past psychiatric, psychologic, or neurological treatment for ADD/ADHD)

- ~~Any family history including: ADD and ADHD, tic disorder, substance abuse disorder, conduct disorder, personality disorder and other anxiety disorders, past or present family stressors, crises, or any abuse or neglect~~
- An interview with parent(s) or guardian(s)
- School information and Standardized Teachers Rating Scales testing reports (such as Test of Variables of Attention [TOVA], achievement test, neuropsychological testing if indicated, Conner's scale, speech and language evaluation)

AND

a. A review of all of the following:

- Diagnostic symptoms of ADD/ADHD
- Presence or absence-child behavior checklist
- Development and context of symptoms and their resulting impairment with family, peers, and in school
- Diagnostic symptoms of possible alternate or comorbid psychiatric diagnosis

OR

ii. All of the following:

1. Patient is 18 years of age or older

AND

2. Documentation in the patient's medical record that an initial evaluation has been done which includes all of the following:

- A complete psychiatric assessment (past and present)
- Diagnostic symptoms of ADD or ADHD
- History of development and context of symptoms and resulting impairment (academic achievement, learning disorder evaluation)

AND

3. Documentation in the patient's medical record that the patient has been assessed for ALL of the following:

- A medical history (including medical or primary neurological diagnoses)
- Any history of other psychiatric disorder(s) and the current treatment regimen
- Review of medications that could be causing symptoms (e.g. phenobarbital, steroids)
- Other possible comorbid psychiatric diagnoses (especially personality disorder, mood disorder, depression or mania, anxiety, dissociative disorder, tic disorder including Tourette's, or substance abuse disorder)

- ~~Family history of ADD or ADHD, tic disorder, substance abuse disorder, conduct disorder, personality disorder, mood disorder and anxiety disorder, possible family stressors, and any history of abuse or neglect~~

AND

4. One of the following:

    a. Patient does not have a history of other psychiatric disorders

OR

    b. Both of the following:

- Patient has a history of other psychiatric disorders
- Documentation in the patient's medical record that they are currently being treated for the other psychiatric disorders or no longer require therapy for the other psychiatric disorders

OR

3. Request meets medical necessity for approval outside of the criteria

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: April 25, 2019

Prior Authorization Criteria being reviewed: ADD/ADHD 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.

Methylphenidate (Methylin, Methylin ER, Ritalin, Ritalin SR and generic products (not methylphenidate ER 72mg tablets) may be approved for narcolepsy:

B. Individual is 6 years of age or older; **AND**
C. One of the following:
1. Individual has a diagnosis of attention deficit hyperactivity disorder (ADHD); **OR**
2. Individual has a diagnosis of narcolepsy.

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: Lisa Todd

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: April 25, 2019

Prior Authorization Criteria being reviewed: ADD/ADHD 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 feels the criteria is overly detailed and fairly expansive in its reach for such a common class of medications. Recommendation would be to eliminate criteria, manage through age limits/ quantity limits, or a simple diagnosis prior authorization.

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: RK 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: April 25, 2019

Prior Authorization Criteria being reviewed: ADD/ADHD 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.

Approval Criteria:

Patient is ≥ 6 years of age

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_____

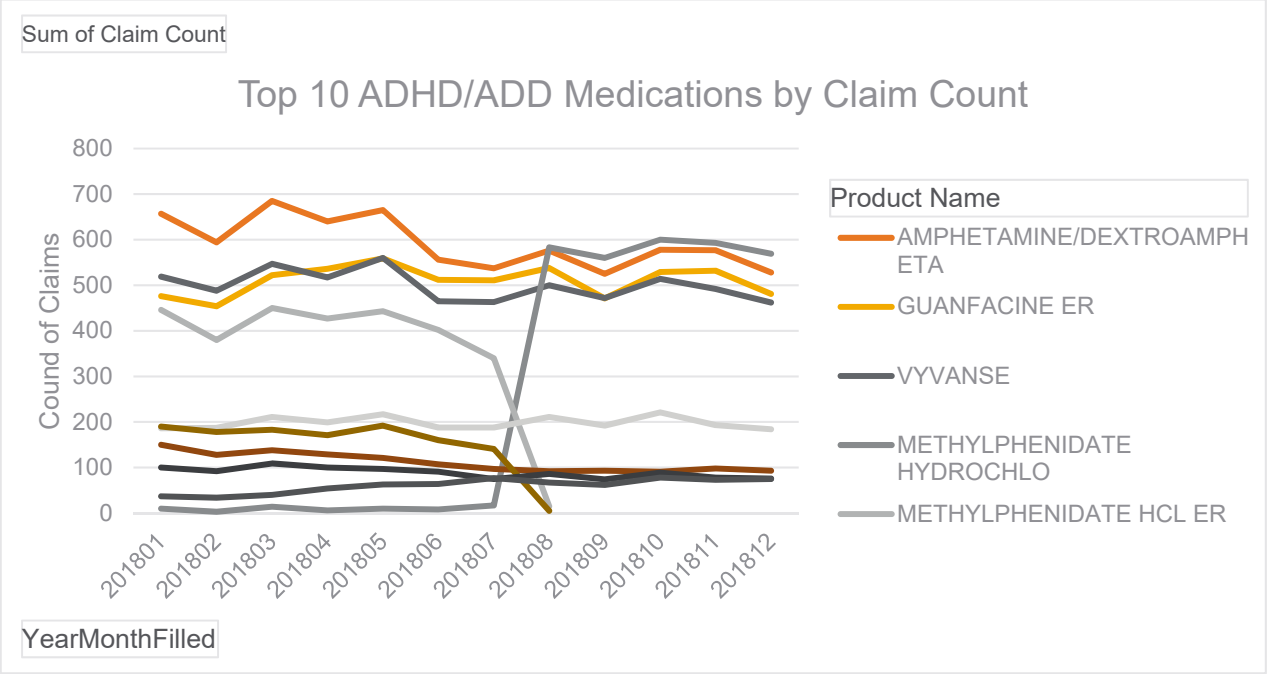
Signature of individual completing this form: _____Tom Beranek_____

ADD/ADHD Medications

Summary of Utilization
January 1, 2018 - December 31, 2018
Fee for Service Medicaid

Product Name	Member Count	Claim Count	Days Supply	Sum of Qty
ADDERALL	50	57	1,650	3,054
ADDERALL XR	2,282	2,377	71,505	74,536
ADZENYS XR-ODT	142	144	4,320	4,530
AMPHETAMINE SULFATE	5	5	135	150
AMPHETAMINE/DEXTROAMPHETA	6,411	7,118	212,145	324,834
ARMODAFINIL	65	72	1,928	1,928
ATOMOXETINE	645	724	21,258	25,601
ATOMOXETINE HYDROCHLORIDE	21	25	759	1,099
CAFFEINE CITRATE	11	11	257	1,446
CAFFEINE/SODIUM BENZOATE	1	1	1	2
CLONIDINE HCL ER	55	61	1,861	4,438
CLONIDINE HYDROCHLORIDE	20	25	750	1,320
CLONIDINE HYDROCHLORIDE E	57	63	2,209	6,099
CLONIDINE HYDROCLORIDE	2	2	60	120
CONCERTA	77	80	2,370	2,670
COTEMPLA XR-ODT	8	8	240	390
DAYTRANA	76	79	2,350	2,370
DEXMETHYLPHENIDATE HCL	341	354	10,482	16,633
DEXMETHYLPHENIDATE HCL ER	245	253	7,404	7,464
DEXMETHYLPHENIDATE HYDROC	21	21	630	630
DEXTROAMPHETAMINE SULFATE	241	278	8,279	17,824
DOPRAM	2	2	2	30
DYANAVEL XR	58	58	1,862	7,263
EVEKEO	4	4	120	120
FOCALIN	7	7	210	240
FOCALIN XR	1,023	1,067	31,522	32,116
GUANFACINE ER	5,544	6,121	182,715	190,134
GUANFACINE HYDROCHLORIDE	32	32	1,017	1,107
INTUNIV	516	585	18,391	19,767
KAPVAY	7	7	210	210
METHAMPHETAMINE HCL	1	1	30	30
METHYLPHENIDATE HCL	1,136	1,220	36,356	68,468
METHYLPHENIDATE HCL CD	105	111	3,450	3,600
METHYLPHENIDATE HCL ER	2,790	2,903	86,150	94,133
METHYLPHENIDATE HYDROCHLO	2,608	2,973	87,623	126,761
METHYLPHENIDATE HYDROCLOR	1	1	30	30
MODAFINIL	232	286	7,539	8,718
MYDAYIS	9	9	270	270
NUVIGIL	12	12	360	630
PHENTERMINE HCL	2	3	38	38
PROVIGIL	76	84	2,437	3,152
QUILLICHEW ER	105	108	3,200	4,055
QUILLIVANT XR	88	88	2,735	19,020

RITALIN	17	31	513	3,908
RITALIN LA	42	42	1,261	1,771
STRATTERA	1,210	1,337	39,987	43,395
VYVANSE	5,767	5,999	177,259	179,026
Grand Total	**32,170**	**34,849**	**1,035,880**	**1,305,130**



ADD/ADHD Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Anthem Nevada Medicaid

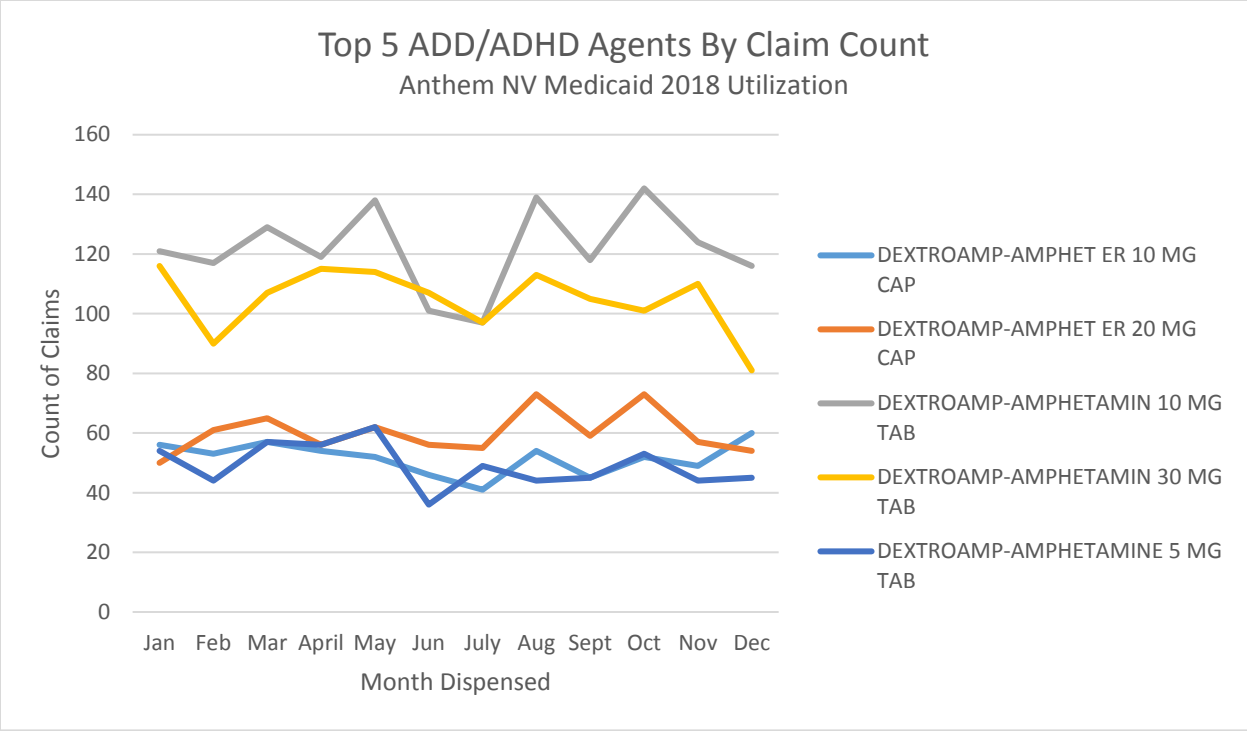
Drug	Count of Members	Count of Claims	Count of Total Days of Therapy	Count of Total Quantity
DEXTROAMP-AMPHETAMIN 10 MG TAB	1461	1461	1461	1461
DEXTROAMP-AMPHETAMIN 30 MG TAB	1256	1256	1256	1256
DEXTROAMP-AMPHET ER 20 MG CAP	721	721	721	721
DEXTROAMP-AMPHET ER 10 MG CAP	619	619	619	619
DEXTROAMP-AMPHETAMINE 5 MG TAB	589	589	589	589
DEXTROAMP-AMPHET ER 30 MG CAP	561	561	561	561
DEXTROAMP-AMPHETAMIN 15 MG TAB	541	541	541	541
METHYLPHENIDATE 10 MG TABLET	517	517	517	517
DEXTROAMP-AMPHET ER 15 MG CAP	499	499	499	499
METHYLPHENIDATE ER 36 MG TAB	445	445	445	445
METHYLPHENIDATE ER 27 MG TAB	425	425	425	425
ATOMOXETINE HCL 40 MG CAPSULE	418	418	418	418
METHYLPHENIDATE 5 MG TABLET	332	332	332	332
METHYLPHENIDATE ER 18 MG TAB	331	331	331	331
VYVANSE 30 MG CAPSULE	314	314	314	314
METHYLPHENIDATE ER 54 MG TAB	297	297	297	297
VYVANSE 40 MG CAPSULE	282	282	282	282
ATOMOXETINE HCL 25 MG CAPSULE	259	259	259	259
METHYLPHENIDATE 20 MG TABLET	241	241	241	241
VYVANSE 70 MG CAPSULE	232	232	232	232

GUANFACINE HCL ER 1 MG TABLET	231	231	231	231
DEXTROAMP-AMPHET ER 25 MG CAP	225	225	225	225
GUANFACINE HCL ER 2 MG TABLET	218	218	218	218
VYVANSE 20 MG CAPSULE	196	196	196	196
ATOMOXETINE HCL 10 MG CAPSULE	180	180	180	180
VYVANSE 50 MG CAPSULE	179	179	179	179
ATOMOXETINE HCL 60 MG CAPSULE	166	166	166	166
DEXTROAMP-AMPHET ER 5 MG CAP	164	164	164	164
GUANFACINE HCL ER 3 MG TABLET	162	162	162	162
VYVANSE 60 MG CAPSULE	159	159	159	159
ATOMOXETINE HCL 80 MG CAPSULE	142	142	142	142
ATOMOXETINE HCL 18 MG CAPSULE	113	113	113	113
DEXMETHYLPHENIDATE ER 15 MG CP	86	86	86	86
METHYLPHENIDATE ER 10 MG TAB	74	74	74	74
DEXMETHYLPHENIDATE 10 MG TAB	72	72	72	72
CLONIDINE HCL ER 0.1 MG TABLET	71	71	71	71
METHYLPHENIDATE ER 20 MG TAB	69	69	69	69
GUANFACINE HCL ER 4 MG TABLET	69	69	69	69
METHYLPHENIDATE CD 20 MG CAP	63	63	63	63
METHYLPHENIDATE CD 30 MG CAP	54	54	54	54
DEXTROAMPHETAMINE 10 MG TAB	54	54	54	54
DEXMETHYLPHENIDATE ER 10 MG CP	52	52	52	52
METHYLPHENIDATE CD 10 MG CAP	52	52	52	52
DEXMETHYLPHENIDATE 5 MG TAB	47	47	47	47
VYVANSE 10 MG CAPSULE	42	42	42	42

DEXTROAMP-AMPHETAM 7.5 MG TAB	37	37	37	37
DEXMETHYLPHENIDATE ER 20 MG CP	37	37	37	37
DEXTROAMPHETAMINE ER 15 MG CAP	37	37	37	37
METHYLPHENIDATE CD 40 MG CAP	37	37	37	37
ATOMOXETINE HCL 100 MG CAPSULE	27	27	27	27
DEXMETHYLPHENIDATE ER 30 MG CP	21	21	21	21
METHYLPHENIDATE ER(LA) 30MG CP	20	20	20	20
METHYLPHENIDATE ER(CD) 10MG CP	19	19	19	19
DEXMETHYLPHENIDATE ER 40 MG CP	19	19	19	19
DEXTROAMP-AMPHETAM 12.5 MG TAB	19	19	19	19
METHYLPHENIDATE LA 30 MG CAP	18	18	18	18
DEXTROAMPHETAMINE 5 MG TAB	18	18	18	18
METHYLPHENIDATE 5 MG CHEW TAB	18	18	18	18
METHYLPHENIDATE LA 20 MG CAP	16	16	16	16
EVEKEO 10 MG TABLET	16	16	16	16
ZENZEDI 30 MG TABLET	16	16	16	16
METHYLPHENIDATE ER(LA) 10MG CP	16	16	16	16
METHYLPHENIDATE ER(CD) 20MG CP	14	14	14	14
METHYLPHENIDATE 10 MG/5 ML SOL	14	14	14	14
VYVANSE 20 MG CHEWABLE TABLET	13	13	13	13
DYANAVEL XR 2.5 MG/ML SUSP	12	12	12	12
DEXTROAMPHETAMINE ER 10 MG CAP	12	12	12	12
VYVANSE 10 MG CHEWABLE TABLET	11	11	11	11
METHYLPHENIDATE ER(LA) 20MG CP	11	11	11	11

ADDERALL 30 MG TABLET	10	10	10	10
DEXMETHYLPHENIDATE ER 25 MG CP	10	10	10	10
VYVANSE 30 MG CHEWABLE TABLET	10	10	10	10
DEXMETHYLPHENIDATE ER 5 MG CAP	10	10	10	10
MYDAYIS ER 37.5 MG CAPSULE	7	7	7	7
METHYLPHENIDATE ER(CD) 40MG CP	7	7	7	7
QUILLIVANT XR 25 MG/5 ML SUSP	7	7	7	7
STRATTERA 60 MG CAPSULE	7	7	7	7
METHYLPHENIDATE ER(CD) 30MG CP	7	7	7	7
METHYLPHENIDATE ER(LA) 40MG CP	6	6	6	6
ADDERALL XR 20 MG CAPSULE	5	5	5	5
METHYLPHENIDATE ER(CD) 50MG CP	5	5	5	5
METHYLPHENIDATE LA 10 MG CAP	5	5	5	5
ADDERALL 20 MG TABLET	4	4	4	4
METHYLPHENIDATE 2.5 MG CHEW TB	3	3	3	3
DEXMETHYLPHENIDATE 2.5 MG TAB	3	3	3	3
METHYLPHENIDATE CD 50 MG CAP	3	3	3	3
APTENSIO XR 15 MG CAPSULE	3	3	3	3
COTEMPLA XR-ODT 17.3 MG TABLET	3	3	3	3
INTUNIV ER 2 MG TABLET	2	2	2	2
ADZENYS XR-ODT 6.3 MG TABLET	2	2	2	2
MYDAYIS ER 25 MG CAPSULE	2	2	2	2
AMPHETAMINE SULFATE 10 MG TAB	2	2	2	2
ADZENYS XR-ODT 9.4 MG TABLET	2	2	2	2
DAYTRANA 10 MG/9 HR PATCH	2	2	2	2

STRATTERA 80 MG CAPSULE	2	2	2	2
METHYLPHENIDATE LA 40 MG CAP	2	2	2	2
CONCERTA ER 27 MG TABLET	2	2	2	2
INTUNIV ER 1 MG TABLET	1	1	1	1
METHYLPHENIDATE 5 MG/5 ML SOLN	1	1	1	1
QUILLICHEW ER 20 MG CHEW TAB	1	1	1	1
CONCERTA ER 18 MG TABLET	1	1	1	1
DAYTRANA 15 MG/9 HR PATCH	1	1	1	1
DEXTROAMPHETAMINE ER 5 MG CAP	1	1	1	1
ADDERALL 15 MG TABLET	1	1	1	1
METHYLPHENIDATE LA 60 MG CAP	1	1	1	1
QUILLICHEW ER 30 MG CHEW TAB	1	1	1	1
COTEMPLA XR-ODT 25.9 MG TABLET	1	1	1	1
DEXMETHYLPHENIDATE ER 35 MG CP	1	1	1	1
METHYLPHENIDATE 10 MG CHEW TAB	1	1	1	1
MYDAYIS ER 50 MG CAPSULE	1	1	1	1
Grand Total	**15623**	**15623**	**15623**	**15623**


Top 5 ADD/ADHD Agents By Claim Count
Anthem NV Medicaid 2018 Utilization
Count of Claims
160
140
120
100
80
60
40
20
0
Jan
Feb
Mar
April
May
Jun
July
Aug
Sept
Oct
Nov
Dec
Month Dispensed
DEXTROAMP-AMPHET ER 10 MG CAP
DEXTROAMP-AMPHET ER 20 MG CAP
DEXTROAMP-AMPHETAMIN 10 MG TAB
DEXTROAMP-AMPHETAMIN 30 MG TAB
DEXTROAMP-AMPHETAMINE 5 MG TAB

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

ADD & ADHD Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
AMPHET/DEXTR TAB 20MG	677	3,863	115,077	234,514	NA
AMPHET/DEXTR TAB 30MG	390	2,554	76,222	149,934	NA
AMPHET/DEXTR TAB 10MG	629	2,408	71,750	125,808	NA
ADDERALL XR CAP 20MG	391	1,584	47,171	53,520	NA
ADDERALL XR CAP 30MG	258	1,404	41,859	46,043	NA
VYVANSE CAP 30MG	392	1,228	36,765	36,940	NA
VYVANSE CAP 40MG	265	1,042	31,114	31,090	NA
ADDERALL XR CAP 10MG	310	880	26,101	26,283	NA
VYVANSE CAP 20MG	297	876	26,143	26,189	NA
AMPHET/DEXTR TAB 5MG	269	797	23,640	37,006	NA
ADDERALL XR CAP 15MG	220	788	23,504	23,654	NA
VYVANSE CAP 50MG	187	777	23,185	23,169	NA
METHYLPHENID TAB 10MG	215	742	22,066	44,492	NA
AMPHET/DEXTR TAB 15MG	191	733	21,668	37,686	NA
VYVANSE CAP 70MG	108	562	16,770	16,770	NA
METHYLPHENID TAB 36MG ER	165	539	16,004	18,706	NA
METHYLPHENID TAB 5MG	181	483	14,256	23,808	NA
ADDERALL XR CAP 25MG	98	458	13,663	14,173	NA
METHYLPHENID TAB 20MG	92	455	13,607	30,093	NA
METHYLPHENID TAB 27MG ER	135	421	12,465	12,465	NA
VYVANSE CAP 60MG	92	408	12,242	12,242	NA
GUANFACINE TAB 2MG ER	102	406	12,146	12,326	NA
METHYLPHENID TAB 54MG ER	89	373	11,127	11,127	NA
GUANFACINE TAB 3MG ER	63	337	10,019	10,289	NA
GUANFACINE TAB 1MG ER	129	316	9,392	9,517	NA
METHYLPHENID TAB 18MG ER	98	259	7,643	7,673	NA
METHYLPHENID TAB 20MG ER	65	248	7,354	9,364	NA
ADDERALL XR CAP 5MG	93	231	6,816	7,250	NA
ATOMOXETINE CAP 40MG	65	203	5,915	6,020	NA
VYVANSE CAP 10MG	85	178	5,310	5,375	NA
GUANFACINE TAB 4MG ER	31	167	5,128	5,128	NA
ATOMOXETINE CAP 80MG	21	117	3,445	3,445	NA
ATOMOXETINE CAP 25MG	39	92	2,672	2,822	NA
METHYLPHENID TAB 10MG ER	39	71	2,114	2,294	NA
DEXMETHYLPH TAB 10MG	18	69	2,070	2,880	NA
METHYLPHENID CAP 20MG ER	25	69	2,070	2,240	NA
DEXTROAMPHET TAB 10MG	13	67	1,983	6,070	NA

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

ADD & ADHD Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
ATOMOXETINE CAP 18MG	31	63	1,804	1,923	NA
METHYLPHENID CAP 30MG ER	18	63	1,857	2,217	NA
ATOMOXETINE CAP 100MG	12	61	1,830	1,830	NA
ATOMOXETINE CAP 60MG	23	60	1,800	1,800	NA
AMPHET/DEXTR CAP 20MG ER	17	49	1,405	1,479	NA
VYVANSE CHW 20MG	24	48	1,416	1,416	NA
METHYLPHENID CAP 40MG	13	47	1,410	1,410	NA
VYVANSE CHW 30MG	17	47	1,410	1,410	NA
METHYLPHENID CAP 20MG	15	46	1,380	1,380	NA
DEXTROAMPHET CAP 15MG ER	6	42	1,237	2,324	NA
AMPHET/DEXTR TAB 7.5MG	12	37	1,110	1,320	NA
VYVANSE CHW 10MG	16	36	1,080	1,080	NA
METHYLPHENID CAP 30MG	11	35	1,050	1,050	NA
AMPHET/DEXTR CAP 10MG ER	11	33	974	974	NA
ATOMOXETINE CAP 10MG	14	33	990	990	NA
DEXMETHYLPHE CAP 20MG ER	11	33	990	990	NA
DEXMETHYLPHE CAP ER 25MG	7	31	930	930	NA
AMPHET/DEXTR CAP 30MG ER	10	28	815	965	NA
MYDAYIS CAP 25MG	6	26	780	780	NA
DEXMETHYLPH CAP 40MG ER	3	24	720	720	NA
DEXMETHYLPHE CAP 10MG ER	9	24	720	720	NA
DEXMETHYLPH TAB 5MG	7	24	720	953	NA
DEXMETHYLPH CAP 15MG ER	6	24	720	720	NA
DEXTROAMPHET CAP 10MG ER	3	24	704	2,502	NA
METHAMPHETAM TAB 5MG	4	21	630	3,030	NA
CONCERTA TAB 54MG	3	21	630	630	NA
DEXMETHYLPH CAP 30MG ER	9	20	600	630	NA
METHYLPHENID SOL 10MG/5ML	4	19	570	7,470	NA
CLONIDINE TAB 0.1MG ER	4	18	515	970	NA
EVEKEO TAB 10MG	6	16	478	1,017	NA
AMPHET/DEXTR TAB 12.5MG	4	16	480	1,050	NA
INTUNIV TAB 1MG	2	15	450	450	NA
METHYLPHENID CAP 50MG	2	15	430	430	NA
VYVANSE CHW 40MG	6	15	450	450	NA
QUILLIVANT SUS 25MG/5ML	5	14	396	1,950	NA
METHYLPHENID CHW 5MG	8	14	420	510	NA
AMPHET/DEXTR CAP 15MG ER	8	14	420	420	NA

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

ADD & ADHD Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

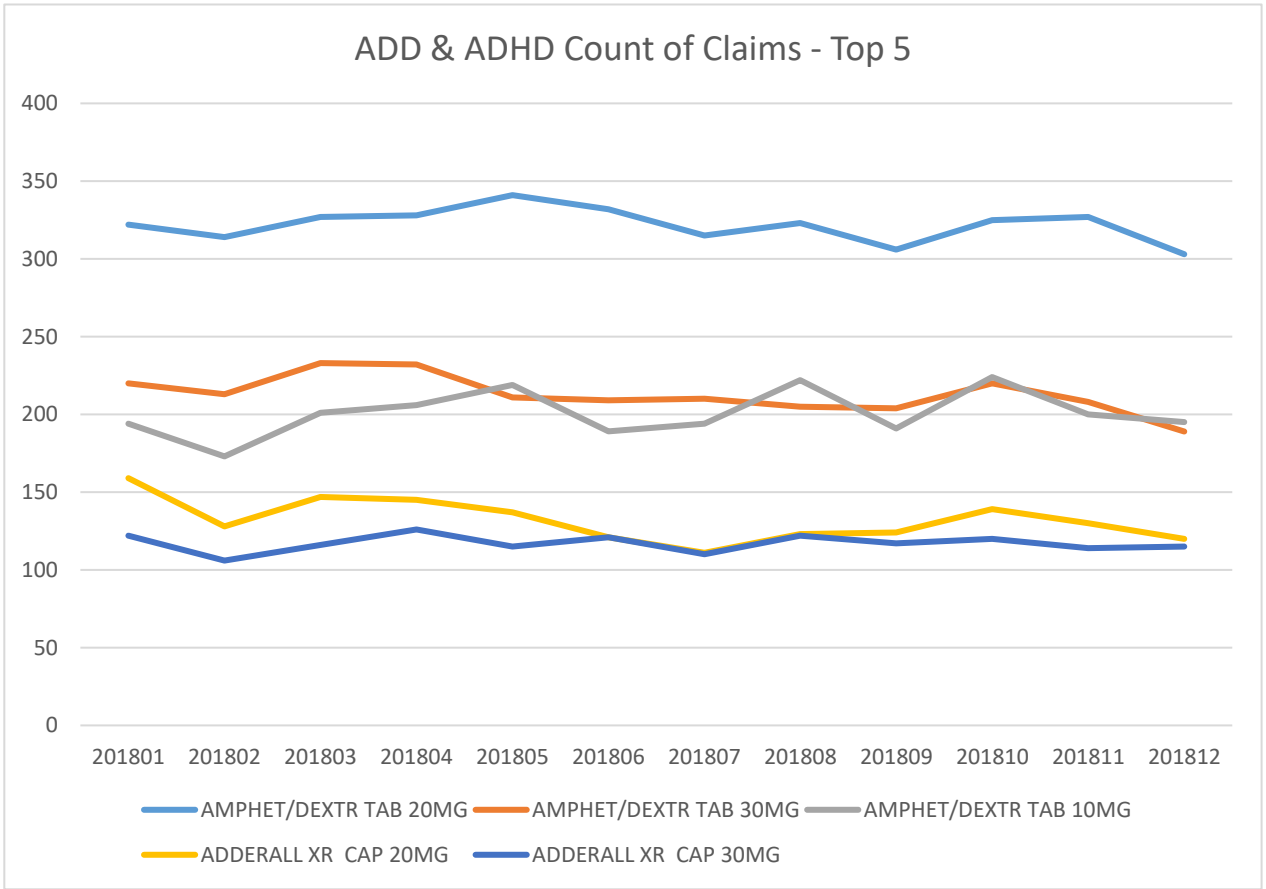
Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
AMPHET/DEXTR CAP 25MG ER	2	13	390	390	NA
STRATTERA CAP 40MG	4	13	390	390	NA
METHYLPHENID CAP 10MG	7	13	360	420	NA
INTUNIV TAB 3MG	1	12	360	360	NA
DYANAVEL XR SUS 2.5MG/ML	3	11	330	1,560	NA
ADZENYS XR TAB 18.8MG	2	11	330	330	NA
STRATTERA CAP 10MG	2	11	330	330	NA
METHYLPHENID CHW 10MG	3	10	277	570	NA
METHYLPHENID CAP 40MG ER	3	9	270	270	NA
STRATTERA CAP 80MG	2	9	250	250	NA
CONCERTA TAB 36MG	5	8	240	390	NA
ADZENYS XR TAB 12.5MG	1	8	240	240	NA
DEXMETHYLPHE CAP ER 35MG	3	7	210	210	NA
DEXMETHYLPH TAB 2.5MG	1	7	210	210	NA
METHYPHENID CAP 10MG ER	6	6	180	180	NA
VYVANSE CHW 60MG	1	6	180	180	NA
VYVANSE CHW 50MG	2	6	180	180	NA
QUILLICHEW CHW 20MG ER	3	6	180	180	NA
AMPHET/DEXTR CAP 5MG ER	4	5	150	150	NA
STRATTERA CAP 60MG	2	5	150	150	NA
DAYTRANA DIS 30MG/9HR	2	5	150	150	NA
DEXTROAMPHET CAP 5MG ER	2	5	150	240	NA
METHYLPHENID SOL 5MG/5ML	3	4	120	900	NA
DAYTRANA DIS 20MG/9HR	1	4	120	120	NA
MYDAYIS CAP 12.5MG	2	4	120	120	NA
QUILLICHEW CHW 30MG ER	1	4	120	120	NA
METHYLPHENID CAP 60MG	1	3	90	90	NA
MYDAYIS CAP 50MG	2	3	90	90	NA
METHLPHENIDA CHW 2.5MG	3	3	90	150	NA
MYDAYIS CAP 37.5MG	2	3	90	90	NA
COTEMPLA TAB 17.3MG	1	3	90	90	NA
CONCERTA TAB 18MG	3	3	90	90	NA
CONCERTA TAB 27MG	2	3	90	90	NA
INTUNIV TAB 4MG	1	2	60	60	NA
DEXTROAMPHET TAB 5MG	1	2	60	60	NA
STRATTERA CAP 25MG	2	2	60	60	NA
ADZENYS XR TAB 15.7 MG	1	2	60	60	NA

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

ADD & ADHD Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
STRATTERA CAP 18MG	1	2	60	60	NA
FOCALIN XR CAP 20MG	1	2	60	60	NA
ADDERALL TAB 10MG	1	1	30	30	NA
ADZENYS XR TAB 6.3MG	1	1	30	30	NA
DEXMETHYLPHE CAP 5MG ER	1	1	30	30	NA
EVEKEO TAB 5MG	1	1	30	30	NA
METHYLPHENID TAB 72MG ER	1	1	7	7	NA
Grand Total	**6,998**	**27,601**	**821,901**	**1,189,062**	**NA**



ADD ADHD Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
AMPHET/DEXTR TAB 20MG	446	864	25,726	47,693	$ 66,213.42
METHYLPHENID TAB 36MG ER	119	226	6,681	7,890	$ 64,748.26
AMPHET/DEXTR CAP 20MG ER	197	356	10,475	11,765	$ 53,594.72
AMPHET/DEXTR TAB 30MG	322	658	19,245	35,045	$ 43,195.99
AMPHET/DEXTR CAP 30MG ER	140	267	7,958	7,958	$ 39,453.75
VYVANSE CAP 40MG	70	139	4,170	4,170	$ 38,641.34
AMPHET/DEXTR TAB 10MG	381	638	18,570	30,123	$ 33,905.65
AMPHET/DEXTR CAP 10MG ER	126	193	5,542	5,842	$ 28,499.55
AMPHET/DEXTR CAP 15MG ER	101	179	5,200	5,290	$ 26,552.10
VYVANSE CAP 30MG	49	87	255	255	$ 24,233.46
ATOMOXETINE CAP 40MG	38	70	2,084	2,084	$ 21,296.02
METHYLPHENID TAB 18MG ER	63	92	2,672	2,639	$ 20,661.16
METHYLPHENID TAB 27MG ER	62	93	2,738	2,722	$ 19,509.37
METHYLPHENID TAB 54MG ER	41	82	2,392	2,392	$ 19,324.68
VYVANSE CAP 50MG	35	67	2,010	2,010	$ 18,294.39
AMPHET/DEXTR TAB 15MG	145	280	8,335	13,765	$ 16,454.67
VYVANSE CAP 60MG	31	57	1,710	1,710	$ 16,371.45
METHAMPHETAM TAB 5MG	2	4	104	2,280	$ 14,656.47
VYVANSE CAP 20MG	26	40	1,169	1,169	$ 10,430.31
DEXTROAMPHET CAP 15MG ER	15	30	835	2,316	$ 10,232.80
ATOMOXETINE CAP 80MG	12	26	757	877	$ 9,772.24
AMPHET/DEXTR TAB 5MG	136	191	5,132	7,502	$ 9,466.20
ATOMOXETINE CAP 10MG	15	31	907	937	$ 9,043.01
VYVANSE CAP 70MG	16	33	964	964	$ 8,236.70
METHYLPHENID TAB 20MG	65	110	3,238	7,411	$ 7,871.72
AMPHET/DEXTR CAP 25MG ER	34	52	1,560	1,590	$ 7,830.54
DEXMETHYLPHE CAP 20MG ER	13	28	840	870	$ 6,780.98
METHYLPHENID TAB 10MG	95	149	4,369	8,317	$ 6,558.81

ADD ADHD Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
ATOMOXETINE CAP 60MG	10	22	660	660	$ 6,423.40
METHYLPHENID TAB 5MG	71	118	3,485	8,001	$ 4,587.15
ATOMOXETINE CAP 25MG	12	14	420	480	$ 4,566.15
AMPHET/DEXTR CAP 5MG ER	29	37	1,051	1,051	$ 4,435.99
METHYLPHENID CAP 30MG	17	31	926	926	$ 4,405.35
DEXMETHYLPH CAP 15MG ER	13	22	638	638	$ 3,909.10
DEXMETHYLPHE CAP ER 25MG	8	20	600	600	$ 3,883.61
METHYLPHENID CAP 20MG	18	32	924	924	$ 3,634.64
MYDAYIS CAP 50MG	7	13	364	364	$ 3,216.77
METHYLPHENID TAB 20MG ER	11	21	630	630	$ 3,140.72
STRATTERA CAP 40MG	4	8	240	240	$ 2,972.02
GUANFACINE TAB 1MG ER	48	71	4,055	2,085	$ 2,869.84
METHYLPHENID TAB 10MG ER	11	16	480	480	$ 2,841.84
DAYTRANA DIS 15MG/9HR	4	8	240	240	$ 2,680.48
GUANFACINE TAB 2MG ER	36	64	1,905	1,905	$ 2,595.54
DEXMETHYLPHE CAP 10MG ER	6	9	270	330	$ 2,562.76
RITALIN LA CAP 20MG	4	9	270	270	$ 2,562.05
DEXTROAMPHET TAB 10MG	9	16	454	1,088	$ 2,382.94
EVEKEO TAB 10MG	2	3	90	360	$ 2,297.04
ADDERALL XR CAP 30MG	3	7	210	270	$ 1,935.81
VYVANSE CAP 10MG	8	12	360	360	$ 1,831.84
MYDAYIS CAP 12.5MG	4	6	180	180	$ 1,634.52
ADDERALL XR CAP 20MG	10	15	425	515	$ 1,600.45
METHYLPHENID CAP 10MG	9	10	300	300	$ 1,406.62
METHYLPHENID CHW 5MG	7	12	360	360	$ 1,370.40
ADDERALL TAB 10MG	1	2	60	180	$ 1,162.40
GUANFACINE TAB 3MG ER	16	32	960	960	$ 1,097.31
METHYLPHENID CAP 40MG	5	6	180	180	$ 1,087.75

ADD ADHD Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
DAYTRANA DIS 10MG/9HR	2	3	90	90	$ 1,055.18
CONCERTA TAB 36MG	2	2	60	90	$ 1,040.92
METHYLPHENID CHW 10MG	3	6	180	180	$ 973.62
ADDERALL XR CAP 10MG	3	5	128	128	$ 919.83
INTUNIV TAB 4MG	2	3	90	90	$ 879.75
METHYLPHENID CAP 30MG ER	5	6	180	180	$ 875.96
STRATTERA CAP 60MG	1	2	60	60	$ 863.42
MYDAYIS CAP 25MG	3	3	90	90	$ 817.26
STRATTERA CAP 10MG	1	2	60	60	$ 794.88
CONCERTA TAB 54MG	4	5	150	150	$ 755.80
METHYLPHENID CAP 40MG ER	3	5	150	150	$ 749.07
GUANFACINE TAB 4MG ER	11	23	690	690	$ 731.02
DEXMETHYLPH TAB 10MG	10	12	360	570	$ 653.26
METHYLPHENID CAP 20MG ER	2	4	120	120	$ 636.87
DYANAVEL XR SUS 2.5MG/ML	2	3	90	480	$ 609.54
RITALIN LA CAP 10MG	2	2	60	60	$ 600.80
DEXMETHYLPHE CAP 5MG ER	1	3	90	90	$ 587.22
DEXMETHYLPH TAB 5MG	5	13	390	750	$ 585.58
ADDERALL TAB 30MG	1	2	60	90	$ 582.45
QUILLIVANT SUS 25MG/5ML	2	2	60	330	$ 551.00
METHYLPHENID CAP 50MG	1	2	60	60	$ 475.54
METHLPHENIDA CHW 2.5MG	4	6	180	180	$ 472.94
ADDERALL XR CAP 5MG	1	2	60	60	$ 430.74
FOCALIN XR CAP 40MG	1	1	30	30	$ 415.14
DEXMETHYLPH CAP 40MG ER	2	2	60	60	$ 411.76
FOCALIN XR CAP 15MG	1	1	30	30	$ 376.64
FOCALIN XR CAP 20MG	1	1	30	30	$ 376.64
FOCALIN XR CAP 5MG	1	1	30	30	$ 360.95

ADD ADHD Agents

Summary of Utilization

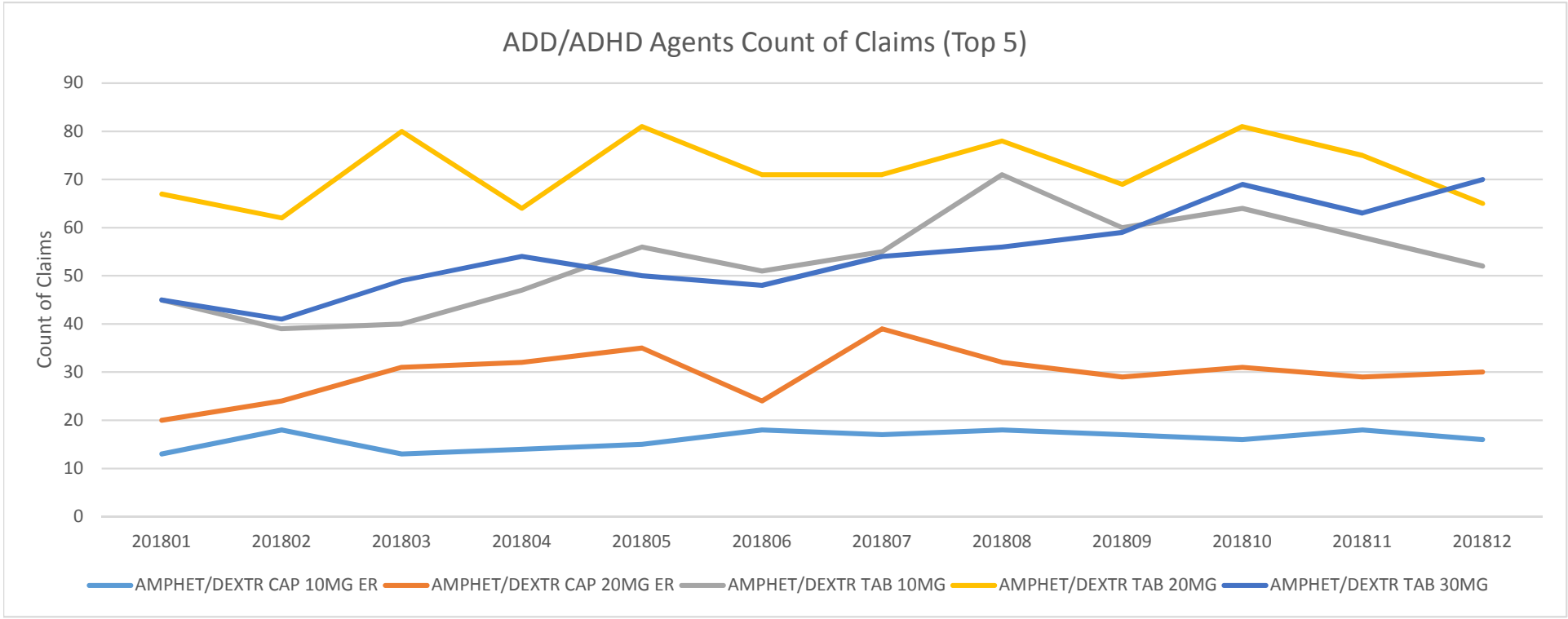
January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
ATOMOXETINE CAP 18MG	6	12	344	344	$ 331.44
ADZENYS XR TAB 12.5MG	1	1	30	30	$ 321.66
ADZENYS XR TAB 15.7 MG	1	1	30	30	$ 321.66
ADZENYS XR TAB 3.1MG	1	1	30	30	$ 321.66
ADZENYS XR TAB 9.4MG	1	1	30	30	$ 321.66
ADDERALL XR CAP 15MG	2	2	60	60	$ 303.14
VYVANSE CHW 20MG	1	1	30	30	$ 296.83
VYVANSE CHW 30MG	1	1	30	30	$ 296.83
ATOMOXETINE CAP 100MG	1	1	30	30	$ 292.68
VYVANSE CHW 10MG	2	4	120	180	$ 241.00
METHYPHENID CAP 10MG ER	1	1	30	30	$ 231.25
DEXTROAMPHET CAP 10MG ER	1	2	60	60	$ 229.13
EVEKEO TAB 5MG	1	1	30	30	$ 192.36
CLONIDINE TAB 0.1MG ER	1	1	30	30	$ 110.99
DEXTROAMPHET CAP 5MG ER	1	1	30	30	$ 98.87
DEXMETHYLPH TAB 2.5MG	4	4	120	180	$ 94.62
ADDERALL TAB 20MG	1	1	30	60	$ 84.21
AMPHET/DEXTR TAB 7.5MG	1	1	30	60	$ 61.52
AMPHET/DEXTR TAB 12.5MG	1	1	30	30	$ 28.71
COTEMPLA TAB 8.6MG	1	1	30	30	$ 25.36
Grand Total	**3,285**	**5,839**	**171,167**	**248,425**	**$ 753,713.61**

ADD ADHD Agents

Summary of Utilization
January 1, 2018 - December 31, 2018
Silversummit Healthplan



C. Agents used for the treatment of Attention Deficit Disorder (ADD)/Attention Deficit Hyperactivity Disorder (ADHD)

Therapeutic Class: ADHD/ADD Agents
Last Reviewed by the DUR Board: January 28, 2016

Agents for the treatment of Attention Deficit Disorder (ADD)/Attention Deficit Hyperactivity Disorder (ADHD) are subject to prior authorization and quantity limits 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 for medications will be given if the following criteria is met and documented:

a. General Criteria (Children and Adults)

1. Only one long-acting stimulant (amphetamine and methylphenidate products) may be used at a time, a 30-day transitional overlap in therapy will be allowed.

2. A diagnosis of ADD/ADHD or other FDA approved diagnosis.

b. ADD/ADHD Criteria (all requests for a diagnosis of ADD/ADHD)

1. The following criteria must be met and documented in the recipient's medical record prior to treatment with ADD/ADHD agents.

a. The decision to medicate for ADD or ADHD must be based on problems that are persistent and sufficiently severe to cause functional impairment in one or more of the following social environments: school, home, work or with peers; and

b. Other treatable causes of ADD/ADHD have been ruled out.

c. ADD/ADHD Criteria (Children up to age 18 years)

1. The recipient is at least three years of age (shorting-acting stimulants) or at least six years of age (long-acting stimulants, long-acting alpha agonists, atomoxetine).

2. An initial evaluation or regular examination has been done within the past 12 months with the treating prescriber and medical notes documenting all of the following:

a. A physical evaluation;

b. A developmental history;

c. Any medical and/or psychological history, any history of the primary neurological diagnosis including any history of past psychiatric, psychologic or neurological treatment for ADD/ADHD;

d. Any family history including: psychiatric diagnoses of ADD/ADHD, tic disorder, substance abuse disorder, conduct disorder, anxiety, etc., past or present, family stressors, crises, abuses or neglect and an interview with parent(s) or guardian(s);

e. A review of diagnostic symptoms of ADD/ADHD, presence or absence-child behavior checklist, development and context of symptoms and resulting impairment, (school, family, peers), possible alternate or comorbid psychiatric diagnosis;

f. School information, which should include standardized teachers rating scales, achievement tests, neuropsychological testing (if indicated) and speech and language evaluations.

d. Adults (18 years or older)

1. An initial evaluation is documented in the recipient's medical record and must include: a complete psychiatric assessment (present and past), diagnostic symptoms of ADD or ADHD, history of development and context of symptoms and resulting impairment (academic achievement, learning disorder evaluation); and

2. All of the following must be met and documented in the recipient's medical record:

a. A medical history, including medical or primary neurological diagnoses, any history of other psychiatric disorder(s) and the current treatment regimen;

b. A medication review to rule out other possible causes of symptoms (e.g. Phenobarbital, steroids);

c. Diagnostic symptoms of ADD and ADHD;

d. An assessment for possible alternate comorbid psychiatric diagnosis (especially: personality disorder, mood disorder, depression or mania, anxiety disorder, dissociatiave disorder, tic disorder including Tourette's disorder and substance abuse disorder): and

e. Any family history including diagnosis of ADD or ADHD, tic disorder, substance abuse disorder, conduct disorder, personality disorder, mood disorder and anxiety disorder, possible family stressors, any history of abuse or neglect.

2. Exception Criteria

a. Prescriptions for ADD/ADHD medications do not require prior authorization for children five years of age, up to 18 years of age, if the following criteria are met and documented:

1. The recipient is at least six years of age for short acting stimulants or at least six years of age for long-acting stimulants, long acting alpha agonists, atomoxetine);

2. The medication is prescribed by a psychiatrist; and

3. An ICD code for Attention Deficit Disorder with or without Hyperactivity is documented on the prescription and transmitted on the claim.

3. 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
Attention-Deficit/Hyperactivity Disorder (ADHD) Agents

INTRODUCTION

- Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder among children, with an estimated prevalence of up to 10% of school-age children in the United States (U.S.). It is more common in boys than girls and frequently persists into adulthood (*Feldman et al 2014*). Epidemiologic studies of adult ADHD have estimated the current prevalence to be 4.4% in the U.S. (*Bukstein 2018*).
  - In children, this chronic disorder is characterized by symptoms of hyperactivity, impulsivity, and/or inattention. These symptoms affect cognitive, academic, behavioral, emotional, and social functioning (*Krull 2019a*). Common comorbid psychiatric disorders include oppositional defiant disorder, conduct disorder, depression, anxiety disorder, and learning disabilities (*Krull 2019b*). Approximately 20% of children with ADHD develop chronic tic disorders and approximately 50% of children with chronic tics or Tourette syndrome have comorbid ADHD (*Krull 2018*).
  - ADHD in adults is characterized by symptoms of inattention, impulsivity, and restlessness. Impairment in executive function and emotional dysregulation frequently occur. Common comorbid psychiatric disorders include mood and anxiety disorders, substance use disorder, and intermittent explosive disorder (*Bukstein 2018*).
- For children < 17 years of age, the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) diagnosis of ADHD requires ≥ 6 symptoms of hyperactivity and impulsivity or ≥ 6 symptoms of inattention. For adolescents ≥ 17 years of age and adults, ≥ 5 symptoms of hyperactivity and impulsivity or ≥ 5 symptoms of inattention are required.
  - The symptoms of hyperactivity/impulsivity or inattention must occur often; be present in more than 1 setting; persist for at least 6 months; be present before the age of 12 years; impair function in academic, social, or occupational activities; and be excessive for the developmental level of the child.
  - Other physical, situational, or mental health conditions that could account for the symptoms must be excluded.
- Treatment of ADHD may involve behavioral/psychologic interventions, medication, and/or educational interventions, alone or in combination (*Krull 2019c*).
  - For preschool children (age 4 through 5 years), behavioral therapy is considered the first-line treatment; when medication is necessary, methylphenidate is generally recommended.
  - For children and adolescents with moderate to severe ADHD, medication and behavioral therapy are recommended. In general, stimulants are the first-line agents; however, non-stimulant medications may be more appropriate for certain children.
    - About 30% of patients do not respond to or may not tolerate the initial stimulant treatment. At least one-half of children who do not respond to one type of stimulant will respond to the other. If there is still no improvement, consideration should be given to switching to or adding a non-stimulant ADHD medication (*Pharmacist's Letter 2015, Krull 2019d*).
- Multiple agents are currently approved by the Food and Drug Administration (FDA) for the treatment of ADHD. They include central nervous system (CNS) stimulants (amphetamine- and methylphenidate-based formulations), as well as non-stimulants: a selective norepinephrine reuptake inhibitor (SNRI), atomoxetine, and 2 alpha$_2$-adrenergic agonists, clonidine extended-release (ER) and guanfacine ER.
  - Due to the potential for abuse, the stimulant agents are classified as Schedule II controlled substances.
  - Several stimulants are also approved for the treatment of narcolepsy and exogenous obesity; the use of stimulants for the treatment of obesity will not be covered in this review. Lisdexamfetamine dimesylate is the only FDA-approved drug for the treatment of binge eating disorder (BED).
- In August of 2018, an extended-release methylphenidate capsule (Jornay PM) was approved by the FDA. In addition, an orally disintegrating amphetamine sulfate tablet (Evekeo ODT) was also approved in late January 2019. Launch dates have not yet been announced for either product.
- Medispan Classes: ADHD Agents – Amphetamines, Dexmethylphenidate, Methylphenidate, Selective Alpha Adrenergic Agonists, Selective Norepinephrine Reuptake Inhibitor

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Stimulants	
Evekeo (amphetamine sulfate)	✔
Evekeo ODT (amphetamine sulfate)†	-
Adderall (mixed amphetamine salts)	✔
Focalin (dexmethylphenidate hydrochloride [HCl])	✔
ProCentra (dextroamphetamine sulfate)	✔
Zenzedi (dextroamphetamine sulfate)	✔
Desoxyn (methamphetamine HCl)	✔
methylphenidate HCl chewable tablets	✔
Methylin Oral Solution (methylphenidate HCl)	✔
Ritalin (methylphenidate HCl)	✔
Dexedrine Spansule (dextroamphetamine sulfate sustained-release)	✔
Adzenys ER (amphetamine ER)	-
Adzenys XR-ODT (amphetamine ER)	-
Dyanavel XR (amphetamine ER)	-
Adderall XR (mixed amphetamine salts ER)	✔
Mydayis (mixed amphetamine salts ER)	-
Focalin XR (dexmethylphenidate HCl ER)	✔
Vyvanse (lisdexamfetamine dimesylate)	-
Aptensio XR (methylphenidate HCl ER)	-
Concerta (methylphenidate HCl ER)	✔
Cotempla XR-ODT (methylphenidate ER)	-
Jornay PM (methylphenidate HCl ER)†	-
methylphenidate HCl ER (CD)	✔
methylphenidate HCl ER	✔
QuilliChew ER (methylphenidate HCl ER)	-
Quillivant XR (methylphenidate HCl ER)	-
Ritalin LA (methylphenidate HCl ER)	✔
Daytrana (methylphenidate transdermal system)	-
Non-stimulants	
Strattera (atomoxetine HCl)	✔
Kapvay (clonidine HCl ER)	✔
Intuniv (guanfacine HCl ER)	✔

†An extended-release methylphenidate capsule (Jornay PM) and an orally disintegrating amphetamine sulfate tablet (Evekeo ODT) have both been recently approved by the FDA; however, launch dates have not yet been announced for either product.

(*Drugs@FDA 2019, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2019, Facts & Comparisons 2019*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Evekeo (amphetamine sulfate)	Evekeo ODT (amphetamine sulfate)	Adzenys ER, Adzenys XR-ODT, Dyanavel XR (amphetamine ER)	Adderall (mixed amphetamine salts)	Adderall XR, Mydayis (mixed amphetamine salts ER)	Strattera (atomoxetine HCl)	Kapvay (clonidine HCl ER)	Focalin (dexmethylphenidate IR); Focalin XR (dexmethylphenidate ER)	ProCentra, Zenzedi (dextroamphetamine sulfate IR); Dexedrine Spansule (dextroamphetamine sulfate SR)	Intuniv (guanfacine HCl ER)	Vyvanse (lisdexamfetamine dimesylate)	Desoxyn (methamphetamine HCl)	Methylin Oral Solution, Ritalin methylphenidate HCl IR); methylphenidate HCl chewable tablets; Metadate ER (methylphenidate ER)	Aptensio XR, Concerta , Cotempla XR-ODT, Daytrana, methylphenidate ER (CD), Jornay PM, QuilliChew ER, Quillivant XR, Ritalin LA (methylphenidate ER)
ADHD*		✓	✓	✓	✓	✓		✓			✓			✓
ADHD, as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, and social) for a stabilizing effect in pediatric patients with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity. The diagnosis of this syndrome should not be made with finality when these symptoms are only of comparatively recent origin. Nonlocalizing (soft) neurological signs, learning disability, and abnormal electroencephalogram (EEG) may or may not be present, and a diagnosis of CNS dysfunction may or may not be warranted.*	✓								✓			✓	✓	
Treatment of ADHD as monotherapy and as adjunctive therapy to stimulant medications							✓			✓				
Narcolepsy**	✓			✓					✓				✓	
Exogenous obesity, as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy	✓											✓		

(eg, repeated diets, group programs, and other drugs).†														
Moderate to severe BED in adults											✓			

(*Prescribing Information*: *Adderall 2017*, *Adderall XR 2018*, *Adzenys ER 2017*, *Adzenys XR-ODT 2018*, *Aptensio XR 2017*, *Concerta 2017*, *Cotempla 2017*, *Daytrana 2017, Desoxyn 2017, Dexedrine Spansule 2019*, *Dyanavel XR 2019*, *Evekeo 2016*, *Evekeo ODT 2019*, *Focalin 2019*, *Focalin XR 2019*, *Intuniv 2018, Jornay PM 2018, Kapvay 2018, Mydayis 2017, Methylin Oral Solution 2017, methylphenidate chewable tablets 2018, methylphenidate ER 2017, methylphenidate ER (CD) 2018, ProCentra 2017*, *QuilliChew ER 2018*, *Quillivant XR 2018*, *Ritalin 2019*, *Ritalin LA 2019*, *Strattera 2017*, *Vyvanse 2018, Zenzedi 2017*)

* Adderall, Evekeo, ProCentra, and Zenzedi are approved for use in children 3 years of age and older. Daytrana, Desoxyn, Dexedrine Spansule, Dyanavel XR, Intuniv, and Kapvay are approved for use in children 6 years of age and older. Adderall XR, Adzenys ER, Adzenys XR-ODT, Aptensio XR, Focalin, Focalin XR, Jornay PM, methylphenidate ER (CD), Methylphenidate ER, Methylin Oral Solution, methylphenidate chewable tablets, QuilliChew ER, Quillivant XR, Ritalin, Ritalin LA, Strattera, and Vyvanse are approved for use in patients 6 years of age and older. Cotempla XR-ODT and Evekeo ODT are approved for use in pediatric patients 6 to 17 years of age. Concerta is approved for use in children 6 years of age and older, adolescents, and adults up to 65 years of age. Mydayis is approved for use in patients 13 years of age and older.
**These drugs are approved for use in patients 6 years of age and older.
†These drugs are not recommended for use in children under 12 years of age for treatment of exogenous obesity. The limited usefulness of these products should be weighed against possible risks inherent in use of the drugs.

- Limitation of use:
  - Lisdexamfetamine: Lisdexamfetamine is not indicated or recommended for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular (CV) adverse events (AEs). The safety and effectiveness of this drug for the treatment of obesity have not been established.
  - Mydayis: Pediatric patients 12 years and younger experienced higher plasma exposure than patients 13 years and older at the same dose and experienced higher rates of AEs, mainly insomnia and decreased appetite.

- 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

- Randomized trials, systematic reviews, and meta-analyses have found stimulants, atomoxetine, and alpha$_2$-adrenergic agonists to be more efficacious than placebo in reducing the core symptoms of ADHD in children and adolescents.
  - Adzenys ER, an amphetamine ER oral suspension, was approved under the 505(b)(2) regulatory pathway and was found to be bioequivalent to Adderall XR. No clinical efficacy studies were conducted.
  - Evekeo ODT, an orally disintegrating amphetamine tablet, was approved under the 505(b)(2) regulatory pathway. The safety and effectiveness of Evekeo ODT for the treatment of ADHD was established based on an adequate and well-controlled study of Evekeo (amphetamine sulfate).
  - Cotempla XR-ODT, a new methylphenidate ER orally disintegrating tablet formulation, was approved based on a randomized, double-blind (DB), multi-center (MC), placebo-controlled (PC) laboratory classroom study (*Childress et al 2017*) (N = 87) which found that the average Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP)-Combined score was significantly better for Cotempla XR-ODT than for placebo (least squares [LS] mean 14.3 [95% CI, 12.2 to 16.4] vs 25.3 [9% CI, 23.0 to 27.6], respectively, $p < 0.0001$).
  - Jornay PM, an ER methylphenidate capsule formulation, was approved based on the results of 2 clinical studies conducted in patients 6 to 12 years of age with ADHD:
    - The first study was a 6-week open-label (OL) dose-optimization study, followed by a 1-week DB, PC withdrawal phase where patients were randomized to continue treatment with Jornay PM or switch to placebo (*Jornay PM Prescribing Information 2018*). The study, which was conducted in an analog classroom setting and included 117 children aged 6 to 12 years, found that Jornay PM was associated with a significant reduction in the SKAMP symptom score over a 12-hour period (difference in least squares [LS] mean -5.9; 95% CI, -9.1 to -2.7).

- A randomized, DB, MC, PC, parallel group, forced-dose titration trial conducted over 3 weeks in 161 children 6 to 12 years of age with ADHD (*Pliszka et al 2017*). The study found that 40 to 80 mg/day of Jornay PM achieved significant improvements vs placebo in ADHD symptoms (LS mean ADHD rating scale-IV 24.1 vs 31.2; p = 0.002) at 3 weeks. Significant improvements were also seen vs placebo in key secondary outcomes including at-home early morning and late afternoon/evening functional impairment at 3 weeks. The most commonly reported treatment-emergent AEs were insomnia and decreased appetite.

- Mydayis, a new mixed amphetamine salts product, was approved for the treatment of ADHD based on the results of 5 MC, DB, PC, randomized controlled trials (RCTs): 3 in adults and 2 in pediatric patients 13 to 17 years of age. The studies found that Mydayis demonstrated a statistically significant treatment effect compared with placebo on various ADHD outcomes measures (eg, ADHD-Rating Scale [ADHD-RS] score, Permanent Product Measure of Performance [PERMP] score) (*Mydayis Prescribing Information 2017, Weisler et al 2017*) (see results below in Table 3 below).

Table 3. Summary of Primary Efficacy Results for Mydayis

Study Number (Age range)	Primary Endpoint	Treatment Group	Mean Baseline Score (SD)	LS Mean Change from Baseline	Placebo-subtracted Difference (95% CI)
Adult Studies					
Study 1 (18 to 55 years)	ADHD-RS	Mydayis 12.5 mg/day§ Mydayis 37.5 mg/day§ Placebo	39.8 (6.38) 39.9 (7.07) 40.5 (6.52)	-18.5 -23.8 -10.4	-8.1 (-11.7 to -4.4) -13.4 (-17.1 to -9.7)
Study 2 (18 to 55 years)	Average PERMP	Mydayis 50 mg/day§ Placebo	239.2 (75.6)† 249.6 (76.7)†	293.23* 274.85*	18.38 (11.28 to 25.47)
Study 3 (18 to 55 years)	Average PERMP	Mydayis 25 mg/day§ Placebo	217.5 (59.6)† 226.9 (61.7)†	267.96* 248.67*	19.29 (10.95 to 27.63)
Pediatric Studies					
Study 4 (13 to 17 years)‡	ADHD-RS-IV	Mydayis 12.5 to 25 mg/day§ Placebo	36.7 (6.15) 38.3 (6.67)	-20.3 -11.6	-8.7 (-12.6 to -4.8)
Study 5 (13 to 17 years)	Average PERMP	Mydayis 25 mg/day§ Placebo	214.5 (87.8)† 228.7 (101)†	272.67* 231.41*	41.26 (32.24 to 50.29)

SD= standard deviation; LS = least squares; CI = confidence interval
†Pre-dose PERMP total score
*LS mean for PERMP is post-dose average score over all sessions of the treatment day, rather than change from baseline
‡Results are for a subgroup of study 4 and not the total population
§Doses statistically significant for placebo

- A systematic (Cochrane) review of 185 RCTs (*Storebø et al 2015*) (N = 12,245) in children and adolescents with ADHD found that methylphenidate may improve teacher-rated ADHD symptoms, teacher-reported general behavior, and parent-reported quality of life (QOL) vs placebo. However, the evidence was of low quality.
- An RCT called the Preschool ADHD Treatment Study (PATS) (*Greenhill et al 2006*) evaluated the efficacy of methylphenidate immediate-release (IR) in 303 preschool children with ADHD and found that it demonstrated significant reductions on ADHD symptom scales; however, the effect sizes (0.4 to 0.8) were smaller than those generally reported for school-age children.
- A systematic (Cochrane) review of 23 PC, RCTs (*Punja et al 2016*) (N = 2675) found that amphetamines were effective at improving the core symptoms of ADHD, but they were also associated with a higher risk of AEs compared to placebo. There was no evidence that one kind of amphetamine was better than another and there was no difference between short-acting and long-acting formulations.
- A meta-analysis of 25 DB, PC, RCTs (*Schwartz et al 2014*) (N = 3928) in children and adolescents with ADHD found atomoxetine to be superior to placebo for overall ADHD symptoms, with a medium effect size (-0.64).

- A meta-analysis of 12 RCTs (*Hirota et al 2014*) (N = 2276) in pediatric patients with ADHD found that alpha$_2$-adrenergic agonists were significantly superior to placebo for overall ADHD symptoms both as monotherapy and, to a lesser extent, as augmentation therapy to stimulants.
  - Meta-analytic results failed to demonstrate a significant difference in efficacy between alpha$_2$-adrenergic agonists. In sub-analyses of individual formulations, the ER formulations separated robustly from placebo whereas the IR formulations did not separate from placebo.
- A systematic review of 16 RCTs and 1 meta-analysis (*Chan et al 2016*) (N = 2668) found evidence supporting the use of methylphenidate ER and amphetamine ER formulations, atomoxetine, and guanfacine ER for the treatment of ADHD in adolescents. For the primary outcome measure of mean change in ADHD-RS total symptom score, both stimulant and non-stimulant medications led to clinically significant reductions of 14.93 to 24.60 points.

- For the treatment of ADHD in children and adolescents, stimulants typically have a slightly larger treatment effect size (standardized mean difference [SMD]) than non-stimulants (approximately 1.0 vs approximately 0.7 for both atomoxetine and alpha$_2$-adrenergic agonists). However, there is insufficient evidence to definitively conclude that one stimulant is more efficacious than another (*Krull 2019d*, *AAP 2011).*
  - An Agency for Healthcare Research and Quality (AHRQ) review of 78 studies (*Jadad et al 1999*) evaluating the efficacy of various interventions for the treatment of ADHD in children and adults found few, if any, differences between methylphenidate and dextroamphetamine.
  - A meta-analysis of 23 DB, PC trials (*Faraone 2010a*) comparing the efficacy of methylphenidate and amphetamine formulations found that amphetamine products may be moderately more efficacious than methylphenidate products.
  - A DB, PC, RCT (*Newcorn et al 2008*) (N = 516) comparing the efficacy of atomoxetine vs methylphenidate ER (osmotic-release formulation) in patients 6 to 16 years of age with ADHD found that both drugs were superior to placebo in terms of response rate, and that methylphenidate ER was superior to atomoxetine.
  - A meta-analysis of 29 DB, PC trials (*Faraone et al 2006*) evaluated the efficacy of various medications (methylphenidate and amphetamine compounds, atomoxetine, pemoline [no longer available in the U.S.], bupropion, and modafinil) for the treatment of ADHD. The effect sizes for non-stimulant medications were significantly less than those for IR stimulants or long-acting stimulants. The 2 classes of stimulant medications did not differ significantly from one another.
  - A meta-analysis of 28 DB, PC, RCTs (*Stuhec et al 2015*) (N = 4699) compared the efficacy of various medications for the treatment of ADHD in children and adolescents. Efficacy in reducing ADHD symptoms compared to placebo was small for bupropion (SMD = -0.32; 95% confidence interval [CI], -0.69 to 0.05), modest for atomoxetine (SMD = -0.68; 95% CI, -0.76 to -0.59) and methylphenidate (SMD = -0.75; 95% CI, -0.98 to -0.52), and highest for lisdexamfetamine (SMD = -1.28; 95% CI, -1.84 to -0.71).
  - A network meta-analysis and mixed treatment comparison of 36 RCTs (*Joseph et al 2017*) evaluating the comparative efficacy and safety of ADHD pharmacotherapies in children and adolescents found that lisdexamfetamine had greater efficacy than guanfacine ER, atomoxetine, and methylphenidate ER. Guanfacine ER had a high posterior probability of being more efficacious than atomoxetine, but their credible intervals overlapped.
  - A network meta-analysis of 48 DB, RCTs (*Padilha et al 2018*) compared the safety and efficacy of various ADHD medications in children and adolescents. Of the 12 trials that were evaluated for efficacy, analysis was performed using the Clinical Global Impression Improvement (CGI-I) scale for 3 drugs, which showed that methylphenidate was more effective than atomoxetine (MD, 3.15; 95% CI, 0.75 to 13.71) and guanfacine (MD, 1.92; 95% CI, 0.64 to 5.94). Thirty-three trials were evaluated for safety. Ranking of AEs showed that lisdexamfetamine was more likely to cause sleep disorders, loss of appetite, and behavior problems compared to other treatments.
- Alpha$_2$-adrenergic agonists have been associated with improvements in ADHD symptoms and comorbid tics.
  - A meta-analysis of 9 DB, PC, RCTs (*Bloch et al 2009*) (N = 477) was conducted to determine the relative efficacy of different medications in treating ADHD and tic symptoms in children with both Tourette syndrome and ADHD.
  - Methylphenidate seemed to offer the greatest improvement of ADHD symptoms and did not seem to worsen tic symptoms.
  - Alpha$_2$-adrenergic agonists offered the best combined improvement in both tic and ADHD symptoms.
  - Atomoxetine significantly improved both tic and ADHD severity compared to placebo.
  - One small study found that tic severity was significantly increased with higher doses of dextroamphetamine treatment.
  - A Cochrane review of 8 RCTs (*Osland et al 2018*) including 510 children with both ADHD and a chronic tic disorder found low-quality evidence for improvement of ADHD symptoms with methylphenidate, atomoxetine, and clonidine, and very low-quality evidence for desipramine, dextroamphetamine, guanfacine, and deprenyl. Tic symptoms improved with guanfacine, desipramine, methylphenidate, clonidine, and a combination of methylphenidate and

clonidine. The authors noted that in 1 study with a short duration (3 weeks), high doses of dextroamphetamine worsened tics.

- There are limited efficacy data regarding the treatment of ADHD in the adult population. Comparison of effect sizes in clinical trials suggests that stimulant medications are more efficacious in adult ADHD than non-stimulants.
  - In a meta-analysis of 12 clinical trials (*Cunill et al 2009*) (N = 3375) comparing atomoxetine with placebo in adult ADHD, atomoxetine led to a modestly greater reduction in ADHD symptom severity, but was associated with higher all-cause discontinuation.
  - A meta-analysis (*Faraone 2010b*) of 19 randomized trials of 13 medications for adult ADHD found a greater average effect size for reduction in ADHD symptoms in patients receiving short- and long-acting stimulant medications (vs placebo; 0.86 and 0.73, respectively) compared with patients receiving non-stimulant medication (vs placebo; 0.39). No difference in effect size was found between short- and long-acting stimulants.
  - A meta-analysis of 20 randomized trials (*Stuhec et al 2018*) compared the efficacy, acceptability, and tolerability of lisdexamfetamine, mixed amphetamine salts, methylphenidate, and modafinil in the treatment of ADHD in adults. The highest effect size in reducing ADHD symptoms was found with lisdexamfetamine (SMD -0.89; 95% CI, -1.09 to -0.70), while moderate reductions in symptoms were seen with mixed amphetamine salts (SMD -0.64; 95% CI, -0.83 to -0.45) and methylphenidate (SMD -0.50; 95% CI, -0.58 to -0.41). No efficacy was reported with modafinil.
  - A Cochrane review of 19 studies (*Castells et al 2018*, N = 2521) comparing dextroamphetamine, lisdexamfetamine, and mixed amphetamine salts for the treatment of ADHD in adults found that overall, amphetamines reduced the patient- and clinician-rated severity of ADHD symptoms compared to placebo; however, they did not improve retention in treatment. Amphetamines were associated with an increased proportion of patients who withdrew because of AEs. When comparing different types of amphetamines, lisdexamfetamine and mixed amphetamine salts reduced the severity of ADHD symptoms as rated by clinicians, but dextroamphetamine did not. No differences in any outcome were found when comparing immediate- and sustained-release formulations.
  - Another meta-analysis (*Cortese et al 2018*) of 133 RCTs comparing the use of amphetamines, atomoxetine, bupropion, clonidine, guanfacine, methylphenidate, and modafinil for the treatment of ADHD found that all drugs were superior to placebo for ADHD core symptoms as rated by clinicians in children and adolescents, and all drugs except for modafinil were more efficacious than placebo in adults.
    - When comparing the various drugs based on teachers' ratings in children and adolescents, only methylphenidate and modafinil were found to be more efficacious than placebo.
    - In head-to-head comparisons, differences in efficacy based on clinicians' ratings were found, favoring amphetamines over modafinil (SMD -0.39; 95% CI -0.67 to -0.12), atomoxetine (SMD -0.46; 95% CI, -0.65 to -0.27), and methylphenidate (SMD-0.24; 95% CI, -0.44 to -0.05) in children and adolescents. Efficacy results based on clinicians' ratings were similar for adults, and favored amphetamines over modafinil (SMD -0.94; 95% CI -1.43 to -0.46), atomoxetine (SMD -0.34; 95% CI, -0.58 to -0.10), and methylphenidate (SMD-0.29; 95% CI, -0.54 to -0.05).
- Lisdexamfetamine dimesylate has demonstrated efficacy in the treatment of BED. Direct comparison trials between lisdexamfetamine and other drugs used off-label to treat BED are lacking.
  - In 2 Phase 3, 12-week, randomized, DB, PC trials (*McElroy et al 2016*) (N = 773) in patients with moderate to severe BED, lisdexamfetamine-treated patients had a statistically significantly greater reduction from baseline in mean number of binge days per week at week 12 vs placebo (treatment difference in study 1: -1.35 [-1.70 to -1.01]; study 2: -1.66 [-2.04 to -1.28]; both $p < 0.001$).
    - A 12-month, OL extension study (*Gasior et al 2017*) (N = 599) in adults with BED found that the long-term safety and tolerability of lisdexamfetamine were generally consistent with the safety profile observed in 3 previous short-term trials in BED as well as its established profile for ADHD. Common treatment-emergent AEs included dry mouth, headache, insomnia, and upper respiratory tract infection. Weight loss and increases in blood pressure and pulse rate were also observed.
  - In a phase 3, DB, randomized, PC, withdrawal study (*Hudson et al 2017*) (N = 418) in adults with moderate to severe BED, responders to lisdexamfetamine during a 12-week OL phase were randomized to placebo or continued lisdexamfetamine during a 26-week, DB phase. The percentage of patients meeting relapse criteria was 3.7% with lisdexamfetamine vs 32.1% with placebo; time to relapse statistically favored lisdexamfetamine ($p < 0.001$). The hazard ratio (HR) was 0.09 (95% CI, 0.04 to 0.23).
  - A systematic review and meta-analysis of 9 waitlist-controlled psychological trials and 25 PC trials evaluating pharmacologic (n = 19) or combination (n = 6) treatment for BED (*Brownley et al 2016*) found that therapist-led CBT, lisdexamfetamine, and second-generation antidepressants (SGAs) increased binge-eating abstinence (relative risk

[RR], 4.95 [95% CI, 3.06 to 8.00], 2.61 [CI, 2.04 to 3.33], and 1.67 [CI, 1.24 to 2.26], respectively), while lisdexamfetamine and SGAs decreased binge-eating frequency (mean difference in days/week, -1.35 [CI, -1.77 to -0.93] and -0.67 [CI, -1.26 to -0.09], respectively). Topiramate and other forms of CBT also increased abstinence and reduced binge-eating frequency.

- A 2018 systematic review and meta-analysis of 45 RCTs (*Ghaderi et al 2018*) compared various psychological, pharmacological, and combined treatments for BED, and found moderate support for the efficacy of cognitive behavioral therapy (CBT) and CBT-guided self-help (moderate quality of evidence), and low quality evidence to support interpersonal psychotherapy, selective serotonin reuptake inhibitors, and lisdexamfetamine for the cessation of or reduction in the frequency of binge eating. Only lisdexamfetamine showed a modest effect on weight loss (SMD for body mass index -5.23; 95% CI, -6.52 to -3.94).

CLINICAL GUIDELINES

ADHD

- Several clinical guidelines have provided recommendations on the treatment of ADHD in children and adolescents.
  - According to the American Academy of Pediatrics (AAP) guidelines (2011), the evidence is particularly strong for stimulant medications, and sufficient but less strong for atomoxetine, guanfacine ER, and clonidine ER (in that order). Guanfacine ER and clonidine ER have evidence to support their use as adjunctive therapy with stimulant medications. Methylphenidate is recommended for preschool-aged children who have had an inadequate response to behavioral interventions.
  - The American Academy of Child and Adolescent Psychiatry (AACAP) guidelines (*Pliszka et al 2007*) state that both methylphenidate and amphetamines are equally efficacious in the treatment of ADHD. The long-acting formulations are equally efficacious as the IR formulations and may be used as initial therapy. Short-acting stimulants are often used as initial treatment in small children (< 16 kg in weight), for whom there are no long-acting preparations in a sufficiently low dose. Some patients may respond similarly to different stimulant classes, whereas other patients may respond preferentially to only 1 of the classes of stimulants. Although stimulants have demonstrated greater efficacy compared to atomoxetine in published studies, atomoxetine may be used first-line in patients with an active substance abuse problem, comorbid anxiety or tics, and in those who experience severe AEs with stimulants.
  - The Medical Letter (2015) recommends that treatment of ADHD in school-age children or adults should begin with an oral stimulant, either a methylphenidate- or amphetamine-based formulation. Mixing short- and long-acting stimulants can be helpful to achieve an immediate effect for early-morning school classes or for reducing rebound irritability or overactivity, especially in the evening. An ER alpha$_2$-adrenergic agonist may be helpful as adjunctive therapy with a stimulant in patients who cannot tolerate usual doses of the stimulant, particularly those with tics. Atomoxetine is an alternative for patients who cannot tolerate stimulants or for whom treatment with a controlled substance is undesirable.
  - The AACAP practice parameter for the treatment of children and adolescents with tic disorders (2013) states that alpha$_2$-adrenergic agonists have demonstrated an effect size of 0.5 for the amelioration of tics and may be preferred by some prescribers over antipsychotics due to their relatively favorable AE profile.

Narcolepsy

- The American Academy of Sleep Medicine (AASM) practice parameters (*Morgenthaler et al 2007*) recommend various drugs for the treatment of daytime sleepiness due to narcolepsy including modafinil (high degree of clinical certainty); amphetamine, methamphetamine, dextroamphetamine, and methylphenidate (moderate degree of clinical certainty); sodium oxybate (high degree of clinical certainty); and selegiline (uncertain clinical certainty).

BED

- According the American Psychiatric Association (APA) practice guidelines on eating disorders (*Yager et al 2006*, *Yager et al 2012* [guideline watch update]), treatment of BED may include the following:
  - Nutritional rehabilitation and counseling
  - Psychosocial treatment
    - CBT, behavior therapy, dialectical behavior therapy (DBT), and interpersonal therapy (IPT) have all been associated with binge frequency reduction rates of 67% or more and significant abstinence rates during active treatment.
    - Self-help programs using self-guided, professionally designed manuals have been effective in reducing the symptoms of BED in the short-run for some patients and may have long-term benefit.
  - Medications

- Antidepressant treatment is associated with short-term reductions in binge-eating but generally does not result in substantial weight loss. Selective serotonin reuptake inhibitors (SSRIs) have the fewest difficulties with AEs and the most evidence for efficacy when used at the high end of the recommended dose range.
- Topiramate can reduce bingeing and decrease weight, but its use may be limited by AEs.

o Combination psychotherapy and pharmacotherapy
- For most patients, adding antidepressant therapy to a behavioral weight control and/or CBT regimen does not have a significant effect on binge suppression.
- Although limited evidence is available, combined treatment is frequently used in clinical practice.

- The American Association of Clinical Endocrinologists and the American College of Endocrinology (AACE/ACE) guidelines for medical care of patients with obesity (*Garvey et al 2016*) recommend the following for patients with overweight or obesity who have BED:
  - o Patients should be treated with a structured behavioral/lifestyle program, combined with CBT or other psychological interventions
  - o Treatment with orlistat or approved medications containing topiramate or bupropion may be considered in conjunction with structured lifestyle therapy, CBT, and/or psychological interventions
- The Task Force on Eating Disorders of the World Federation of Societies of Biological Psychiatry (*Aigner et al 2011*) concluded that for the treatment of BED, grade A evidence supports the use of imipramine (moderate risk-benefit ratio), sertraline (good risk-benefit ratio), citalopram/escitalopram (good risk-benefit ratio), orlistat (low to moderate risk-benefit ratio), and topiramate (moderate risk-benefit ratio). Atomoxetine has grade B evidence supporting its use.

SAFETY SUMMARY

- Due to the potential for abuse, the stimulants are classified as Schedule II controlled substances. Atomoxetine, clonidine ER, and guanfacine ER are not classified as controlled substances.
- Various stimulants are contraindicated for use in patients with advanced arteriosclerosis, symptomatic CV disease, moderate to severe hypertension, hyperthyroidism, hypersensitivity to sympathomimetic amines, glaucoma, agitated states, history of drug abuse, tics, and in those using monoamine oxidase inhibitors (MAOIs). The stimulants carry a boxed warning for potential drug abuse and dependence. They also have warnings for increased risks of serious CV reactions, psychiatric AEs, suppression of growth, peripheral vasculopathy, and priapism. Amphetamines have a warning for risk of serotonin syndrome when used in combination with other drugs affecting the serotonergic neurotransmitter systems.
  - ○ Common AEs of stimulants include anorexia, decreased weight, tachycardia, anxiety, irritability, and insomnia.
  - ○ Refer to the prescribing information for details on warnings, precautions, and AEs for individual products. For example:
    - QuilliChew ER can be harmful to patients with phenylketonuria (PKU) since it contains phenylalanine.
    - Because the Concerta tablet is nondeformable and does not appreciably change in shape in the gastrointestinal tract, it should not ordinarily be administered to patients with preexisting severe gastrointestinal narrowing.
    - The use of Daytrana may result in chemical leukoderma and contact sensitization; in addition, exposure of the application site to external heat sources should be avoided due to increased absorption of the drug.
- Atomoxetine is contraindicated for use in patients with narrow angle glaucoma, pheochromocytoma, severe CV disorders, hypersensitivity to any component of the product, and in those taking MAOIs. It carries a boxed warning for rare increased risk of suicidal ideation in children and adolescents. It also has warnings for serious CV events, effects on blood pressure and heart rate, effects on growth, psychiatric AEs, rare cases of severe liver injury, and priapism.
  - ○ Common AEs associated with atomoxetine include somnolence, nausea, and vomiting.
- The alpha$_2$-adrenergic agonists are contraindicated in patients known to be hypersensitive to any constituent of the product. They carry warnings for increased risk of hypotension, bradycardia, and syncope; sedation and somnolence; rebound hypertension; and cardiac conduction abnormalities.
  - ○ Common AEs associated with clonidine ER include somnolence, fatigue, and irritability while common AEs with guanfacine ER include somnolence, fatigue, and hypotension.

DOSING AND ADMINISTRATION

Table 4. Dosing and Administration

Drug	Duration of action*	Available Formulations	Route	Usual Recommended Frequency	Comments
Stimulants					
Evekeo (amphetamine)	4 to 6 h	Tablets	Oral	*ADHD, narcolepsy*: Daily up to divided doses daily *Exogenous obesity*: Divided doses daily	*ADHD and narcolepsy* The first dose should be given upon awakening; additional doses at intervals of 4 to 6 hours.
Evekeo ODT (amphetamine)	4 to 6 h	Orally disintegrating tablets	Oral	Once or twice daily in the morning	As soon as the blister pack is opened, the tablet should be placed on the patient's tongue and allowed to disintegrate without chewing or crushing. The tablet will disintegrate in saliva so that it can be swallowed.
Adzenys ER (amphetamine ER)	10 to 12 h	Suspension	Oral	Daily in the morning	
Adzenys XR-ODT (amphetamine ER)	10 to 12 h	Orally disintegrating tablets	Oral	Daily in the morning	As soon as the blister pack is opened, the tablet should be placed on the patient's tongue and allowed to disintegrate without chewing or crushing. The tablet will disintegrate in saliva so that it can be swallowed.
Dyanavel XR (amphetamine ER)	Up to 13 h	Suspension	Oral	Daily in the morning	The bottle should be shaken before administration.
Adderall (mixed amphetamine salts)	4 to 6 h	Tablets	Oral	*ADHD, narcolepsy*: Daily up to divided doses daily	The first dose should be given on awakening, then additional doses at intervals of 4 to 6 hours.
Adderall XR (mixed amphetamine salts ER)	10 to 12 h	Capsules	Oral	Daily in the morning	Capsules may be taken whole, or the capsule may be opened and the entire contents

Drug	Duration of action*	Available Formulations	Route	Usual Recommended Frequency	Comments
					sprinkled on applesauce and consumed immediately. The dose of a single capsule should not be divided.
Mydayis (mixed amphetamine salts ER)	16 h	Capsules	Oral	Daily in the morning	Dosage adjustment is needed for severe renal impairment. Use in end stage renal disease (ESRD) is not recommended. Capsules may be taken whole, or the capsule may be opened and the entire contents sprinkled on applesauce and consumed immediately in its entirety without chewing. The dose of a single capsule should not be divided.
Focalin (dexmethylphenidate)	5 to 6 h	Tablets	Oral	Twice daily	
Focalin XR (dexmethylphenidate ER)	10 to 12 h	Capsules	Oral	Daily in the morning	ER capsules may be taken whole, or the capsule may be opened and the entire contents sprinkled on applesauce.
ProCentra, Zenzedi (dextroamphetamine)	4 to 6 h	Solution (ProCentra) Tablets (Zenzedi)	Oral	*ADHD, narcolepsy*: Daily up to divided doses daily	The first dose should be given upon awakening; additional doses at intervals of 4 to 6 hours
Dexedrine Spansule (dextroamphetamine SR)	6 to 8 h	Capsules	Oral	*ADHD* Daily or twice daily Narcolepsy Daily	

Drug	Duration of action*	Available Formulations	Route	Usual Recommended Frequency	Comments
Vyvanse (lisdexamfetamine)	10 to 12 h	Capsules, chewable tablets	Oral	*ADHD, BED*: Daily in the morning	Dosage adjustment is needed for renal impairment/ESRD. The capsules may be swallowed whole or can be opened, emptied, and mixed with yogurt, water, or orange juice and consumed immediately. A single capsule should not be divided. The chewable tablets must be chewed thoroughly before swallowing. A single dose should not be divided.
Desoxyn (methamphetamine)	3 to 5 h	Tablets	Oral	*ADHD*: Daily to twice daily *Obesity*: 30 min before each meal	
Methylin, Ritalin (methylphenidate)	3 to 5 h	Chewable tablets, tablets (Ritalin), solution (Methylin)	Oral	Twice daily to 3 times daily	The chewable tablets should be taken with at least 8 ounces (a full glass) of water or other fluid. The liquid should be given 30 to 45 minutes before meals. The ER tablets may be used in place of the IR tablets when the 8-hour dosage of the ER product corresponds to the titrated 8-hour dosage of the IR products.
Methylphenidate ER	3 to 8 h	Tablets			

Drug	Duration of action*	Available Formulations	Route	Usual Recommended Frequency	Comments
					The ER tablets must be swallowed whole and never crushed or chewed.
Aptensio XR (methylphenidate ER)	12 h	Capsules	Oral	Daily in the morning	The capsules may be taken whole or they can be opened and sprinkled onto applesauce; the applesauce should be consumed immediately and it should not be chewed. The dose of a single capsule should not be divided.
Concerta (methylphenidate ER)	10 to 12 h	Tablets	Oral	Daily in the morning	The tablets should not be chewed or crushed. Note: An FDA analysis of methylphenidate ER products manufactured by UCB/Kremers (formerly Kudco) and Mallinckrodt indicated that in some individuals, they may deliver the drug in the body at a

Drug	Duration of action*	Available Formulations	Route	Usual Recommended Frequency	Comments
Methylphenidate ER					slower rate during the 7- to 12-hour range. As a result, the FDA changed the therapeutic equivalence of these products from AB to BX. Because these manufacturers have subsequently failed to demonstrate that their products are bioequivalent to the brand-name reference drug, the FDA proposes to withdraw their approval (*FDA 2016*).
Cotempla XR-ODT (methylphenidate ER)	12 h	Orally disintegrating tablets	Oral	Daily in the morning	As soon as the blister pack is opened, the tablet should be placed on the patient's tongue and allowed to disintegrate without chewing or crushing. The tablet will disintegrate in saliva so that it can be swallowed.
Jornay PM (methylphenidate ER)	Peak concentration occurs 14 hours after dose with gradual decline thereafter.	Capsules	Oral	Daily in the evening	The capsules may be swallowed whole or it may be opened and the contents sprinkled onto applesauce and given immediately. The capsule contents must not be crushed or chewed, the dose of a single capsule should not be divided, and the contents of the entire capsule should be taken at the same time.

Drug	Duration of action*	Available Formulations	Route	Usual Recommended Frequency	Comments
Methylphenidate ER (CD)	8 to 12 h	Capsules	Oral	Daily in the morning	The capsule may be swallowed whole or it may be opened and the contents sprinkled onto a small amount (tablespoon) of applesauce and given immediately. The capsule contents must not be crushed or chewed.
QuilliChew ER (methylphenidate ER)	12 h	Chewable tablets	Oral	Daily in the morning	A 10 mg or 15 mg dose can be achieved by breaking in half the functionally scored 20 mg and 30 mg tablets, respectively.
Quillivant XR (methylphenidate ER)	12 h	Suspension	Oral	Daily in the morning	The bottle of Quillivant XR should be shaken vigorously for 10 seconds prior to administration. The suspension is stable for up to 4 months once reconstituted.
Ritalin LA (methylphenidate ER)	8 to 12 h	Capsules	Oral	Daily in the morning	The capsule may be swallowed whole or may be administered by sprinkling the capsule contents on a small amount of applesauce; the contents should not be crushed, chewed, or divided. The mixture should be consumed immediately.
Daytrana (methylphenidate transdermal system)	10 to 12 h	Transdermal system	Transdermal	The patch should be applied 2 hours before an effect is needed and removed within 9	

Drug	Duration of action*	Available Formulations	Route	Usual Recommended Frequency	Comments
				hours. It may be removed earlier than 9 hours if a shorter duration of effect is desired or late day side effects appear.	
Non-stimulants					
Strattera (atomoxetine)	24 h	Capsules	Oral	Daily in the morning or divided dose in the morning and late/afternoon early evening	Dosage adjustment is recommended for patients with moderate or severe hepatic insufficiency. The capsules are not intended to be opened and should be taken whole.
Kapvay (clonidine ER)	12 h	Tablets	Oral	Daily at bedtime or twice daily divided doses.	With twice daily dosing, either an equal or higher split dosage should be given at bedtime. The tablets should not be crushed, chewed, or broken prior to swallowing. The initial dosage should be based on the degree of renal impairment.
Intuniv (guanfacine ER)	8 to 24 h	Tablets	Oral	Daily in the morning or evening	The tablets should not be crushed, chewed, or broken prior to swallowing; they should not be administered with high fat meals, due to increased exposure It may be necessary to reduce the dosage in patients with significant renal and hepatic impairment.

See the current prescribing information for full details
*References: Prescribing information for individual products, *Medical Letter 2015, Pharmacist's Letter 2016, Krull 2019d*

CONCLUSION

- Both CNS stimulants and non-stimulants may be used for the treatment of ADHD. In general, stimulants are first-line treatment due to their superior efficacy. Clinical evidence suggests that methylphenidate and amphetamines are equally efficacious, but some patients may respond to one stimulant and not the other. Various short-, intermediate- and long-acting formulations (eg, tablets/capsules, chewable/orally disintegrating tablets, solution/suspension, transdermal patch) are available to provide a range of dosing options. Although non-stimulants such as atomoxetine and alpha$_2$-adrenergic agonists have smaller effect sizes, they may be used in patients who have failed or are intolerant to stimulants or when there is concern about possible abuse or diversion. The alpha$_2$-adrenergic agonists are approved both as monotherapy and as adjunctive therapy to stimulants, and they have been shown to improve both tic and ADHD symptoms in patients with comorbid tic disorder.
  - Current consensus clinical guidelines for the treatment of children and adolescents with ADHD recommend that stimulants are highly effective for reducing core symptoms of ADHD in children (*AACAP 2007*; *AAP 2011*).
- Ultimately, the choice of the initial agent for treatment of ADHD depends upon various factors such as: duration of desired coverage; ability of the child to swallow pills; coexisting tic disorder (use of alpha$_2$-adrenergic agonists may be warranted); potential AEs, history of substance abuse in the patient or household member (eg, avoid stimulants or use stimulants with less potential for abuse [eg, lisdexamfetamine, osmotic-release preparation, methylphenidate patch]); and preference of the patient and parent/guardian (*Krull 2019d*).
- Various stimulants are indicated for treatment of narcolepsy and are generally considered to be second-line agents after modafinil/armodafinil due to their sympathomimetic AEs (*Scammell 2019*).
- Lisdexamfetamine is the only FDA-approved drug indicated for the treatment of moderate to severe BED, with demonstrated efficacy in reduction of mean binge days per week vs placebo. Direct comparison trials between lisdexamfetamine and other drugs used off-label to treat BED are lacking.

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Publication Date: March 1, 2019

Androgen/Testosterone replacement agents

Prior Authorization Guideline

Guideline Name Xyosted (testosterone enanthate)

1 . Indications

Drug Name: Xyosted (testosterone enanthate) **Indications** Testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

2 . Criteria

Product Name: Xyosted (testosterone enanthate)

Diagnosis	Hypogonadism
Approval Length	14 days
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of hypogonadism (e.g., testicular hypofunction, male hypogonadism, ICD-10 code E29.1)

AND

2. Male patient at birth

AND

3. One of the following:

    a. Two pre-treatment serum total testosterone levels less than 300 ng/dL (< 10.4 nmol/L) or less than the reference range for the lab

    OR

    b. Both of the following:

        i. Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity)

        AND

        ii. One pre-treatment calculated free or bioavailable testosterone level less than 5 ng/dL (< 0.17 nmol/L) or less than the reference range for the lab

    OR

    c. Patient has a history of one of the following:

- Bilateral orchiectomy
- Panhypopituitarism
- A genetic disorder known to cause hypogonadism (e.g., congenital anorchia, Klinefelter's syndrome)

Product Name: Xyosted (testosterone enanthate)

Diagnosis	Gender Dysphoria (off-label)
Approval Length	6 months for patients new to testosterone therapy; or 12 months for patients continuing testosterone therapy but without a current authorization on file with OptumRx
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Using hormones to change physical characteristics.

AND

2. Diagnosis of gender dysphoria, as defined by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM)

AND

3. Patient is a female-to-male transsexual

Product Name: Xyosted (testosterone enanthate)

Diagnosis	Male hypogonadism or Gender dysphoria
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1. One of the following:

    a. Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy, or 12 months for patients continuing testosterone therapy, is within or below the normal limits of the reporting lab

    OR

    b. Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy, or 12 months for patients continuing testosterone therapy, is outside of upper limits of normal for the reporting lab and the dose is adjusted

    OR

    c. Both of the following:

        i. Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity)

        AND

        ii. One of the following:

            1. Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy, or 12 months for patients continuing testosterone therapy, is within or below the normal limits of the reporting lab

            OR

2. Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy, or 12 months for patients continuing testosterone therapy, is outside of upper limits of normal for the reporting lab and the dose is adjusted

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: April 25, 2019

Prior Authorization Criteria being reviewed: Androgens

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: ____Lisa Todd_____

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: April 25, 2019

Prior Authorization Criteria being reviewed: Androgens

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 recommends the following in addition to the OptumRx FFS criteria.
HYPOGONADISM:

- Change initial approval length to 12 months from 14 days
- Diagnosis of hypogonadism
- One of the following: a. Significant reduction in weight (less than 90% ideal body weight) (e.g., AIDS wasting syndrome), b. Osteopenia, c. Osteoporosis, d. Decreased bone density, e. Decreased libido, f. Organic cause of testosterone deficiency (eg, injury)
- Patient is not taking any of the following: a. One of the following growth hormones, unless diagnosed with panhypopituitarism: (list growth hormones); b. Aromatase inhibitor (eg, anastrozole, letrozole, exemestane)
- If the request is for a non-preferred product, the patient has a history of failure, contraindication, or intolerance to generic testosterone 1% topical gel

GENDER DYSPHORIA:

- Remove "patient is a female-to-male transsexual"
- Include the 3rd and 4th bullets from HYPOGONADISM criteria

REAUTH CRITERIA FOR BOTH INDICATIONS – include 3rd bullet above

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: RK 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: April 25, 2019

Prior Authorization Criteria being reviewed: Androgens

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.

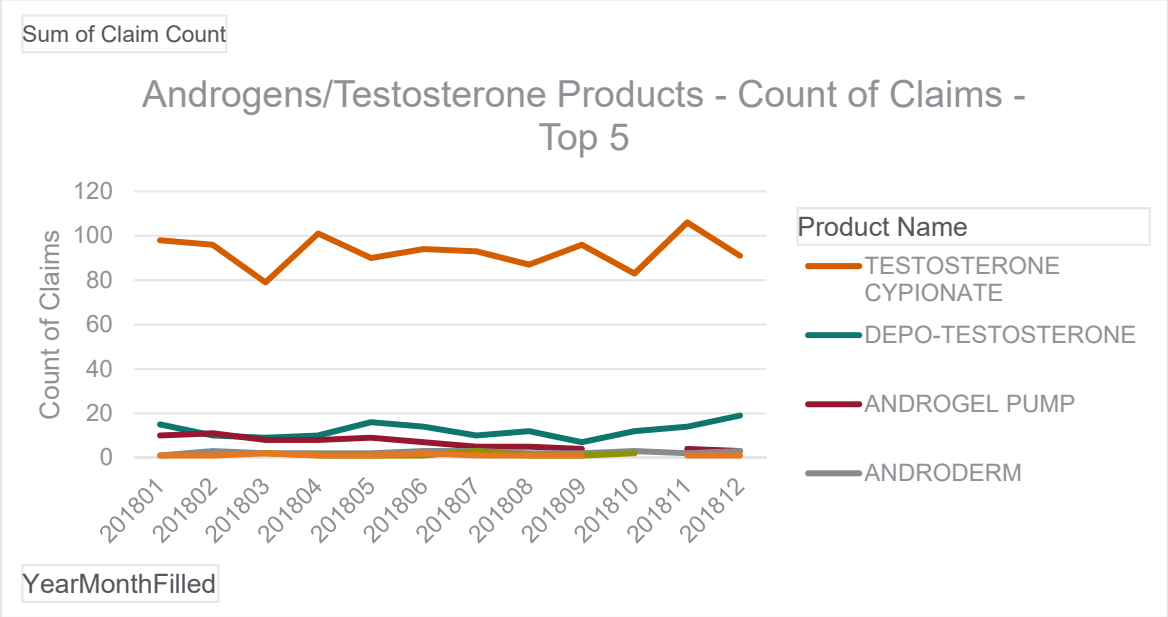
Please print the name of the individual completing this form: Tom Beranek

Signature of individual completing this form: Tom Beranek

Androgens/Testosterone Products

Summary of Utilization
January 1, 2018 - December 31, 2018
Fee for Service Medicaid

Product Name	Member Count	Claim Count	Days Supply	Sum of Qty
FORTESTA GEL 10MG/ACT	1	1	30	60
TESTOSTERONE SOL 30MG/ACT	4	11	367	1,530
TESTOSTERONE GEL PUMP 1%	1	3	90	450
ANDROGEL GEL 1%(50MG)	3	7	390	1,950
ANDRODERM DIS 4MG/24HR	3	18	540	810
TESTOPEL MIS PELLETS	1	7	7	7
TESTOST CYP INJ 200MG/ML	293	1,212	43,336	3,985
DEPO-TESTOST INJ 200MG/ML	32	143	261	142
DEPO-TESTOST INJ 100MG/ML	2	4	4	4
ANDRODERM DIS 2MG/24HR	2	10	330	330
TESTOST CYP INJ 100MG/ML	21	34	2,616	350
DANAZOL CAP 100MG	2	8	360	450
TESTOSTERONE GEL 1%(50MG)	2	6	180	900
TESTOST ENAN INJ 200MG/ML	8	14	362	650
ANDROGEL GEL 1.62%	20	88	2,740	10,500
TESTOSTERONE GEL 1%(25MG)	2	6	240	1,050
ANADROL-50 TAB 50MG	2	13	450	345
Total	**399**	**1,585**	**52,303**	**23,512**



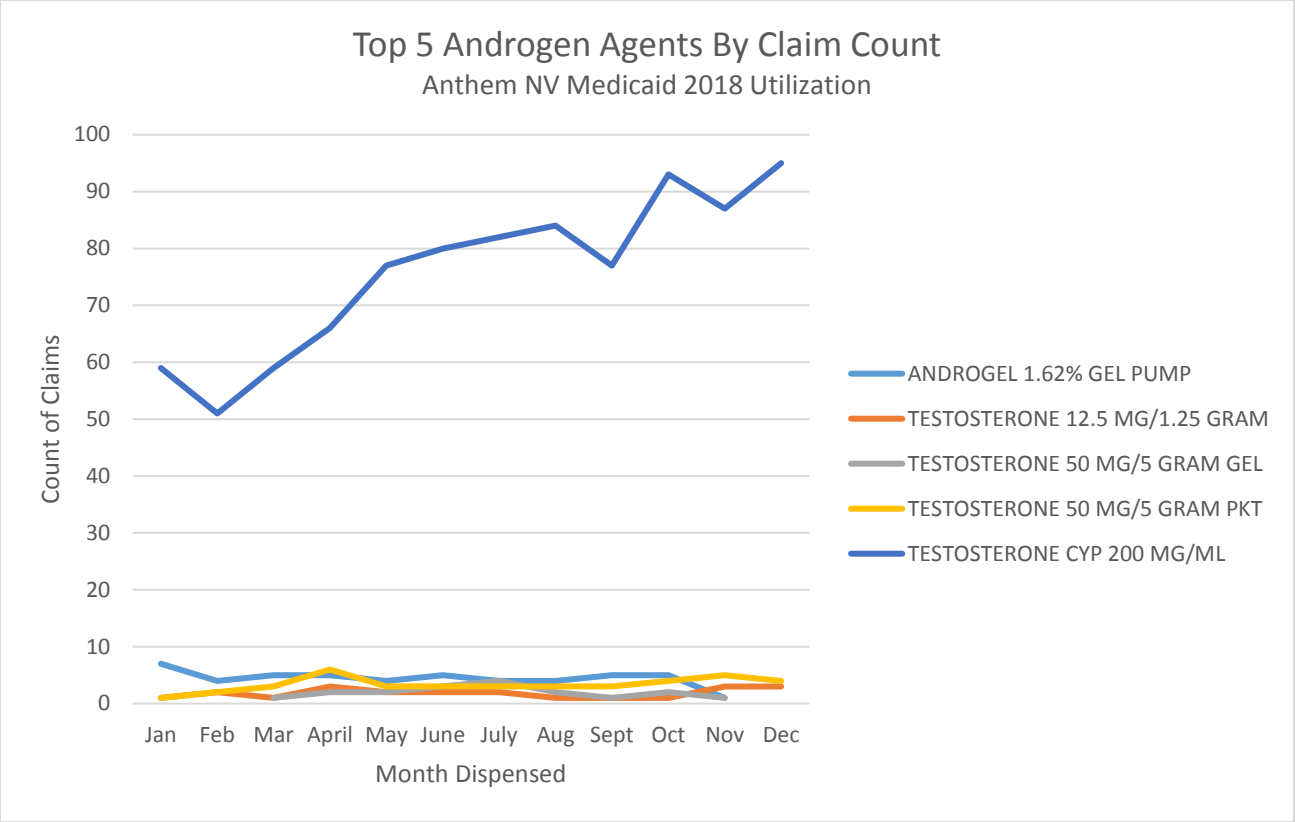
Androgen Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Anthem Nevada Medicaid

Drug	Count of Members	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
TESTOSTERONE CYP 200 MG/ML	910	910	24669	2275
ANDROGEL 1.62% GEL PUMP	49	49	1170	3675
TESTOSTERONE 50 MG/5 GRAM PKT	40	40	1200	6240
TESTOSTERONE 12.5 MG/1.25 GRAM	22	22	595	3225
TESTOSTERONE 50 MG/5 GRAM GEL	18	18	540	2700
TESTOSTERON CYP 2,000 MG/10 ML	11	11	318	120
TESTOSTERONE 30 MG/1.5 ML PUMP	6	6	180	540
ANDROGEL 1.62%(2.5G) GEL PCKT	6	6	180	450
TESTOSTERONE ENAN 200 MG/ML	5	5	150	25
TESTOSTERON CYP 1,000 MG/10 ML	5	5	146	50
TESTOSTERONE 1.62% GEL PUMP	5	5	120	375
TESTOSTERONE 25 MG/2.5 GM PKT	4	4	120	375
TESTOSTERONE CYP 100 MG/ML	2	2	60	20
DEPO-TESTOSTERONE 200 MG/ML	2	2	58	8
ANDROGEL 1.62%(1.25G) GEL PCKT	1	1	30	37.5
NATESTO NASAL 5.5 MG/0.122 GM	1	1	30	21.96
ANDRODERM 4 MG/24HR PATCH	1	1	30	30
TESTOSTERON ENAN 1,000 MG/5 ML	1	1	30	5
Grand Total	**1089**	**1089**	**29626**	**20172.46**

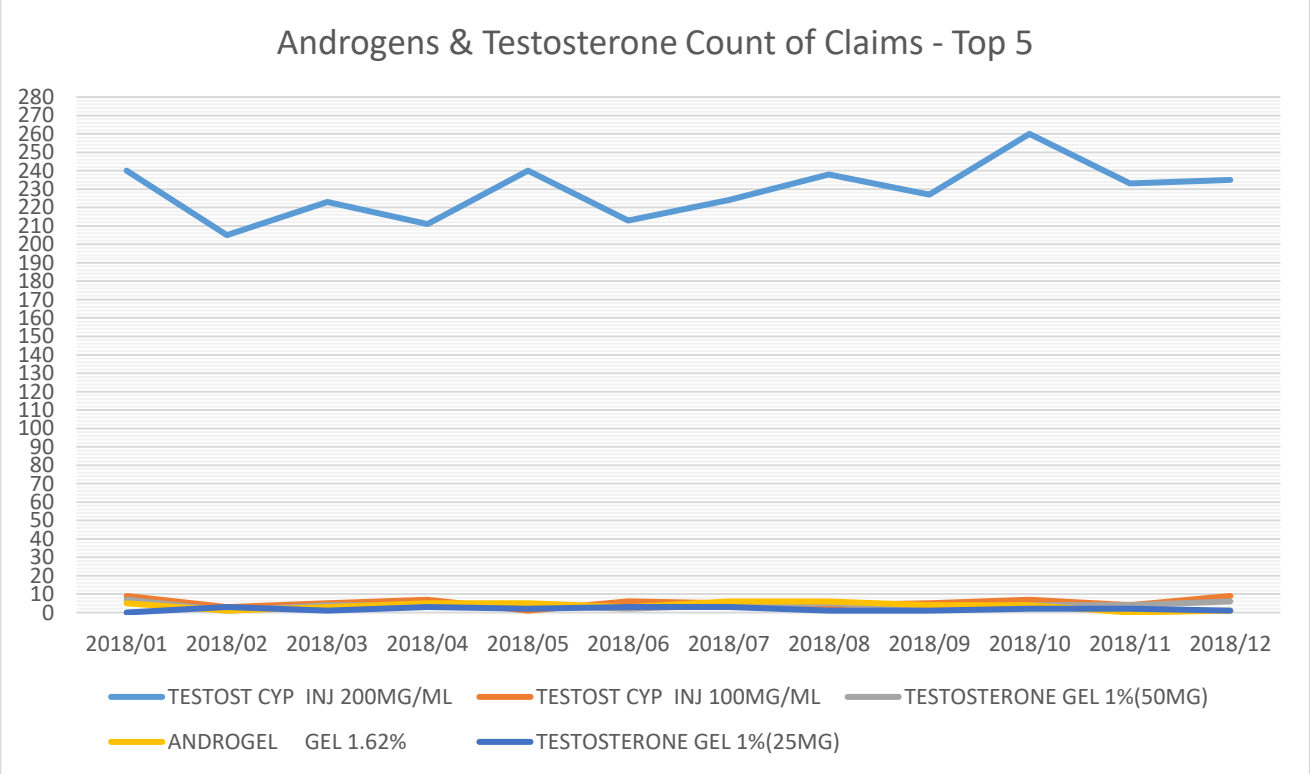

Top 5 Androgen Agents By Claim Count
Anthem NV Medicaid 2018 Utilization
Count of Claims
100
90
80
70
60
50
40
30
20
10
0
Jan
Feb
Mar
April
May
June
July
Aug
Sept
Oct
Nov
Dec
Month Dispensed
ANDROGEL 1.62% GEL PUMP
TESTOSTERONE 12.5 MG/1.25 GRAM
TESTOSTERONE 50 MG/5 GRAM GEL
TESTOSTERONE 50 MG/5 GRAM PKT
TESTOSTERONE CYP 200 MG/ML

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Androgens & Testosterone Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
TESTOST CYP INJ 200MG/ML	536	2,749	73,616	7,455	NA
TESTOST CYP INJ 100MG/ML	42	65	2,185	642	NA
TESTOSTERONE GEL 1%(50MG)	13	48	1,391	7,020	NA
ANDROGEL GEL 1.62%	11	43	1,273	3,450	NA
TESTOSTERONE GEL 1%(25MG)	6	22	660	2,025	NA
TESTOSTERONE SOL 30MG/ACT	4	8	180	900	NA
ANDRODERM DIS 4MG/24HR	3	8	240	240	NA
TESTOSTERONE GEL PUMP 1%	1	7	210	825	NA
TESTOSTERONE GEL 1.62%	5	7	210	450	NA
TESTOST ENAN INJ 200MG/ML	4	7	211	35	NA
TESTOSTERONE GEL 10MG/ACT	3	4	120	300	NA
DEPO-TESTOST INJ 200MG/ML	2	2	60	14	NA
ANDRODERM DIS 2MG/24HR	1	1	30	60	NA
DEPO-TESTOST INJ 100MG/ML	1	1	30	10	NA
Grand Total	**632**	**2,972**	**80,416**	**23,426**	**0**



Androgens Testosterone Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan

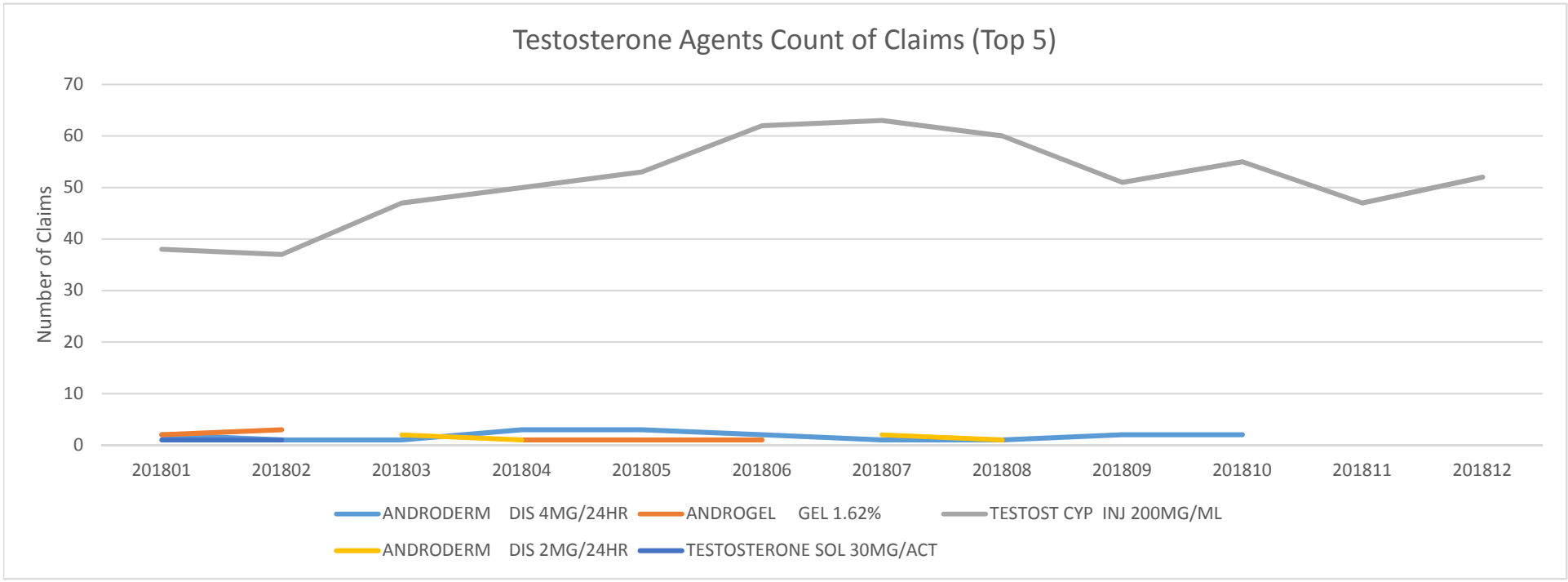
Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
TESTOST CYP INJ 200MG/ML	86	615	16,881	1,579	$ 27,973.74
ANDRODERM DIS 4MG/24HR	4	20	600	600	$ 11,296.80
ANDROGEL GEL 1.62%	3	10	295	863	$ 5,029.10
ANDRODERM DIS 2MG/24HR	2	6	180	180	$ 1,698.30
TESTOSTERONE SOL 30MG/ACT	1	3	98	270	$ 1,148.58
TESTOSTERONE GEL 1%(25MG)	1	3	90	210	$ 813.57
TESTOSTERONE GEL 1%(50MG)	1	2	60	300	$ 692.23
TESTOSTERONE GEL 1.62%	1	1	30	75	$ 560.70
TESTOSTERONE GEL 10MG/ACT	1	3	102	360	$ 504.93
DEPO-TESTOST INJ 200MG/ML	1	6	180	12	$ 242.95
TESTOST CYP INJ 100MG/ML	1	1	30	10	$ 50.60
Grand Total	**102**	**670**	**18,546**	**4,459**	**$ 50,011.50**

Androgens Testosterone Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan



DD. Androgel®, Androderm®, Testim® (Testosterone gel and transdermal system)

Therapeutic Class: Androgenic Agents
Last Reviewed by the DUR Board: July 22, 2010

Topical Androgens are subject to prior authorization.

1. Coverage and Limitations

   Recipients must meet all of the criteria for coverage:

2. Criteria for approval

   a. Recipient is a male;

   b. Use is for the FDA Approved Indication:

      Primary (congenital or acquired) or secondary (congenital or acquired) hypogonadism with an ICD code for hypogonadism;

   c. The patient has two morning pre-treatment testosterone levels below the lower limit of the normal testosterone reference range of the individual laboratory used;

   d. The patient does not have breast or prostate cancer, a palpable prostate nodule or induration, prostate-specific antigen greater than 4 ng/ml or severe lower urinary symptoms with an International Prostate Symptom Score (IPSS) > 19;

   e. The patient does not have a hematocrit > 50%;

   f. The patient does not have untreated severe obstructive sleep apnea; and

   g. The patient does not have uncontrolled or poorly controlled heart failure.

3. Prior Authorization Guidelines

   a. Prior authorization approval will be for up to one year.

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

   c. Length of authorization: one year.

INTRODUCTION

- Male hypogonadism is characterized by a lack of function of the gonads (testes). It can be categorized by the level of the reproductive system in which the defect occurs (*Dandona and Rosenberg, 2010*).
  - Primary hypogonadism is hypogonadism resulting from a defect of the gonads.
  - Secondary hypogonadism, also known as hypogonadotropic hypogonadism, results from defects in the hypothalamus or pituitary.
- Male hypogonadism may manifest with testosterone deficiency and/or infertility. Clinical signs and symptoms depend primarily on the age at the onset of the condition (*Petak et al, 2002*).
- Postpubertal hypogonadism usually results in slowly evolving clinical manifestations that may include a progressive decrease in muscle mass, loss of libido, impotence, oligospermia or azoospermia, poor ability to concentrate, and an increased risk of osteoporosis and fractures (*Petak et al, 2002*).
- Intramuscular (IM) and topical testosterone preparations are generally recommended for the management of hypogonadism in adult male patients. The oral alkylated androgens are generally not recommended because of poor androgen effects, adverse lipid changes, and hepatic side effects (*Bhasin et al, 2018; Mulhall et al, 2018; Petak et al, 2002; Wang et al, 2008*).
- Androgens included in this review are Androderm (testosterone) transdermal system; Androgel, Fortesta, Testim, and Vogelxo (testosterone) topical gels; Methitest (methyltestosterone) oral tablets, methyltestosterone oral capsules; Aveed (testosterone undecanoate) injection; testosterone topical solution; danazol oral capsules; Depo-Testosterone (testosterone cypionate) injection; Natesto (testosterone) nasal gel; Striant (testosterone) buccal system; Testopel (testosterone) pellets for subcutaneous implantation; and testosterone enanthate injections including Xyosted subcutaneous autoinjector.
- With the exception of danazol, all agents in this review are Food and Drug Administration (FDA)-approved for the management of male hypogonadism. Danazol is FDA-approved for the treatment of endometriosis and hereditary angioedema.
- Methyltestosterone capsules and tablets; Testopel (testosterone) pellets for subcutaneous implantation; and testosterone enanthate are also FDA-approved for the treatment of delayed puberty in males.
- Methyltestosterone capsules and tablets and testosterone enanthate are also FDA-approved for metastatic mammary cancer in females.
- All testosterone products are controlled substances (C-III). Danazol, an androgen, is not a controlled substance.
- Testosterone gels and solutions have risk evaluation and mitigation strategy (REMS) programs consisting of a medication guide with information on proper application, potential adverse effects, and preventing inadvertent exposure to others, specifically women and children. Aveed has a REMS program related to post-injection reactions (*Drugs@FDA, 2019*).
- This review primarily focuses on the use of androgens for the management of male hypogonadism.
- Non-labeled indications, such as anemia, hormone therapy for transgender patients, and acquired immunodeficiency syndrome (AIDS)-associated wasting syndrome are not addressed in this review.
  - Due to the number of branded products in different formulations, generic names and formulations will be used throughout the review.
  - The agents included in this review are listed in Table 1.
  - Other androgen products are not included in this review.
    - Oxandrolone is a synthetic testosterone derivative FDA-indicated for cachexia.
    - Oxymetholone is an anabolic steroid with androgenic properties FDA-indicated for anemias and myelofibrosis (*Micromedex, 2019*).
- Compounded products and combination products containing testosterone are not included in this review.
- Medispan therapeutic class: Androgens

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Androderm (testosterone transdermal system) patch	-
Androgel, Fortesta, Testim, Vogelxo (testosterone) topical gel	✔ *
Methitest (methyltestosterone) tablets, methyltestosterone capsules	-/ ✔ §
Aveed (testosterone undecanoate)	-
testosterone topical solution	✔ ¥
danazol	✔ †
Depo-Testosterone (testosterone cypionate)	✔
Natesto (testosterone) nasal gel	-
Striant (testosterone) buccal system	-
Testopel (testosterone) pellets for subcutaneous implantation	-
testosterone enanthate	✔ ‡
Xyosted (testosterone enanthate) autoinjector for subcutaneous injection	-

* A-B rated generics are available for Androgel 1% and 1.62% gel. An authorized generic is also available for Androgel 1.62%, Testim, Vogelxo, and Fortesta. In addition, the FDA has determined that Testim and Vogelxo are therapeutically equivalent.
¥ Branded product, Axiron, is no longer manufactured, but it is still available as a generic.
† Branded product, Danocrine, is no longer manufactured, but it is still available as a generic.
‡ Branded product, Delatestryl, is no longer manufactured, but it is still available as a generic.
§ Branded products, Android and Testred (methyltestosterone capsules), are no longer manufactured, but are still available as generics. Methitest is only available as a branded product.

(*Drugs@FDA, 2019; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2019*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	danazol	methyltestosterone	testosterone buccal	testosterone gel	testosterone nasal gel	testosterone implant	testosterone patch	testosterone topical solution	testosterone cypionate	testosterone enanthate	testosterone undecanoate*	testosterone enanthate autoinjector
Replacement therapy in males for deficiency or absence of endogenous testosterone due to primary hypogonadism (congenital or acquired)		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Replacement therapy in males for deficiency or absence of endogenous testosterone due to hypogonadotropic hypogonadism (congenital or acquired)		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Stimulation of puberty in carefully selected males with clearly delayed puberty that is not secondary to a pathological disorder		✔				✔				✔		
Treatment of metastatic mammary cancer in women with inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal		✔								✔		
Treatment of endometriosis amenable to hormonal management	✔											
Prevention of attacks of angioedema of all types	✔											
Limitations of Use:												
Safety and efficacy in men with "age-related hypogonadism" have not been established		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Safety in males under the age of 18 years has not been established			✔	✔	✔		✔	✔			✔	✔
Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure				✔ †								

*Aveed should only be used in patients who require testosterone replacement therapy and in whom the benefits of the product outweigh the serious risks of pulmonary oil microembolism (POME) and anaphylaxis.
† Androgel, Testim, and Vogelxo only

(*Prescribing information: Androderm, 2018; Androgel 1%, 2016; Androgel 1.62%, 2016; Android, 2015; Aveed, 2018; danazol, 2018; Depo-Testosterone, 2018; Fortesta, 2017; Methitest, 2016; Natesto, 2016; Striant, 2016; Testim, 2018; Testopel, 2018; testosterone enanthate, 2017; testosterone topical solution, 2018; Testred, 2015; Vogelxo, 2017; Xyosted 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

- Male Hypogonadism
  - In clinical studies, testosterone transdermal system (Androderm), topical gel (Androgel, Fortesta, Testim), and topical solution have been shown to increase serum testosterone and lean body mass, decrease body fat, and improve sexual function in men with hypogonadism. Increases in hemoglobin, hematocrit, and prostate specific antigen (PSA) were observed (*Brock et al, 2016, Dobs et al, 2012; Grober et al, 2008; McNicholas et al, 2003; Roy et al, 2017; Steidle et al, 2003; Swerdloff et al, 2000; Wang et al, 2000; Wang et al, 2004; Wang et al, 2011*).
  - A network meta-analysis of 87 randomized and 51 non-randomized studies concluded that testosterone replacement therapies, as a class, improved quality of life, libido, depression, and sexual function as compared to placebo (*Elliott et al, 2017*). Additionally, individual product comparisons were also made. Most endpoints did not reveal significant differences between products, but the 1% testosterone gel was significantly better than the patch for improvement in libido.
  - A 36-month extension study demonstrated that long-term treatment with testosterone topical gel (Androgel) maintained increased levels of serum testosterone as well as improvements in sexual function, positive mood, and body composition. A gradual but significant improvement in hip and spine bone mineral density was also observed. Increases in hemoglobin and hematocrit plateaued at 12 months, and clinically insignificant increases in high-density lipoprotein cholesterol, serum creatinine, and total bilirubin were seen. Serum levels of PSA showed no further significant increases past 6 months of treatment. Treatment-emergent adverse events included application site reactions, acne, and gynecomastia (*Wang et al, 2004*).
  - Head-to-head studies comparing testosterone topical gel (Androgel, Testim) to testosterone patch (Androderm) have shown greater improvement in serum testosterone levels, lean body mass, and sexual function as well as fewer adverse events with testosterone gel compared to testosterone patches in men with hypogonadism (*McNicholas et al, 2003; Steidle et al, 2003; Swerdloff et al, 2000; Wang et al, 2000*).
  - In an open-label study, hypogonadal men on testosterone replacement therapy with suboptimal response underwent brand substitution and switched between Androgel and Testim. More patients who switched from Androgel to Testim experienced improvements in libido, erectile function, and energy levels compared to those who switched from Testim to Androgel. Changing from Testim to Androgel eliminated or minimized unwanted adverse effects (*Grober et al, 2008).*
  - Testosterone buccal system (Striant) was compared to testosterone transdermal system or testosterone topical gel in 2 randomized controlled studies with hypogonadal men. Testosterone buccal system was shown to lead to serum testosterone levels within normal ranges that were similar to testosterone topical gel and transdermal system (*Dobs et al, 2004; Korbonits et al, 2004*).
  - A double-blind, randomized controlled trial showed that testosterone cypionate improved grip strength and increased hemoglobin compared to placebo in hypogonadal men (*Sih et al, 1997*).
  - An open-label trial comparing 4 different dosing regimens of testosterone enanthate in men with primary hypogonadism showed that testosterone enanthate 200 mg every 2 weeks and 300 mg every 3 weeks were most effective in suppressing serum luteinizing hormone to normal, while 100 mg every week and 200 mg every 2 weeks were effective in suppressing follicle-stimulating hormone to normal (*Snyder et al, 1980*).
  - In a small, open-label study, methyltestosterone was associated with improvement in sexual function in men with profound testosterone deficiency but no noticeable changes in levels of energy, mood, or feeling of well-being (*Morales et al, 1994*).
  - Aveed was approved via the 505(b)(2) pathway. The primary clinical trial submitted for its approval was a Phase 3, multi-center, open-label, 84-week, pharmacokinetic and safety study of testosterone undecanoate in hypogonadal men. Adult males with primary or secondary hypogonadism and testosterone levels < 300 ng/dL were given 750 mg of testosterone undecanoate IM at baseline, 4 weeks, and every 10 weeks thereafter for a total of 9 injections (N = 130). At week 14 (after the third dose), the percentage of the 117 patients still enrolled with an average serum total testosterone concentration within the normal range (300 to 1000 ng/dL) was 94% (95% confidence interval [CI], 89.7 to 98.3%). The percentage of patients with a maximum total testosterone concentration < 1500 ng/dL was 92%. The authors concluded that testosterone undecanoate 750 mg achieved sustained, consistent serum testosterone in the normal range during a 10-week dosing interval (*Morgentaler et*

al, 2008). Additional trials of testosterone undecanoate have been completed, but published results are limited. In 1 trial, the dose was not specified, but testosterone undecanoate was demonstrated to be effective in a large number of patients (*Zitzmann et al, 2013*). One study demonstrated improvement in scores on the Aging Male Symptoms (AMS) scale, which is 1 measurement of health-related quality of life, when testosterone undecanoate 1000 mg was used (*Ho et al, 2012*).

- One study with a 6-year follow up measured mortality in patients with type 2 diabetes (N = 581) with low vs. normal testosterone levels (some of whom were treated with testosterone gel or testosterone undecanoate to maintain normal levels). The authors found that patients with low testosterone had higher mortality rates than those with normal levels (17.2 vs. 9%; p = 0.003) (*Muraleedharan et al, 2013*).
- The Testosterone Trials were a coordinated set of clinical trials designed to determine whether testosterone would benefit men with age-related low testosterone levels. Initial results from 3 of the 7 trials have been published (*Snyder et al, 2016*). Each participant was enrolled in 1 or more of the 3 trials (the Sexual Function Trial, the Physical Function Trial, and the Vitality Trial). In addition to the results for the individual trials, the primary efficacy outcome of each trial was assessed among participants across all 3 trials. Patients (N = 790) aged ≥ 65 years with serum testosterone levels < 275 ng/dL were assigned to receive either testosterone gel (Androgel 1%) or placebo for 1 year.
  - Sexual function: Participants taking testosterone experienced an increase in sexual activity as assessed by question 4 on the Psychosexual Daily Questionnaire (PDQ-Q4) in both the Sexual Function Trial (mean difference, 0.58; p < 0.001) and among all trial participants (mean difference, 0.62; p < 0.001). Testosterone treatment was also associated with increased sexual desire and improved erectile function.
  - Physical function: Among patients enrolled in the Physical Function Trial, testosterone was not associated with a significant difference vs. placebo in the percentage of patients achieving a ≥ 50 meter increase in the 6-minute walking distance (6MWD) (odds ratio [OR], 1.42; p = 0.2); there was also no difference in the mean change from baseline in 6MWD. There was no significant difference in the percentage of patients with an increase of ≥ 8 points in the physical function domain (PF-10) of the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36); however, there was a significant difference in the mean change from baseline in PF-10 score (mean difference, 2.75 points; p = 0.03). When results from the 3 trials combined were considered, there was a significant difference in the percentage of patients with a ≥ 50 meter increase in 6MWD (OR, 1.76; p = 0.003) as well as each of the secondary physical function endpoints.
  - Vitality: Among patients in the Vitality Trial, testosterone was not associated with a significant difference vs. placebo in vitality as determined by an increase of ≥ 4 points on the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale (OR, 1.23; p = 0.3). However, improvements were observed on several secondary endpoints, including the SF-36 vitality score (mean difference, 2.41 points; p = 0.03), the positive and negative affect schedule (PANAS) positive affect score (mean difference, 0.47 points; p = 0.04), the PANAS negative affect score (mean difference, -0.49 points; p < 0.001), and the patient health questionnaire (PHQ-9) depression score (mean difference, -0.72 points; p = 0.004). There was no significant difference in the percentage of patients with an increase of ≥ 4 points on the FACIT-Fatigue score when results of the 3 trials combined were considered (OR, 1.23; p = 0.22); however, the effect of testosterone on the mean change from baseline in the FACIT-Fatigue score was significant (mean difference, 1.27; p = 0.006).
  - Safety: No significant differences between groups were demonstrated in cardiac adverse events. Seven men in each group had major adverse cardiovascular events (myocardial infarction, stroke, or death from cardiovascular causes) during the treatment period, and 2 patients in the testosterone group and 9 in the placebo group had major adverse cardiovascular events in the subsequent year. More patients assigned to testosterone had an increase in PSA of ≥ 1 ng/dL (23 vs 8); 1 man (in the testosterone group) was diagnosed with prostate cancer during the treatment period, and 2 patients in the testosterone group and 1 in the placebo group were diagnosed in the subsequent year. A hemoglobin level ≥ 17.5 g/dL was observed in 7 men in the testosterone group and none in the placebo group. No difference was seen in the international prostate symptom score (IPSS).

- Conclusions: Testosterone supplementation had small-to-moderate effects on all measures of sexual function and some measures of physical function, mood, and depressive symptoms. Although cardiovascular events were not increased with testosterone supplementation, the trial was not large enough to exclude smaller increases in risk. In addition, safety with respect to prostate cancer and urinary symptoms cannot be generalized because men with a high risk of prostate cancer and men with moderately severe urinary symptoms were excluded from the trial.

- Separate publications reported additional results from the Testosterone Trials. The Cognitive Function Trial included a subgroup of men (n = 493) with age-associated memory impairment (*Resnick et al, 2017*). Testosterone replacement did not improve delayed paragraph recall in these patients at 6 and 12 months (adjusted estimated difference, -0.07; p = 0.88). In the Cardiovascular Trial (n = 170) coronary computed tomographic angiography (CCTA) was used to determine whether testosterone slowed the progression of noncalcified coronary artery plaque. It was found that testosterone treatment was associated with a significantly greater increase in noncalcified plaque volume after 12 months of treatment compared with placebo: estimated difference, 41 mm^3; p = 0.003 (*Budoff et al, 2017*). The Bone Trial (n = 211) found testosterone treatment to significantly improve mean spine and hip volumetric bone mass density compared with placebo (*Snyder et al, 2017*).
- A randomized, double-blind, placebo-controlled trial found that once daily application of testosterone 2% solution for 12 weeks restored normal testosterone levels, and led to significant improvements in sex drive in men with hypogonadism; improvements in energy levels were variable (*Brock et al, 2016*).
- Meta-analyses have evaluated the potential adverse effects associated with testosterone use. One found that patients treated with testosterone had higher rates of cardiovascular-related events than patients treated with placebo (*Xu et al, 2013*). However, another meta-analysis that included both randomized controlled and epidemiological studies found no difference in the risk of major cardiovascular events between testosterone and placebo (*Corona et al, 2018*). Calof and colleagues found that patients treated with testosterone had a greater rate of prostate events and elevated hematocrit compared to patients treated with placebo (*Calof et al, 2005*).
- The efficacy and safety of Xyosted were evaluated in an open-label, single-arm, dose-blinded, 52-week study in 150 men with hypogonadism (*Kaminetsky et al, 2018*). Patients were started on 75 mg Xyosted self-administered on a weekly basis with dose adjustments made at week 7 based on total testosterone trough concentrations. Results revealed that 92.7% of subjects achieved an average total testosterone concentration of 300 to 1100 ng/dL at week 12 with a maximum serum concentration of < 1500 ng/dL achieved by 91.3% of patients and 0 patients with levels > 1800 ng/dL. At week 52, the mean testosterone trough concentration was 487.2 ± 153.33 ng/dL. The most frequently reported treatment-related adverse events were increases in hematocrit, hypertension, and PSA; no serious treatment-related adverse events were reported.

- Delayed puberty and delayed growth
  - Testosterone products, including testosterone enanthate and methyltestosterone have been studied in the treatment of delayed growth and puberty in adolescent males. These products have demonstrated increased growth (weight and height) in the time periods studied, but it is difficult to determine the long-term effects on bone health as the trials had relatively limited durations and study populations (*Kaplan et al, 1973; Rosenfeld et al, 1982; Soliman et al, 1995*).
- Endometriosis
  - Danazol is used for the palliative treatment of endometriosis in patients in whom alternative hormonal therapy (eg, estrogen and progestin or testosterone) is ineffective, intolerable or contraindicated (*Micromedex, 2019*). A meta-analysis of 5 placebo-controlled trials concluded that danazol was effective in relieving pain and improving laparoscopic scores in women with endometriosis; however, its use was limited by the occurrence of androgenic adverse effects (*Selak et al, 2007*).
- Hereditary angioedema
  - Studies have reported that danazol was beneficial in reducing the frequency and severity of acute attacks and increasing the serum levels of C1 esterase inhibitor and the fourth component of complement (*Bork et al, 2008; Gelfand et al, 1976*).
- Treatment of metastatic mammary cancer
  - Studies on the use of methyltestosterone have not been included in the detailed review. Endocrine therapy (including androgens) may be used for metastatic breast cancer in post-menopausal women.

Androgens are rarely used (often considered last-line therapy) in the treatment of metastatic breast cancer. While response rates may be reasonable, adverse effects, including virilization, edema, and jaundice, limit their clinical applicability compared to other treatment options (*Ma, 2018*).

CLINICAL GUIDELINES

- Male hypogonadism
  - The American Urological Association recommends the use of testosterone replacement therapy in men with testosterone deficiency but provides no specific guidance other than to avoid methyltestosterone (*Mulhall et al, 2018*). The European Association of Urology (EAU) recommends that choice of therapy should be based on risk vs benefit decisions between the provider and patient and states that short-acting therapies may be preferred when initiating therapy (*Dohle et al, 2018*). The Endocrine Society recommends all testosterone products in appropriate doses, with the exceptions of danazol and methyltestosterone (*Bhasin et al, 2018*). A joint statement by the International Society of Andrology (ISA), International Society for the Study of the Aging Male (ISSAM), EAU, European Academy of Andrology (EAA), and American Society of Andrology (ASA) agrees that decisions should be made based on patient and prescriber preference and tolerability, but states that methyltestosterone should be avoided due to potential liver toxicity (*Wang et al, 2008*). The American Association of Clinical Endocrinologists (AACE) also agrees with the recommendation to avoid methyltestosterone (*Petak et al, 2002*).
- Endometriosis
  - Both the American Society for Reproductive Medicine (ASRM) and American Congress of Obstetricians and Gynecologists (ACOG) have guidelines for the treatment of endometriosis, but only the ASRM specifically addresses danazol (*ACOG, 2010 [reaffirmed in 2018]; ASRM, 2014*). This guideline states that danazol has been used for the treatment of endometriosis, but hyperandrogenic side effects (hirsutism, acne, weight gain, and deepening of the voice) are common (*ASRM, 2014*).
- Hereditary angioedema
  - The international World Allergy Organization/European Academy of Allergy and Clinical Immunology 2017 guideline for the management of hereditary angioedema does not advise using danazol for on-demand treatment of attacks as the drug shows no or only minimal effects when used in this manner (*Maurer et al*, 2018). For long-term prevention of attacks, danazol is a recommended second-line therapy after C1-inhibitor administration.

SAFETY SUMMARY

- Boxed Warnings:
  - Danazol: use in pregnancy is contraindicated; thromboembolism, thrombotic and thrombophlebitic events, and life-threatening or fatal strokes have been reported; experience with long-term therapy is limited; and therapy has been associated with several cases of benign intracranial hypertension.
  - Testosterone, topical gel and solution: virilization has been reported in children who were secondarily exposed to testosterone gel.
  - Testosterone undecanoate has a boxed warning for post-injection pulmonary oil microembolism (POME) and anaphylactic reactions.
  - Xyosted has a boxed warning regarding increases in blood pressure that may elevate the risk of major adverse cardiovascular events. Blood pressure should be monitored before initiation, and periodically during, therapy.
- REMS programs
  - Testosterone topical gel and solution have REMS programs consisting of a medication guide to promote proper use, limit unwanted exposure, and provide safety information.
  - Testosterone undecanoate products have a single shared REMS program that restricts its use to specific healthcare facilities and providers who have been adequately trained to assess and treat post-injection reactions, including POME and anaphylaxis.
- Major contraindications include active thrombosis or thromboembolic disease (danazol only); androgen-dependent tumors or breast or prostate cancer; known hypersensitivity; serious cardiac, hepatic, or renal disease; use in pregnant or breastfeeding women or women who may become pregnant; porphyria (danazol only); and undiagnosed abnormal genital bleeding (danazol only).

- Although Depo-Testosterone, methyltestosterone, Testopel, and testosterone enanthate do not specifically list breastfeeding as a contraindication within their prescribing information, breastfeeding should be halted if these agents are required (*Briggs et al, 2017*).
- Key warnings include bone growth changes, adverse effects on spermatogenesis, cardiovascular risk (eg, myocardial infarction, stroke, etc.), serum lipid changes, blood glucose changes, edema with or without heart failure, gynecomastia, hepatic adverse effects, polycythemia, prostate cancer, priapism, virilizing effects in women and/or children, worsening of benign prostatic hyperplasia (BPH), and the potential for abuse of testosterone products. Additionally, use of testosterone has been subject to abuse leading to serious cardiovascular and psychiatric adverse reactions. If suspected, serum testosterone concentrations should be monitored.
- Transdermal testosterone patches contain aluminum that may burn the skin if worn during a magnetic resonance imaging scan. Testosterone gel and topical solution formulations are flammable until dry.
- Common side effects include application-related reactions for topical and buccal products, injection site reactions for injected products, edema, hepatic adverse effects, prostate effects, increased hematocrit, weight gain, and virilizing effects.
- In January 2014, the FDA announced that it was investigating the risk of cardiovascular events (ie, stroke, heart attack, and death) in men taking FDA-approved testosterone products, based on the results of 2 trials that suggested an increased cardiovascular risk. At that time, the FDA had not made any conclusions and recommended that patients not discontinue prescribed testosterone products without first discussing any questions or concerns with their health care provider (*FDA drug safety communication, 2014*). On March 3, 2015, the FDA issued an updated safety announcement clarifying the approved uses of prescription testosterone products for men who have low testosterone caused by certain medical conditions and not for treating low testosterone due to aging. Additionally, the manufacturers of all approved testosterone products were required to add information to the labeling about a possible increased risk of heart attacks and strokes in patients taking testosterone. Manufacturers are also required to conduct a well-designed clinical trial to more clearly address the question of whether an increased risk of heart attack or stroke exists among users of these products. In April 2015, the FDA approved labeling revisions to several sections of the prescribing information for all of the testosterone products to clarify the approved uses, confirm the medical condition causing low testosterone using lab testing, and add a new warning related to potential increased cardiovascular risk (*FDA drug safety communication, 2015*). In October 2016, the FDA finalized labelling regarding abuse and dependence of testosterone along with the adverse health outcomes associated with abuse (*FDA drug safety communication, 2016*). The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) issued a joint position statement in September 2015 on the association of testosterone and cardiovascular risk. Although they agreed with the FDA that the risk/benefit of testosterone replacement therapy is not well established in aging-associated hypogonadism and large-scale, prospective, randomized controlled trials are needed, the joint committee determined that the FDA directive lacked clarity. They recommended that decisions on testosterone replacement should be guided by the signs, symptoms, and testosterone concentrations rather than the underlying cause (*Goodman et al, 2015*). Newer data suggest that increases in cardiovascular events may be due to widespread use of testosterone therapies without appropriate monitoring, and patients with cardiovascular disease may safely receive androgen therapy for the treatment of hypogonadism (*Tanna et al, 2016*).
- A trial (N = 308) was designed to determine the effect of testosterone administration on subclinical atherosclerosis progression in men ≥ 60 years of age with low or low-normal baseline testosterone levels. Treatment continued for a 3-year period. In this study, testosterone replacement did not result in a significant difference in the rate of change in common carotid artery intima-media thickness or coronary artery calcium. However, the trial was not designed to determine the effects of testosterone replacement on cardiovascular events (*Basaria et al, 2015*).
- A European observational study of hypogonadal, elderly men (mean age 59 years) (N = 115) evaluated the effects of testosterone undecanoate on various parameters for up to 10 years of use. Injections of testosterone were given every 12 weeks. Body weight and body mass index were significantly reduced from the previous year for 8 years and waist circumference was significantly lower from the previous year for 7 years. The hemoglobin A1C and ratio of triglycerides to high-density lipoprotein were significantly reduced from the second year onward. Fasting blood glucose showed improvement after

the first year of testosterone replacement. No major cardiovascular events were observed (*Yassin et al, 2016*).

- A European observational study of hypogonadal men with a history of cardiovascular disease (N = 77, mean age 61 years) evaluated the effects of testosterone therapy for up to 8 years. A marked and significant weight loss was observed after 8 years of continuous use. Beneficial effects were also observed on body mass index, lipid parameters, blood pressure, and glycemic control. No patient suffered a major adverse cardiovascular event during the full observation time (*Haider et al, 2016*).
- In a European multinational longitudinal disease registry of 99 men with hypogonadism, 750 (75%) initiated testosterone replacement therapy. CV event rates for men receiving testosterone were not statistically different from untreated men (p = 0.70). Regardless of treatment assignment, CV event rates were higher in older men and in those with increased CV risk factors or a prior history of CV events (*Maggi et al, 2016*).
- In a European prospective registry of men with hypogonadism, 360 men who received testosterone undecanoate were compared to 296 men who did not receive testosterone treatment (*Traish et al, 2017*). Deaths and CV parameters were tracked for 8 years. In contrast to previous studies, patients receiving testosterone had a lower mortality rate than the control group (estimated incidence difference, 0.0804; 95% CI, 0.0189 to 0.3431). In this cohort, there were no CV-related deaths in the testosterone group and 19 CV-related deaths in the control group.
- Although testosterone therapy was previously thought to be contraindicated in men with a history of prostate cancer, recent data suggest that use does not increase risk of de novo prostate cancer, progression of the disease, or biochemical recurrence in men with hypogonadism and a history of non-high-risk prostate cancer; safety data for testosterone use in high-risk cancer patients are limited and use in this patient population remains controversial (*Davidson et al, 2016; Nguyen et al, 2016*).

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Androderm (testosterone transdermal system) (C-III)	Transdermal system	top	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): Apply once nightly	Apply patches to back, abdomen, upper arms or thighs. Rotate the site of application with an interval of 7 days between applications to the same site. Avoid swimming, showering or washing the application site for a minimum of 3 hours after application. When discarding a used patch, it should be folded in half so the sticky sides stick together and thrown away in household trash.
Androgel, Fortesta, Testim, Vogelxo (testosterone) (C-III)	Topical gel	top	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism	Apply the topical gel in the following area: Androgel 1%: shoulders, upper arms and/or abdomen Androgel 1.62%: upper arms and shoulders

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			(congenital or acquired in males): Apply once daily (preferably in the morning)	Fortesta: front and inner thighs Testim, Vogelxo: shoulders and/or upper arms Allow application sites to dry before dressing. Cover the application sites with clothing to prevent transfer to another person. Wash hands with soap and water after application. Avoid swimming, showering or washing the application site for a minimum of: ○ 2 hrs after Androgel 1.62%, Fortesta, Vogelxo, and Testim ○ 5 hrs after Androgel 1%
Methitest, (methyltestosterone) tablets, methyltestosterone capsules (CIII)	Capsules Tablets	oral	Delayed puberty (males): 10-50 mg/d for a limited duration (eg, 4-6 mos) Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): 10-50 mg/d Metastatic mammary cancer (females): 50-200 mg/d	Dosage will depend on age, sex, diagnosis, patient's response to treatment, and appearance of adverse effects.
Aveed (testosterone undecanoate) (C-III)	Injectable solution	IM	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males):	Observe patients in the healthcare setting for 30 minutes following injection for symptoms of serious POME reactions or anaphylaxis. Inject deeply into the gluteal muscle at a 90°

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			Inject at initiation, 4 wks, and every 10 wks thereafter	angle over 60 to 90 seconds. Between consecutive injections, alternate the injection site between the left and right buttock.
Testosterone (C-III)	Topical solution	top	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): Apply once daily in the morning	Apply to the axilla with an applicator. Use at least 2 minutes after antiperspirant or deodorant use. Allow application sites to dry before dressing. Cover the application sites with clothing to prevent transfer to another person. Rinse the metered dose pump applicator with water after application. Avoid swimming, showering or washing the application site for a minimum of 2 hours after application.
Danazol	Capsules	oral	Treatment of endometriosis (females): Twice daily; continue uninterrupted for 3-6 mos (up to 9 mos) Treatment of hereditary angioedema: Twice to 3 times daily; after a favorable response, decrease dose by 50% or less at intervals of 1 to 3 months or longer depending on the frequency of attacks; individualize dose based on patient response	Treatment of endometriosis should begin during menstruation; otherwise, ensure that patient is not pregnant while on treatment.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Depo-Testosterone (testosterone cypionate) (C-III)	Injectable solution	IM	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): Inject every 2-4 wks	Dosage will depend on age, sex, diagnosis, patient's response to treatment, and appearance of adverse effects. Inject the preparation slowly and deeply into the gluteal muscle.
Natesto (testosterone nasal gel) (C-III)	Nasal gel	intranasal	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): Apply intranasally 3 times daily	Administer once in the morning, afternoon, and evening (6 to 8 hrs apart). Clear nasal passage prior to intranasal administration. Do not blow the nose or sniff for 1 hour after administration.
Striant (testosterone buccal system) (C-III)	Buccal system	oral	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): Apply to gum region twice daily	The buccal system should be placed against the gum and held firmly in place with a finger over the lip and against the product for 30 seconds to ensure adhesion. Place Striant in a comfortable position just above the incisor tooth (on either side of the mouth). Rotate sides of mouth with each application. Remove by gently sliding it downwards from the gum. The system should be removed before brushing or flossing the teeth. Do not chew or swallow.
Testopel (testosterone) pellets for subcutaneous implantation (C-III)	Pellets	SC	Delayed puberty (males): Doses vary based on needs and are typically less than for hypogonadotropic hypogonadism; inject SC for a limited duration (eg, 4 to 6 months of treatment) Hypogonadotropic hypogonadism (congenital or	In the face of complications, the pellets should be removed. In addition, pellets may slough out. Pellet implantation is less flexible for dosage adjustment. Great care should be used when estimating the amount of testosterone needed.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			acquired in males) and primary hypogonadism (congenital or acquired in males): Inject SC every 3-6 mos	Lower doses may be used on initiation and then increased gradually. Approximately one-third of the material is absorbed in the first month, one-fourth in the second month, and one-sixth in the third month. Frequency may vary based on patient needs.
testosterone enanthate (C-III)	Injectable solution	IM	Delayed puberty: Inject IM every 2-4 wks for a limited duration (eg, 4-6 mos) Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): Inject IM every 2-4 wks Metastatic mammary cancer (females): Inject IM every 2-4 wks	Inject the preparation slowly and deeply into the gluteal muscle. Dosage and duration of therapy will depend on age, sex, diagnosis, patient's response to treatment and appearance of adverse effects.
Xyosted (testosterone enanthate) autoinjector for subcutaneous administration	Autoinjector	SC	Hypogonadotropic hypogonadism (congenital or acquired in males) and primary hypogonadism (congenital or acquired in males): Inject SC once weekly	Inject in the abdominal region only.

See the current prescribing information for full details

CONCLUSION

- Androgens included in this review are Androderm (testosterone) transdermal system; Androgel, Fortesta, Testim, and Vogelxo (testosterone) topical gels; methyltestosterone oral capsules; Aveed (testosterone undecanoate) injection; testosterone topical solution; danazol oral capsules; Depo-Testosterone (testosterone cypionate) injection; Methitest (methyltestosterone) oral tablets; Natesto (testosterone) nasal gel; Striant (testosterone) buccal system; Testopel (testosterone) pellets for subcutaneous implantation; and testosterone enanthate injection including Xyosted subcutaneous autoinjector.

- With the exception of danazol, all agents in this review are FDA-approved for the management of male hypogonadism. Danazol is FDA-approved for the treatment of endometriosis and hereditary angioedema.
- All androgen products, with the exception of danazol, are controlled substances (C-III). Testosterone gels and solutions have REMS programs consisting of a medication guide with information on proper application, potential adverse effects, and preventing inadvertent exposure to others, specifically women and children. Aveed has a REMS program related to post-injection reactions (*Drugs@FDA, 2019*).
- In clinical studies, testosterone buccal and topical products have been shown to increase serum testosterone levels and/or improve lean body mass, decrease body fat, and improve sexual function in men with hypogonadism (*Dobs et al, 2004; Dobs et al, 2012; Grober et al, 2008; Korbonits et al, 2004; McNicholas et al, 2003; Steidle et al, 2003; Swerdloff et al, 2000; Wang et al, 2000; Wang et al, 2004; Wang et al, 2011*).
- Initial results from a coordinated set of clinical trials in men with age-related low testosterone levels demonstrated small-to-moderate improvements in sexual function and some measures of physical function, mood, and depressive symptoms (*Snyder et al, 2016*).
- Head-to-head studies comparing testosterone topical gel to testosterone transdermal system have shown greater improvement in serum testosterone levels, lean body mass, and sexual function as well as fewer adverse events with testosterone gel compared to testosterone patches in men with hypogonadism (*McNicholas et al, 2003; Steidle et al, 2003; Swerdloff et al, 2000; Wang et al, 2000*).
- Increases in hemoglobin, hematocrit, and PSA have been observed in clinical studies (*Wang et al, 2000*). Severe hepatotoxicity has been associated more commonly with oral androgen than topical androgen therapy, and liver function tests should be monitored periodically.
- Meta-analyses have demonstrated an increased risk of cardiovascular events and prostate events, whereas a long-term observational study found reduced mortality in patients with type 2 diabetes who had low testosterone vs normal testosterone levels. A European 10-year observational study of elderly men demonstrated improvement in weight, body mass index, and glycemic parameters with no reports of major adverse cardiovascular events. Similarly, a European 8-year observational study of hypogonadal men with a history of cardiovascular disease demonstrated improvement in weight, body mass index, lipid parameters, blood pressure, and glycemic control with no major adverse cardiovascular events during the full observation time. Another European 8-year observational study observed lower rates of mortality, including CV-related deaths, in hypogonadal men receiving testosterone compared to those not receiving treatment (*Calof et al, 2005; Muraleedharan et al, 2013; Xu et al, 2013, Yassin et al, 2016, Haider et al, 2016; Traish et al, 2017*).
- Although testosterone therapy was previously thought to be contraindicated in men with a history of prostate cancer, recent data suggest that use does not increase risk of de novo prostate cancer, progression of the disease, or biochemical recurrence in men with hypogonadism and a history of non-high-risk prostate cancer; safety data for testosterone use in high-risk cancer patients are limited and use in this patient population remains controversial (*Davidson et al, 2016; Nguyen et al, 2016*).
- In March 2015, the FDA issued a safety announcement clarifying the approved uses of prescription testosterone products for men who have low testosterone caused by certain medical conditions, discouraging the treatment of low testosterone due to aging, and requiring manufacturers of all approved testosterone products to add information to the labeling regarding a possible increased risk of heart attacks and strokes in patients taking testosterone and to conduct a well-designed clinical trial to more clearly address the question of whether an increased risk of heart attack or stroke exists among users of these products. In April 2015, the FDA approved labeling revisions to several sections of the prescribing information for all of the testosterone products to clarify the approved uses, confirm the medical condition causing low testosterone using lab testing, and add a new warning related to a potential increased cardiovascular risk (*FDA drug safety communication, 2015*). The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) issued a joint position statement in September 2015 recommending testosterone replacement be guided by the signs, symptoms, and testosterone concentrations rather than the underlying cause (*Goodman et al, 2015*). Newer data suggest that increases in cardiovascular events may be due to widespread use of testosterone therapies without appropriate monitoring, and patients with cardiovascular disease may safely receive androgen therapy for the treatment of hypogonadism (*Tanna et al, 2016*).

- According to current consensus guidelines, IM and topical testosterone preparations are generally recommended for the management of hypogonadism in adult male patients while the oral (capsule or tablet) androgen therapies are generally not recommended for this condition due to poor androgen effects, adverse lipid changes, and hepatic side effects. The selection of a specific testosterone replacement therapy should be a joint decision between an informed patient and physician after considering patient preferences, the pharmacokinetic profiles of the respective agents, treatment burden, and cost. Furthermore, currently available guidelines do not give preference to one topical preparation vs. another (*Bhasin et al, 2018; Dohle et al, 2018; Mulhall et al, 2018; Petak et al, 2002; Wang et al, 2008*).

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Publication Date: February 21, 2019

Fentanyl

Prior Authorization Guideline

Guideline Name Fentanyl (Duragesic) transdermal

1. Indications

Drug Name: Transdermal fentanyl patch

Indications

Chronic Pain: Management of pain in opioid-tolerant patients, severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

2. Criteria

Product Name: Fentanyl patch

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

Approval Criteria

1. Diagnosis of pain severe enough to require daily, around-the-clock, long-term opioid (agent is contraindicated in the management of mild or intermittent pain, acute pain, and postoperative pain)

AND

2. Patient requires continuous opioid administration

AND

3. Patient's condition cannot be managed by lesser means such as acetaminophen-opioid combinations, nonsteroidal analgesics, or PRN dosing with a short acting opioid

AND

4. The prescriber has been encouraged to check the Nevada State BOPs Prescription Monitoring Program (PMP) prior to prescribing narcotic analgesics.

AND

5. One of the following:

    a. Patient is transitioning to fentanyl patch from another opioid AND one of the following:

- Morphine equivalent dose is 134 mg/day or less, and the requested fentanyl dose is 25 mcg/hour (every 3 days)
- Morphine equivalent dose is 135 to 224 mg/day, and the requested fentanyl dose is 50 mcg/hour (every 3 days)
- Morphine equivalent dose is 225 to 314 mg/day, and the requested fentanyl dose is 75 mcg/hour (every 3 days)
- Morphine equivalent dose is 315 to 404 mg/day, and the requested fentanyl dose is 100 mcg/hour (every 3 days)
- Morphine equivalent dose is 405 to 494 mg/day, and the requested fentanyl dose is 125 mcg/hour (every 3 days)
- Morphine equivalent dose is 495 to 584 mg/day, and the requested fentanyl dose is 150 mcg/hour (every 3 days)
- Morphine equivalent dose is 585 to 674 mg/day, and the requested fentanyl dose 175 mcg/hour (every 3 days)
- Morphine equivalent dose is 675 to 764 mg/day, and the requested fentanyl dose is 200 mcg/hour (every 3 days)
- Morphine equivalent dose is 765 to 854mg/day, and the requested fentanyl dose is 225 mcg/hour (every 3 days)
- Morphine equivalent dose is 855 to 944mg/day, and the requested fentanyl dose is 250 mcg/hour (every 3 days)
- Morphine equivalent dose is 945 to 1034 mg/day, and the requested fentanyl dose is 275 mcg/hour (every 3 days)
- Morphine equivalent dose is 1035 to 1124 mg/day, and the requested fentanyl dose is 300 mcg/hour (every 3 days)

OR

b. The patient is not transitioning to fentanyl patches from another opioid AND one of the following:

- The requested dose is 12 mcg/hr (1 patch every 3 days)
- The requested dose is 25 mcg/hr (1 patch every 3 days)

Prior Authorization Guideline

Guideline Name Oral Fentanyl Products

1 . Indications

Drug Name: Abstral (fentanyl) **Indications** **Breakthrough pain** Indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine daily, or at least 25 mcg of transdermal fentanyl/hour, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily or at least 25 mg oral oxymorphone daily, or an equianalgesic dose of another opioid medication daily for a week or longer. Patients must remain on around-the-clock opioids when taking Abstral. Limitations of Use: As a part of the TIRF REMS Access program, Abstral may be dispensed only to outpatients enrolled in the program. For inpatient administration of Abstral (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.
Drug Name: Actiq (fentanyl citrate) oral transmucosal lozenge **Indications** **Breakthrough pain** Indicated for the management of breakthrough pain in cancer patients 16 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine daily, at least 25 mcg of transdermal fentanyl/hour, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily, at least 25 mg oral oxymorphone daily, or an equianalgesic dose of another opioid daily for a week or longer. Patients must remain on around-the-clock opioids when taking Actiq. This product must not be used in opioid non-tolerant patients because life-threatening respiratory depression and death could occur at any dose in patients not on a chronic regimen of opioids. For this reason, Actiq is contraindicated in the management of acute or postoperative pain. Actiq is intended to be used only in the care of opioid-tolerant cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain. Limitations

of Use: As a part of the TIRF REMS Access program, Actiq Q may be dispensed only to outpatients enrolled in the program. For inpatient administration of Actiq (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.

Drug Name: Fentora (fentanyl buccal tablet)

Indications

Breakthrough pain Indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine daily, at least 25 mcg/hr of transdermal fentanyl, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily, at least 25 mg oral oxymorphone daily, or an equianalgesic dose of another opioid daily for a week or longer. Patients must remain on around-the-clock opioids while taking Fentora. This product must not be used in opioid non-tolerant patients because life-threatening hypoventilation and death could occur at any dose in patients not on a chronic regimen of opioids. For this reason, Fentora is contraindicated in the management of acute or postoperative pain. Fentora is intended to be used only in the care of opioid tolerant cancer patients and only by healthcare professionals who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain. Limitations of Use: As a part of the TIRF REMS Access program, Fentora may be dispensed only to outpatients enrolled in the program. For inpatient administration of Fentora (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.

Drug Name: Lazanda (fentanyl) nasal spray

Indications

Breakthrough pain Indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least: 60 mg of oral morphine/day, 25 mcg of transdermal fentanyl/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid for a week or longer. Patients must remain on around-the-clock opioids when taking Lazanda. Lazanda is contraindicated for patients who are not already tolerant to opioids because life-threatening respiratory depression and death could occur in patients not taking chronic opioids. For this reason, Lazanda is contraindicated in the management of acute or postoperative pain, including headache/migraine, or dental pain. Lazanda is intended to be prescribed only by healthcare professionals who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain. Limitations of Use: As a part of the TIRF REMS Access program, Lazanda may be dispensed only to outpatients enrolled in the program.For inpatient administration of Lazanda (e.g., hospitals, hospices, and long-term care facilities that prescribefor inpatient use), patient enrollment is not required.

Drug Name: Subsys (fentanyl sublingual spray)

Indications

Breakthrough pain Indicated for the management of breakthrough pain in adult cancer patients who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine daily, at least 25 mcg of transdermal fentanyl/hour, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid daily for a week or longer. Patients must remain on around-the-clock opioids when taking Subsys . This product must not be used in opioid non-tolerant patients because life-threatening respiratory depression and death could occur at any dose in patients not on a chronic regimen of opioids. For this reason, Subsys is contraindicated in the management of acute or postoperative pain. Subsys is intended to be used only in the care of cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain. Limitations of Use As part of the Transmucosal Immediate-Release Fentanyl (TIRF) REMS ACCESS Program, Subsys may be dispensed only to outpatients enrolled in the program. For inpatient administration (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use) of Subsys, patient enrollment is not required.

2 . Criteria

Product Name: Abstral, Actiq, Fentora, Lazanda, Subsys or generic fentanyl lozenges

Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1. For the management of breakthrough cancer pain

AND

2. Patient must have at least a one week history of one of the following medications to demonstrate tolerance to opioids:

- Morphine sulfate at doses of greater than or equal to 60 mg/day
- Fentanyl transdermal patch at doses greater than or equal to 25 µg/hr
- Oxycodone at a dose of greater than or equal to 30 mg/day
- Oral hydromorphone at a dose of greater than or equal to 8 mg/day
- Oral oxymorphone at a dose of greater than or equal to 25 mg/day
- An alternative opioid at an equianalgesic dose (e.g., oral methadone greater than or equal to 20 mg/day)

AND

3. The patient is currently taking a long-acting opioid around the clock for cancer pain

AND

4. Prescribed by or in consultation with one of the following:

- Pain specialist
- Oncologist
- Hematologist
- Hospice care specialist
- Palliative care specialist

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: April 25, 2019

Prior Authorization Criteria being reviewed: Fentanyl

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

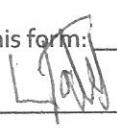
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

Oral forms of fentanyl are included in the Anthem transmucosal PA criteria. All transmucosal forms of fentanyl require clinical PA. All transmucosal fentanyl agents and are non-preferred with the exception of generic fentanyl citrate lozenge which is preferred.

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: Lisa Todd

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: April 25, 2019

Prior Authorization Criteria being reviewed: Fentanyl (Transdermal)

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.

The transdermal fentanyl agents are included in the Anthem Long-Acting Opioid PA criteria. All LA opioids require clinical PA.

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: Lisa Todd

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: April 25, 2019

Prior Authorization Criteria being reviewed: Fentanyl

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 recommends the following changes to the proposed OptumRx FFS criteria for fentanyl IR:

- ADD "Submission of medical records demonstrating use is for the management of pain associated with a cancer diagnosis (cancer diagnosis must be documented)."
- REMOVE specialist requirement
- ADD - One of the following:
    - The patient is not concurrently receiving an alternative fentanyl transmucosal product OR The patient is currently receiving an alternative transmucosal fentanyl product AND the prescriber is requesting the termination of all current authorizations for alternative transmucosal fentanyl products in order to begin treatment with the requested medication. Only one transmucosal fentanyl product will be approved at a time. If previous authorizations cannot be terminated, the PA request will be denied.
- ADD (for products that are NOT fentanyl citrate lozenges (generic Actiq) only)
    - History of failure, contraindication, or intolerance to Fentanyl citrate lozenges (generic Actiq)
- ROLL fentanyl transdermal patch requirements in already existing long-action opioid PA

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: _____RK 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: April 25, 2019

Prior Authorization Criteria being reviewed: Fentanyl

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.

Oral

Initial Approval Criteria:

- Member is on fentanyl transdermal patches;
- Age ≥ 16 years (for Actiq requests) OR age ≥ 18 years (for Abstral, Fentora, Lazanda, or Subsys requests);
- Failure of a trial of two formulary short-acting opioid analgesics unless all are contraindicated or clinically significant adverse effects are experienced;
- For Abstral, Fentora, Lazanda and Subsys requests: Failure of a trial of generic fentanyl citrate oral transmucosal lozenge (Actiq) unless contraindicated or clinically significant adverse effects are experienced;

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.

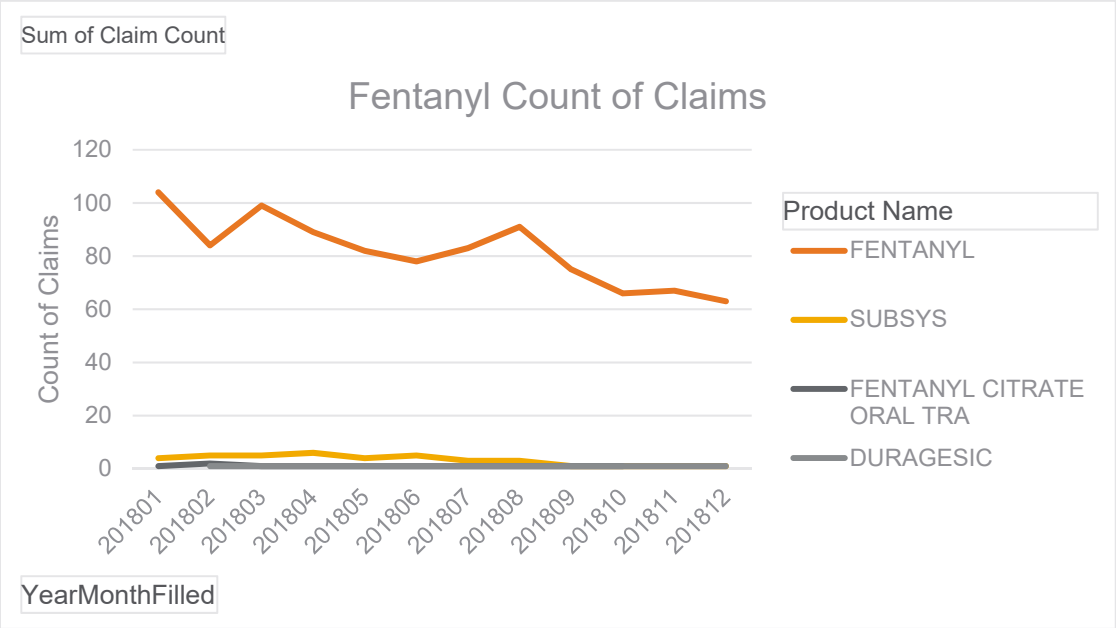
Please print the name of the individual completing this form: Tom Beranek

Signature of individual completing this form: Tom Beranek

Fentanyl Products

Summary of Utilization
January 1, 2018 - December 31, 2018
Fee for Service Medicaid

Product Name	Member Count	Claim Count	Days Supply	Sum of Qty
DURAGESIC DIS 100MCG/H	1	2	60	30
DURAGESIC DIS 75MCG/HR	3	15	450	170
FENTANYL DIS 100MCG/H	27	158	4,065	1,614
FENTANYL DIS 12MCG/HR	54	178	4,727	1,693
FENTANYL DIS 25MCG/HR	110	426	11,336	4,115
FENTANYL DIS 37.5MCG	8	39	1,140	420
FENTANYL DIS 50MCG/HR	83	305	8,016	2,899
FENTANYL DIS 75MCG/HR	43	236	6,222	2,222
FENTANYL OT LOZ 200MCG	2	2	2	2
FENTANYL OT LOZ 600MCG	1	10	300	1,170
SUBSYS SPR 200MCG	1	15	225	900
SUBSYS SPR 600MCG	3	12	344	1,440
SUBSYS SPR 800MCG	1	12	360	1,440
Total	**337**	**1,410**	**37,247**	**18,115**



Fentanyl Transdermal Patches

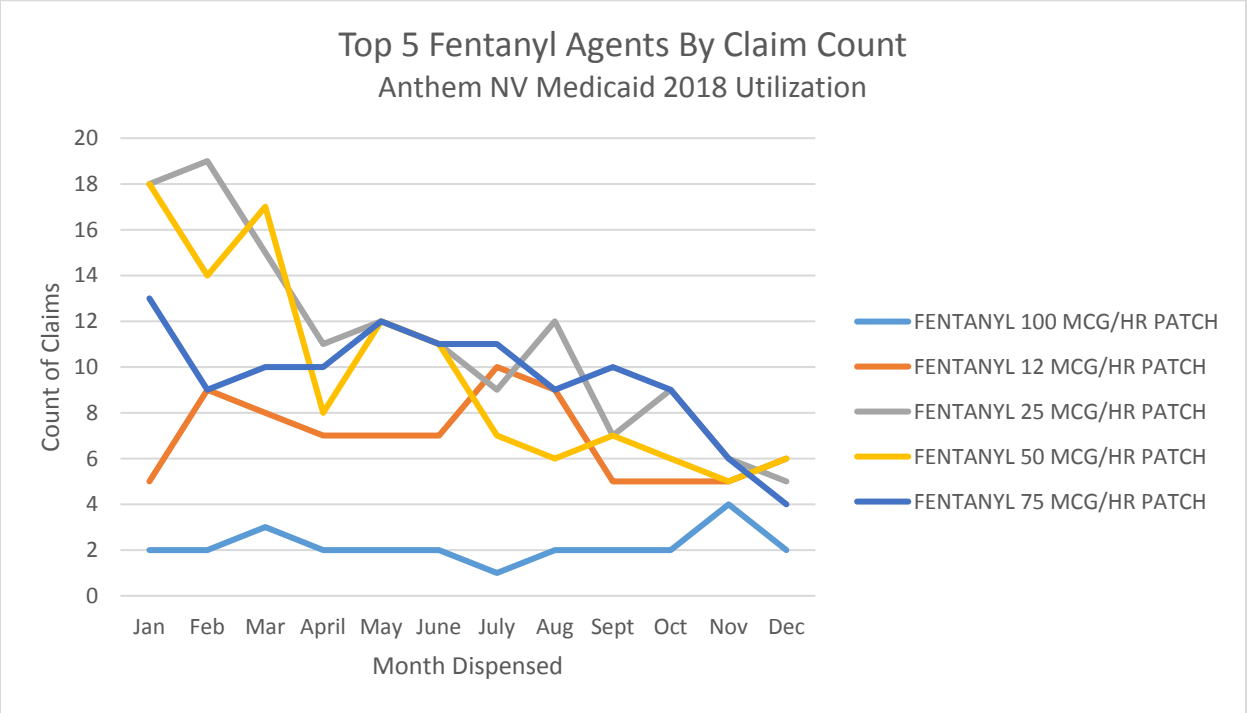
Summary of Utilization

January 1, 2018 - December 31, 2018

Anthem Nevada Medicaid

Drug	Count of Members	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
FENTANYL 25 MCG/HR PATCH	134	134	3752	1279
FENTANYL 50 MCG/HR PATCH	117	117	3281	1282
FENTANYL 75 MCG/HR PATCH	114	114	3393	1410
FENTANYL 12 MCG/HR PATCH	83	83	2331	835
FENTANYL 100 MCG/HR PATCH	26	26	780	335
FENTANYL 37.5 MCG/HR PATCH	11	11	303	101
Grand Total	**485**	**485**	**13840**	**5242**

Note: *No paid claims for oral, IV, powder forms of fentanyl in 2018*

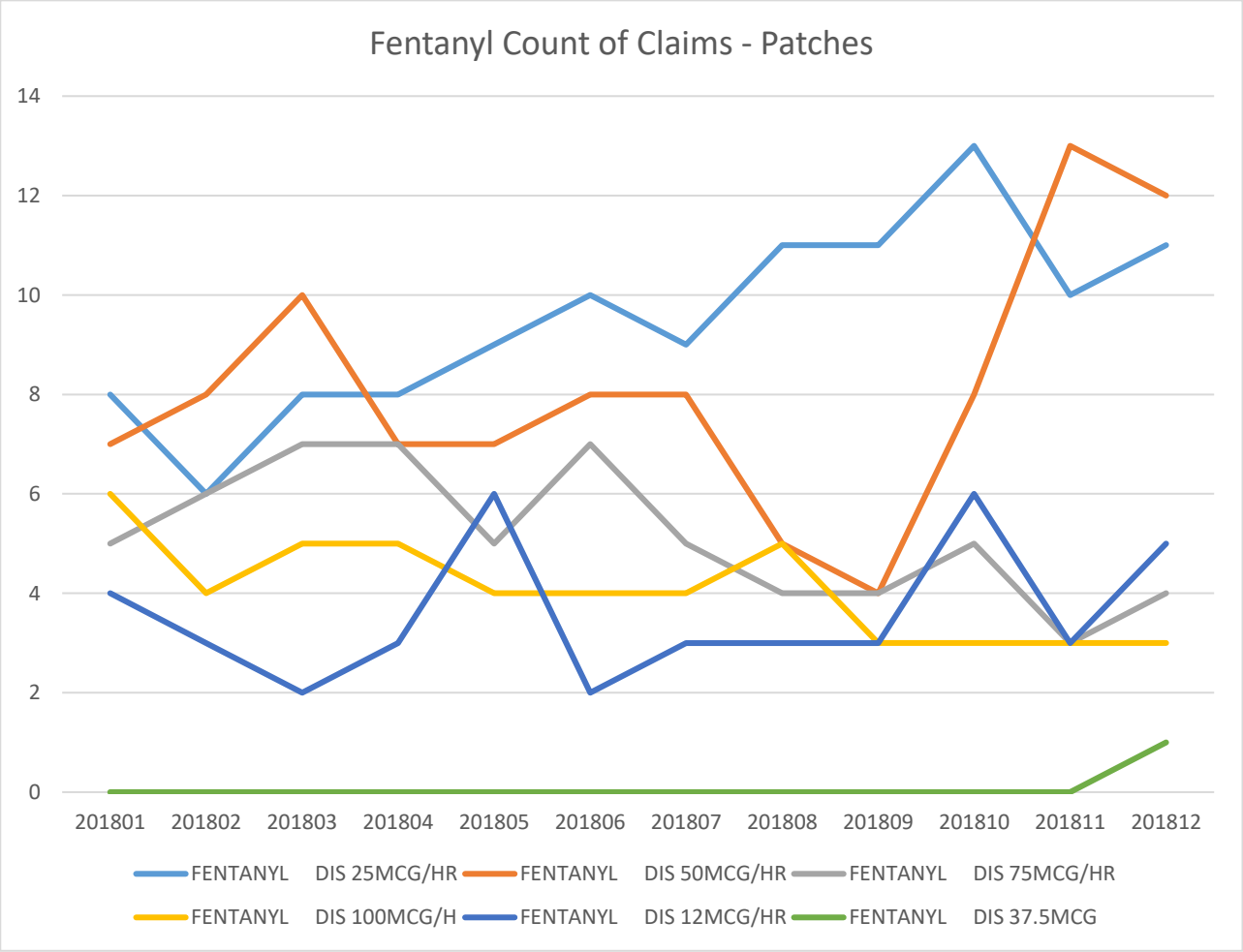


HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Fentanyl Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
Fentanyl Patches					
FENTANYL DIS 25MCG/HR	36	114	3,255	1,164	NA
FENTANYL DIS 50MCG/HR	32	97	2,705	1,013	NA
FENTANYL DIS 75MCG/HR	12	62	1,845	700	NA
FENTANYL DIS 100MCG/H	8	49	1,417	842	NA
FENTANYL DIS 12MCG/HR	16	43	1,136	428	NA
FENTANYL DIS 37.5MCG	1	1	30	15	NA
Total	**105**	**366**	**10,388**	**4,162**	**NA**

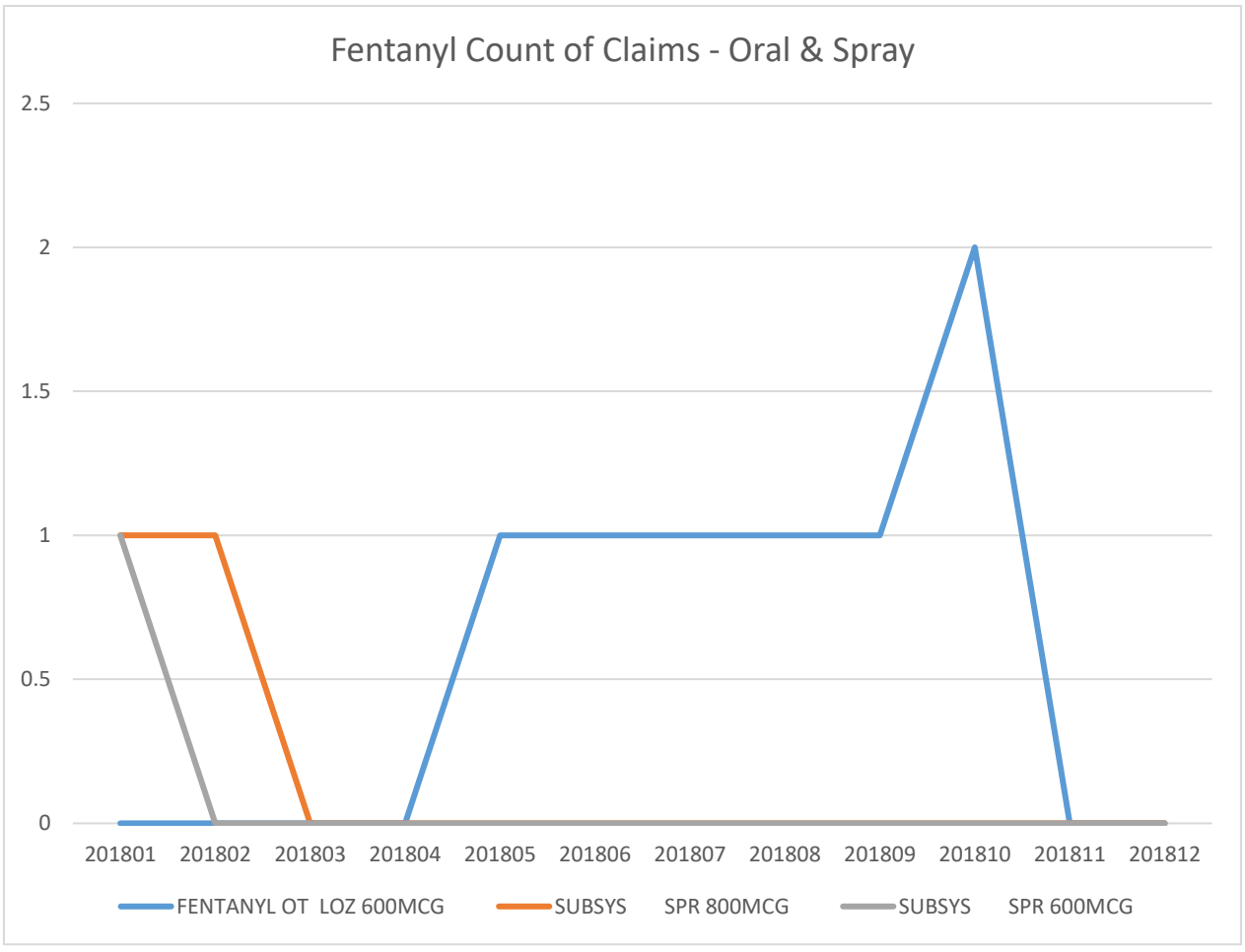


HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Fentanyl Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
Fentanyl Oral/Spray					
FENTANYL OT LOZ 600MCG	1	7	204	174	NA
SUBSYS SPR 800MCG	1	2	60	240	NA
SUBSYS SPR 600MCG	1	1	30	120	NA
Total	**3**	**10**	**294**	**534**	**NA**



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Fentanyl Utilization

January 1, 2018 - December 31, 2018
Health Plan of Nevada

Drug Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
Fentanyl Injectibles					
Total	**0**	**0**	**0**	**0**	**NA**

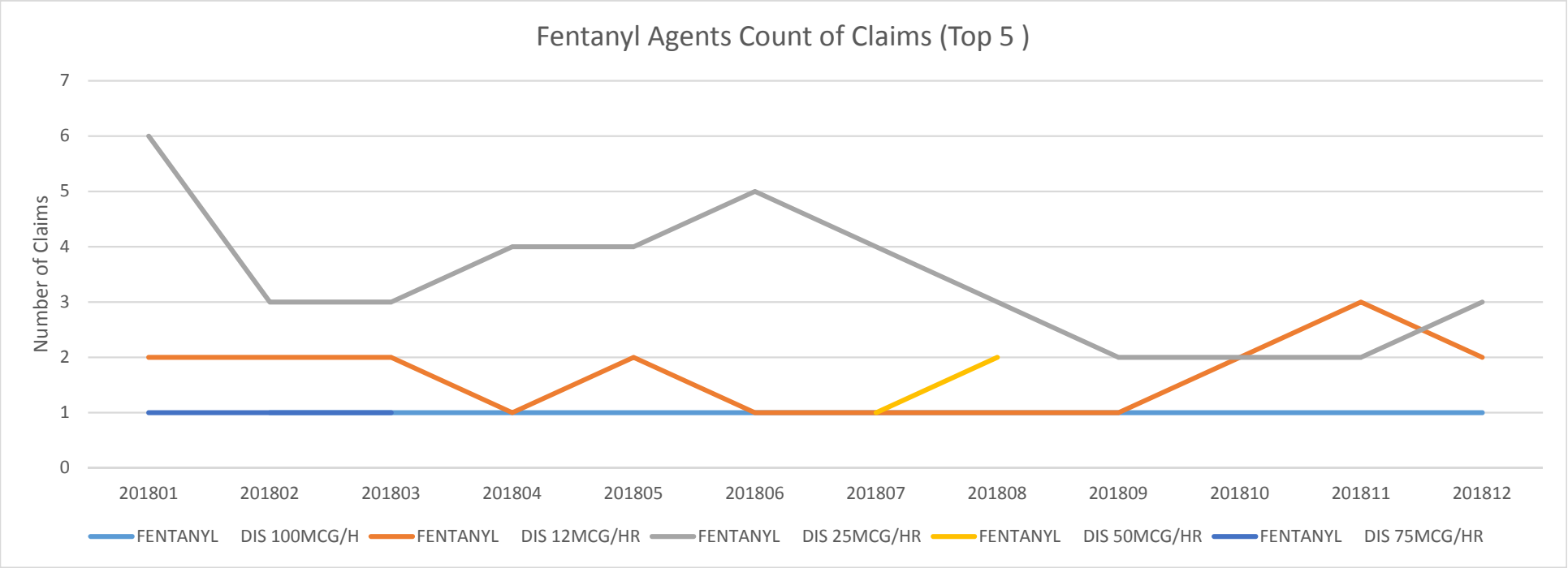
Fentanyl Agents

Summary of Utilization

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty	Sum of Amt Paid
FENTANYL DIS 25MCG/HR	21	41	1206	417	$ 3,468.97
FENTANYL DIS 12MCG/HR	9	20	540	180	$ 2,651.31
FENTANYL DIS 100MCG/H	5	11	330	150	$ 2,904.80
FENTANYL DIS 50MCG/HR	5	6	162	54	$ 562.55
FENTANYL DIS 75MCG/HR	3	5	150	65	$ 961.52
FENTANYL DIS 37.5MCG	1	4	120	40	$ 2,186.48
DURAGESIC DIS 75MCG/HR	1	3	90	45	$ 5,431.08
SUBSYS SPR 200MCG	1	1	15	60	$ 4,675.38
Grand Total	**46**	**91**	**2,613**	**1,011**	**$ 22,842.09**



Preliminary Report:
Opioid (Synthetic Narcotics [T40.4]) Counts and Crude Rates by year, Nevada Residents, 2014-2018*

Year	Synthetic Narcotics		Fentanyl	
	N.	Rate	N.	Rate
2014	31	1.1	19	0.7
2015	31	1.1	18	0.6
2016	49	1.7	28	0.9
2017	64	2.1	40	1.3
2018*	68	2.2	45	1.5

**Data for 2018 are preliminary and subject to changes.*
Crude rates are per 100,000 population, provided by the State Demographer (vintage 2018).
Deaths with any of the following ICD-10 codes as an underlying cause of death were first selected:

X40-X44	*Accidental poisonings by drugs*
X60-X64	*Intentional self poisoning by drugs*
X85	*Assault by drug poisoning*
Y10-Y14	*Drug poisoning of underdetermined intent*

Opioids listed as a contributing cause of death:

T40.4	*Synthetic narcotics*

For Fentanyl deaths:
Deaths with ICD-10 codes T40.4 were manually scanned for the term fentanyl in the cause of death field of the death certificate.

G. Immediate-Release Fentanyl Products

Therapeutic Class: Analgesics, Narcotic
Last Reviewed by the DUR Board: July 25, 2013

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

1. Coverage and Limitations

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

a. Subsys® (fentanyl sublingual spray), Onsolis® (fentanyl citrate buccal film), Fentora® (fentanyl citrate buccal tablet), Lazanda® (fentanyl citrate nasal spray), Abstral® (fentanyl citrate sublingual tablet) and Actiq® (fentanyl citrate transmucosal lozenge):

The recipient must meet all of the following:

1. The recipient is ≥ 18 years of age or ≥ 16 years of age if requesting fentanyl citrate transmucosal lozenge (Actiq®); and

2. The recipient has pain resulting from a malignancy; and

3. The recipient is already receiving and is tolerant to opioid therapy; and

4. The recipient is intolerant of at least two of the following immediate-release opioids: hydrocodone, hydromorphone, morphine or oxycodone.

2. Prior Authorization Guidelines

a. Prior Authorization approval will be for six months.

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

F. Transdermal Fentanyl

Therapeutic Class: Analgesics, Narcotic
Last Reviewed by the DUR Board: January 22, 2015

Transdermal fentanyl, a narcotic agonist analgesic, is indicated in the management of chronic pain in patients requiring continuous opioid analgesia for pain that cannot be managed by lesser means such as acetaminophen-opioid combinations, non-steroidal analgesics or PRN dosing with short-acting opioids. Transdermal fentanyl 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

Because serious or life-threatening hypoventilation could occur, fentanyl transdermal is contraindicated in management of acute or postoperative pain, mild or intermittent pain responsive to PRN or non-opioid therapy, or in doses exceeding 25 mcg/hr at the initiation of opioid therapy. Therefore, patients must meet the following criteria in order to gain prior authorization approval:

a. Patient cannot be managed by lesser means such as acetaminophen-opioid combinations, nonsteriodal analgesics or PRN dosing with short-acting opioid.

b. Patient requires continuous opioid administration.

c. Prescribers are encouraged to check the Nevada State BOPs Prescription Monitoring Program (PMP) prior to prescribing narcotic analgesics. Refer to the PMP website at http://bop.nv.gov/links/PMP/.

d. If transitioning from another opioid, daily morphine equivalent doses are used to calculate the appropriate fentanyl patch dose.

1. Morphine 60-134 mg/day PO; Initial Transdermal Fentanyl dose 25 mcg/hr.

2. Morphine 135-224 mg/day PO; initial Transdermal Fentanyl dose 50 mcg/hr.

3. Morphine 225-314 mg/day PO; initial Transdermal Fentanyl dose 75 mcg/hr.

4. Morphine 315-404 mg/day PO; initial Transdermal Fentanyl dose 100 mcg/hr.

5. Morphine 405-494 mg/day PO; initial Transdermal Fentanyl dose 125 mcg/hr.

6. Morphine 495-584 mg/day PO; initial Transdermal Fentanyl dose 150 mcg/hr.

7. Morphine 585-674 mg/day PO; initial Transdermal Fentanyl dose 175 mcg/hr.

8. Morphine 675-764 mg/day PO; initial Transdermal Fentanyl dose 200 mcg/hr.

9. Morphine 765-854 mg/day PO; initial Transdermal Fentanyl dose 225 mcg/hr.

10. Morphine 855-944 mg/day PO; initial Transdermal Fentanyl dose 250 mcg/hr.

11. Morphine 945-1034 mg/day PO; initial Transdermal Fentanyl dose 275 mcg/hr.

12. Morphine 1035-1124 mg/day PO; initial Transdermal Fentanyl dose 300 mcg/hr.

2. Prior Authorizations

Prior approval will be given for a 12 month time period.

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

INTRODUCTION

- Pain originates from somatic or visceral structures. Somatic pain is localized and typically results from injury or disease of the skin, musculoskeletal structures, and joints. Visceral pain arises from internal organ dysfunction or from functional pathology.
- Pain can be acute or chronic. Acute pain often results from injury or inflammation and may have a survival role and assist in the healing process by minimizing re-injury. In contrast, chronic pain, often defined as pain persisting for over three to six months, may be considered a disease in that it serves no useful purpose (*Cohen et al 2016*).
  - Chronic pain is estimated to affect 100 million Americans and the total annual incremental cost of health care in 2010 due to pain ranges from $560 billion to $635 billion in the United States (U.S.). This includes medical costs and costs related to disability days and lost wages and productivity (*American Academy of Pain Medicine [AAPM] 2018*).
- Pain may be classified as nociceptive and neuropathic pain.
  - Nociceptive pain, including cancer pain, results from an injury or disease affecting somatic structures such as skin, muscle, tendons and ligaments, bone, and joints. It is typically treated with nonopioid analgesics or opioids.
  - Neuropathic pain results from disease or injury to the peripheral or central nervous systems (CNS) and is less responsive to opioids. It is often treated with adjuvant drugs such as antidepressants and antiepileptics. Opioids are recommended as second- or third-line agents (*Cohen et al 2016*).
- Several pharmacologic and nonpharmacologic options are currently available for the management of pain. Treatment options include pharmacologic treatment, physical medicine, behavioral medicine, neuromodulation, interventional, and surgical approaches. Pharmacologic therapy should not be the sole focus of pain treatment; however, it is the most widely utilized option (*Cohen et al 2016*).
  - Major pharmacologic categories used in the management of pain include non-opioid analgesics, tramadol, opioid analgesics (full and partial agonists), alpha-2 (α_2) adrenergic agonists, antidepressants, anticonvulsants, muscle relaxants, N-methyl-d-aspartate (NMDA) receptor antagonists, and topical analgesics. Opioids are available in both short-acting and long-acting or sustained release formulations (*Cohen et al 2016*).
  - Combining different types of treatments, including multiple types of analgesics, may provide an additive analgesic effect without increasing adverse effects (*Cohen et al 2016, The Medical Letter 2013*).
- It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. The use of opioid analgesics presents serious risks, including overdose and opioid use disorder. From 1999 to 2014, there were more than 165,000 deaths due to opioid analgesic overdoses in the U.S. (*Dowell et al 2016*).
- The long-acting opioids have gained increasing attention regarding overuse, abuse, and diversion. Some manufacturers have addressed concerns about abuse and misuse by developing new formulations designed to help discourage the improper use of opioid medications.
  - In January 2013, the Food and Drug Administration (FDA) released draft guidance for industry regarding abuse deterrent opioids. This document was finalized in April 2015. The guidance explains the FDA's current direction regarding studies conducted to demonstrate that a given formulation has abuse deterrent properties. The guidance also makes recommendations about how those studies should be performed and evaluated (*FDA Industry Guidance 2015*). The 2015 guidance does not address generic opioids. Subsequently in November 2017, the FDA issued a final guidance to support industry in the development of generic versions of abuse-deterrent opioids (*FDA Industry Guidance 2017*).
  - In 2013, reformulated OxyContin (oxycodone) became the first long-acting opioid to be approved with labeling describing the product's abuse deterrent properties consistent with the FDA's guidance for industry (*Hale et al 2016*).
  - Since the approval of reformulated OxyContin, several other long-acting opioids have been approved with abuse deterrent labeling, including, Arymo ER (morphine), Embeda (morphine and naltrexone), Hysingla ER (hydrocodone), Morphabond (morphine), Targiniq ER (oxycodone and naloxone), Troxyca ER (oxycodone and naltrexone), Vantrela

ER (hydrocodone), and Xtampza ER (oxycodone) (*Drugs@FDA 2018, Hale et al 2016*). However, Targiniq ER, Troxyca ER, and Vantrela ER were never launched and were recently discontinued (*Drugs@FDA 2018*).

- A number of federal agencies have recently implemented measures to combat drug abuse and misuse. The Centers for Medicare & Medicaid Services (CMS) has issued guidance in an effort to improve drug utilization review controls in Part D prescription plans. The Drug Enforcement Agency (DEA) issued a nationwide alert regarding fentanyl products laced with heroin, causing significant drug incidents and overdoses nationwide. The U.S. Office of Disease Prevention and Health Promotion announced a new interactive training tool, "Pathways to Safer Opioid Use," which teaches healthcare providers how to implement opioid-related recommendations from the adverse events action plan. Additionally, the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), has a number of studies and initiatives to educate providers and patients about opioid addiction and treatment. On July 13, 2017, the National Academies of Science, Engineering, and Medicine (NASAM) also released a consensus report, commissioned by the FDA, which outlined the state of the science regarding prescription opioid abuse and misuse, as well as the evolving role that opioids play in pain management. (*CMS 2018, DEA 2016, Office of Disease Prevention and Health Promotion 2015, NASAM 2017, NIDA 2015*).
- In March 2016, the Centers for Disease Control and Prevention (CDC) issued a guideline for prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risks and addressing harms of opioid use. The guideline encourages prescribers to follow best practices for responsible opioid prescribing due to the risks of opioid use (*Dowell et al 2016*).
- Methadone is FDA-approved for detoxification and maintenance treatment of opioid addiction.
  - Methadone products when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners or institutions by formal agreement with the program sponsor) certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR 8.12) (*Prescribing information: Dolophine 2018, methadone oral solution 2018, Methadose 2018*).
- Included in this review are the long-acting opioids, which are primarily utilized in the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time. Long-acting opioids are available in a variety of different dosage forms, and currently several agents are available generically (*Drugs@FDA 2018*).
  - All of the long-acting opioids are classified as Schedule II controlled substances by the FDA, with the exception of transdermal and buccal buprenorphine, a partial opioid agonist, which is a Schedule III controlled substance (*Drugs@FDA 2018*).
- Since some agents are available under multiple brand names, many tables in this review are arranged by generic name.
- Medispan class: Opioid Agonists

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Single Entity Agents	
Arymo ER†, Avinza¶, Kadian, Morphabond†, MS Contin (morphine sulfate)	✔
Belbuca, Butrans (buprenorphine)	✔
Dolophine, Methadose (methadone)	✔
Duragesic (fentanyl)	✔
Exalgo (hydromorphone)	✔
Hysingla ER†, Zohydro ER§ (hydrocodone bitartrate)	-
levorphanol	✔
Nucynta ER (tapentadol)	-
Opana ER* (oxymorphone)	✔
OxyContin†, Xtampza ER† (oxycodone)	✔
Combination Products	

Drug	Generic Availability
Embeda† (morphine sulfate/naltrexone)	-

*Generic products of the pre-reformulated Opana ER are available. The branded versions of Opana ER (pre- and post-reformulation) are no longer available on the market.
†Approved as an abuse deterrent (AD) formulation, which is consistent with the FDA's 2015 guidance for industry, *Abuse-Deterrent Opioids – Evaluation and Labeling.*
‡OxyContin had various patents extending out to 2027. Patent litigation on OxyContin reached an agreement between manufacturers. In late 2014, a number of generic products launched.
§In February 2015, a new formulation of Zohydro ER was FDA-approved with AD properties; however, it has not been deemed to meet the FDA requirements for labeling as an AD opioid.
¶Avinza branded products were discontinued by Pfizer in July 2015.
(*Drugs@FDA 2018, FDA Industry Guidance 2015, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Single Entity Agents										Combination Products
	buprenorphine	fentanyl	hydrocodone	hydromorphone	levorphanol	methadone	morphine	oxycodone	oxymorphone	tapentadol	morphine sulfate/ naltrexone
Pain Management											
Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate in adults.	✔		✔			✔ *	✔	✔	✔	✔	✔
Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate in opioid-tolerant pediatric patients ≥ 11 years of age who are already receiving and tolerate a minimum daily opioid dose of at least 20 mg oxycodone orally or its equivalent.								✔ †			
Management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.					✔						
Management of pain in opioid-tolerant patients, severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.		✔ ‡		✔ ‡							
For the management of acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.											
Management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) in adults severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate										✔	
Opioid Addiction											
Detoxification treatment of opioid addiction (heroin or other morphine-like drugs)						✔					
Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with social and medical services						✔					
Limitations of Use											
Limitations of Use: Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release (ER) opioid formulations, reserve this agent for	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔

Indication	Single Entity Agents										Combination Products
	buprenorphine	fentanyl	hydrocodone	hydromorphone	levorphanol	methadone	morphine	oxycodone	oxymorphone	tapentadol	morphine sulfate/ naltrexone
use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.											
Limitations of Use: Not indicated as an as-needed (prn) analgesic.	✔	✔	✔	✔		✔	✔	✔	✔	✔	✔

*Methadone tablets and oral solution only
†OxyContin only
‡Patients considered opioid tolerant are those who are receiving, for one week or longer, at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid.

(Prescribing information: Arymo ER 2017, Belbuca 2016, Butrans 2017, Dolophine 2018, Duragesic 2018, Embeda 2016, Exalgo 2016, Hysingla ER 2016, Kadian 2016, levorphanol 2016, methadone oral solution 2018, Methadose 2018, Morphabond 2018, MS Contin 2016, Nucynta ER 2016, Opana ER 2016, OxyContin 2016, oxymorphone extended-release 2017, Xtampza ER 2017, Zohydro ER 2016)

- 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

- As a class, the long-acting opioids are a well-established therapy for the treatment of moderate to severe pain. In general, opioids are used for the treatment of non-cancer and cancer pain; however, data establishing their effectiveness in the treatment of neuropathic pain are available. Head-to-head trials of long-acting opioids do exist and for the most part the effectiveness of the individual agents, in terms of pain relief, appears to be similar. Small differences between the agents exist in side effect profiles, and associated improvements in quality of life or sleep domains (*Agarwal et al 2007, Aiyer et al 2017, Allan et al 2001, Allan et al 2005, Bao et al 2016, Bekkering et al 2011, Bruera et al 2004, Buynak et al 2010, Caldwell et al 2002, Caraceni et al 2011, Chou et al 2015, Clark et al 2004, Conaghan et al 2011, Felden et al 2011, Finkel et al 2005, Finnerup et al 2015, Gimbel et al 2003, Gordon et al [a], 2010, Gordon et al [b], 2010, Karlsson et al 2009, Hale et al 2007, Hale et al 2010, Katz et al 2010, King et al 2011, Kivitz et al 2006, Langford et al 2006, Ma et al 2008, Melilli et al 2014, Mercadante et al 2010, Mesgarpour et al 2014, Morley et al 2003, Musclow et al 2012, Nicholson et al 2017, Park et al 2011, Pigni et al 2011, Quigley et al 2002, Rauck et al 2014, Schwartz et al 2011, Slatkin et al 2010, Sloan et al 2005, Watson et al 2003, Whittle et al 2011, Wiffen et al 2013, Wild et al 2010*).
- Recent systematic reviews and meta-analyses recommend opioids as a potential treatment option for various forms of non-cancer and cancer-related pain. No single opioid is recommended over the others (*Chou et al 2015, Finnerup et al 2015, Mesgarpour et al 2014*).
  - The Agency for Healthcare Research and Quality (AHRQ) conducted a systematic review (N=39 studies, 40 publications) of the effectiveness and risks of long-term (>3 months) opioid therapy for chronic pain and included both randomized and observational studies. Findings indicated that three randomized, head-to-head trials of various long-acting opioids found no differences in one-year outcomes related to pain or function. One good-quality case-control study found current opioid use to be associated with increased risk for hip, humerus, or wrist fracture versus non-use (adjusted odds ratio [OR], 1.27; 95% confidence interval [CI], 1.21 to 1.33). The risk was highest with one prescription (OR, 2.7; 95% CI, 2.34 to 3.13) and decreased with higher numbers of prescriptions, with no increased risk with more than 20 cumulative prescriptions. One fair-quality cohort study found that a cumulative opioid supply of at least 180 days over a 3.5-year period was associated with an increased risk for myocardial infarction versus no long-term opioid therapy (adjusted incidence rate ratio, 2.66; 95% CI, 2.3 to 3.08) (*Chou et al 2015*).
  - The Special Interest Group on Neuropathic Pain of the International Association for the Study of Pain conducted a systematic review and meta-analysis of randomized, double-blinded studies of oral and topical therapy for neuropathic pain and required a number needed to treat (NNT) for 50% pain relief as the primary measure. For tapentadol ER, the review identified one negative study and one positive enrichment study with a potential bias and a high NNT of 10.2 (95% CI, 5.3 to 185.5) in 67% of the patients responding to the open phase. Thirteen trials were identified with strong opioids, in which oxycodone (10 to 120 mg/day) and morphine (90 to 240 mg/day) were used mainly in peripheral neuropathic pain. The final quality of evidence was moderate. Ten trials were positive with a combined NNT of 4.3 (95% CI, 3.4 to 5.8) and a number needed to harm of 11.7 (95% CI, 8.4 to 19.3). Maximum effectiveness seemed to be associated with 180 mg morphine or equivalent (*Finnerup et al 2015*).
  - Another systematic review evaluated long-acting opioids in the treatment of moderate to severe cancer pain. The review included only double-blinded, randomized controlled trials for efficacy assessments; open-label and controlled observational studies were allowed for safety assessments. A total of five RCTs and four observational studies met criteria for inclusion. Similar pain intensity improvements were demonstrated for oxycodone ER, oxycodone/naloxone ER, hydromorphone ER, and oxycodone ER. However, the average equivalent dose of oxycodone ER was significantly different from hydromorphone ER. The Morphine ER and hydromorphone ER groups had similar improvements in average cancer pain in the past 24 hours and “current pain in the morning;” however, the “worst pain in the past 24 hours” and “current pain in the evening” were significantly lower in the hydromorphone ER group. The quality of life scores were comparable between oxycodone ER and oxycodone/naloxone ER as well as morphine ER and hydromorphone ER in two trials. The rate of discontinuation due to lack of efficacy was similar among patients treated with morphine ER, hydromorphone ER, oxycodone ER or oxycodone/naloxone ER and ranged from 1.1% (oxycodone/naloxone ER) to 6.5% (hydromorphone ER). The risk of experiencing serious adverse events was comparable in patients treated with morphine ER or hydromorphone ER, morphine ER or fentanyl ER, and morphine ER or oxycodone ER. Overall, the reviewers concluded that there was no difference in efficacy and risk of harms among ER opioids in the treatment of cancer-related pain based on current evidence (*Mesgarpour et al 2014*).

- A recent pragmatic, 12-month, randomized trial (N=240) compared opioid vs non-opioid medications on pain-related function, pain intensity, and adverse effects in patients with moderate to severe chronic back pain or hip or knee osteoarthritis pain despite analgesic use *(Krebs et al 2018)*.
  - Each intervention had its own prescribing strategy that included multiple medication options in 3 steps. In the opioid group, the first step was immediate-release morphine, oxycodone, or hydrocodone/acetaminophen. For the nonopioid group, the first step was acetaminophen or a nonsteroidal anti-inflammatory drug (NSAID). Medications were changed, added, or adjusted within the assigned treatment group according to individual patient response.
  - Groups did not significantly differ on pain-related function over 12 months (p = 0.58); mean 12-month Brief Pain Inventory (BPI) interference was 3.4 for the opioid group and 3.3 for the nonopioid group (difference, 0.1 [95% CI, −0.5 to 0.7]). Pain intensity was significantly better in the nonopioid group over 12 months (p = 0.03); mean 12-month BPI severity was 4.0 for the opioid group and 3.5 for the nonopioid group (difference, 0.5 [95% CI, 0.0 to 1.0]). Adverse medication-related symptoms were significantly more common in the opioid group over 12 months (p = 0.03); mean medication-related symptoms at 12 months were 1.8 in the opioid group and 0.9 in the nonopioid group (difference, 0.9 [95% CI, 0.3 to 1.5]).
- Arymo ER and Morphabond were approved based on bioequivalence to MS Contin. In lieu of conducting new nonclinical studies and clinical studies of the safety and efficacy, the manufacturers relied on previous findings of efficacy and safety for MS Contin (*FDA Summary Review: Arymo ER 2017, Morphabond 2018*).
- The efficacy of buprenorphine buccal films was evaluated in three 12-week, double-blind (DB), placebo-controlled (PC) trials in opioid-naïve and opioid-experienced patients with moderate-to-severe chronic low back pain. In the trials, the DB treatment phase was preceded by an OL dose titration period. Patients were eligible for randomization into the 12-week DB treatment phase if they were able to titrate to a tolerable and effective buprenorphine dose. The primary efficacy variable was the patients' pain scores (based on a 0 to 10 numeric rating scale). Two of these studies demonstrated efficacy in patients with low back pain. One trial did not show a statistically significant pain reduction for Belbuca compared to placebo, and the results of this trial are not included in the Prescribing Information (*Belbuca Prescribing Information 2016, Gimbel et al 2016, Rauck et al 2016*).
  - In one study of opioid-naïve patients, pain scores increased more in the placebo group vs. the buprenorphine group during the DB phase; mean (standard deviation [SD]) changes from baseline to week 12 were 0.94 (1.85) and 1.59 (2.04) in the buprenorphine and placebo groups, respectively, with a significant between-group difference (-0.67, 95% confidence interval [CI]: -1.07 to -0.26; p = 0.0012). A higher proportion of buprenorphine patients (62%) had at least a 30% reduction in pain score from prior to OL titration to study endpoint when compared to patients who received placebo (47%) (*Rauck et al 2016*).
  - In another study, opioid-experienced patients experienced a higher increase in their pain scores in the placebo vs. buprenorphine group after randomization. The difference between groups in the mean change from baseline to week 12 was -0.98 (95% CI: -1.32 to -0.64; p < 0.001). A significantly larger percentage of patients receiving buprenorphine than placebo had pain reductions ≥ 30% and ≥ 50% (p < 0.001 for both) (*Gimbel et al 2016*).

CLINICAL GUIDELINES

- Clinical guidelines do not state a preference for the use of one long-acting opioid over another for the use in moderate to severe pain (*Attal et al 2010, Bril et al 2011, Chou et al 2009, Hochberg et al 2012, Manchikanti et al 2017, Qaseem 2017, Paice et al 2016, The Medical Letter 2013*). However, opioid rotation is recommended if a patient experiences adverse effects from one agent (*Chou et al 2009*). In addition, methadone safety guidelines from the 2014 American Pain Society recommend buprenorphine as an alternative to methadone for the treatment of opioid addiction in patients with risk factors or known QTc prolongation (*Chou et al 2014*).

- In March 2016, the CDC issued a guideline for prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use. Recommendations in the CDC guideline include the following (*Dowell et al 2016*):
  - Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate (category A, evidence 3).

- Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (category A, evidence 4).
- Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (category A, evidence 3).
- When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of ER/long-acting opioids (category A, evidence 4).
- Clinicians should prescribe opioids at the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥ 90 MME/day or carefully justify a decision to titrate dosage to ≥ 90 MME/day (category A, evidence 3).
- Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed (category A, evidence 4).
- Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (category A, evidence 4).
- Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥ 50 MME/day), or concurrent benzodiazepine use, are present (category A, evidence 4).
- Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months (category A, evidence 4).
- When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs (category B, evidence 4).
- Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible (category A, evidence 3).
- Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (category A, evidence 2).

Category of Recommendations:

- Category A: Applies to all persons; most patients should receive the recommended course of action.
- Category B: Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

Evidence Type:

- Type 1: Randomized clinical trials or overwhelming evidence from observational studies.
- Type 2: Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies.
- Type 3: Observational studies or randomized clinical trials with notable limitations.
- Type 4: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

- In February 2017, the American College of Physicians published clinical practice guidelines for noninvasive treatments of acute, subacute, and chronic low back pain. The guidelines state that clinicians should only consider opioids as an option in patients who have failed other treatments (e.g., non-pharmacological treatment, NSAIDs, tramadol, duloxetine)

and only if the potential benefits outweigh the risks for individual patients and after a discussion of known risks and realistic benefits with patients (*Qaseem et al 2017*).
  - There is moderate-quality evidence that show strong opioids (tapentadol, morphine, hydromorphone, and oxymorphone) are associated with a small short-term improvement in pain scores (about 1 point on a pain scale of 0 to 10) and function compared with placebo. There is moderate-quality evidence that show no differences among different long-acting opioids for pain or function, and low-quality evidence shows no clear differences in pain relief between long- and short-acting opioids.

- In February 2017, the American Society of Interventional Pain Physicians (ASIPP) also published new practice guidelines for responsible, safe, and effective prescription opioids for chronic non-cancer pain. Similar to other guidelines, they do not recommend one opioid agent over the others. They do provide the following recommendations and conclusions for long-term opioid therapy (*Manchikanti et al 2017*):
  - Initiate opioid therapy with low dose, short-acting drugs, with appropriate monitoring (Evidence: Level II; Strength of Recommendation: Moderate).
  - Consider up to 40 MME as low dose, 41 to 90 MME as a moderate dose, and greater than 91 MME as high dose (Evidence: Level II; Strength of Recommendation: Moderate).
  - Avoid long-acting opioids for the initiation of opioid therapy (Evidence: Level I; Strength of Recommendation:
  - Strong).
  - Recommend methadone only for use after failure of other opioid therapy and only by clinicians with specific training in its risks and uses, within FDA recommended doses (Evidence: Level I; Strength of Recommendation: Strong).
  - Understand and educate patients of the effectiveness and adverse consequences (Evidence: Level I; Strength of Recommendation: Strong).
  - Similar effectiveness for long-acting and short-acting opioids with increased adverse consequences of long-acting opioids (Evidence: Level I-II; Strength of recommendation: Moderate to strong).
  - Recommend long-acting or high dose opioids only in specific circumstances with severe intractable pain (Evidence: Level I; Strength of Recommendation: Strong).

- The guidelines from the American College of Physicians and the American Society of Interventional Pain Physicians state that buprenorphine has lower quality evidence and is a third-line opioid for the treatment of pain (*Manchikanti et al 2017, Qaseem et al 2017*).

SAFETY SUMMARY

- On July 9, 2012, the FDA approved a Risk Evaluation and Mitigation Strategy (REMS) program for all ER and long-acting opioids included in this review, with the exception of levorphanol. This program has been updated to include new formulations and medications. The REMS program is part of the national prescription drug abuse plan announced in 2011 to combat prescription drug misuse and abuse. Program components include prescriber education and training, patient education, and a communication plan for prescribers.
- All of the long-acting opioids are classified as Schedule II controlled substances by the FDA, with the exception of buprenorphine buccal and transdermal systems, which are Schedule III controlled substances.
- Most long-acting opioids are associated with boxed warnings regarding the potential for abuse and misuse, life-threatening respiratory depression, neonatal opioid withdrawal syndrome, an interaction with alcohol, and accidental ingestion risks. Dolophine and methadone products have additional boxed warnings regarding life-threatening QT prolongation. Duragesic, Hysingla ER, OxyContin, Xtampza ER, and Zohydro ER also have a Boxed Warning for an interaction with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers). An additional Boxed Warning for Duragesic cautions against exposure to heat due to increases in fentanyl release.
- Key contraindications across the class include acute or severe bronchial asthma, significant respiratory depression, and known or suspected paralytic ileus.
- There are multiple warnings and precautions with each agent. Key safety concerns associated with the opioid analgesics include respiratory depression, driving and operating machinery, hypotension, interactions with other CNS depressants, neonatal opioid withdrawal syndrome, use in special populations, and use in those with gastrointestinal conditions.

- The frequency of adverse reactions varies to some degree with each agent; however, overall adverse reactions are similar within the class. The most common adverse events in adults include nausea, vomiting, constipation, and somnolence.
- OxyContin is approved in patients aged ≥ 11 years. The most frequent adverse events in pediatric patients were vomiting, nausea, headache, pyrexia, and constipation.
- In March 2016, the FDA issued a drug safety communication warning about several safety issues with opioids and describing new class-wide labeling requirements. The warnings include the following (*FDA Drug Safety Communication 2016*):
  - Opioids can interact with antidepressants and migraine medications to cause serotonin syndrome.
  - Taking opioids may rarely lead to adrenal insufficiency.
  - Long-term opioid use may be associated with decreased sex hormone levels and symptoms such as reduced interest in sex, impotence, or infertility.
- In August 2016, the FDA announced that it is requiring class-wide changes to drug labeling, including patient information, in order to help inform health care providers and patients of the serious risks associated with the combined use of certain opioid medications and benzodiazepines (*FDA Drug Safety Communication 2016*).
  - Among the changes, the FDA is requiring boxed warnings and patient-focused Medication Guides for prescription opioid analgesics, opioid-containing cough products, and benzodiazepines – nearly 400 products in total – with information about the serious risks associated with using these medications concomitantly. Risks include extreme sleepiness, respiratory depression, coma, and death.
- On March 14, 2017, the FDA Drug Safety Risk Management and Anesthetic and Analgesic Drug Products Advisory Committees voted 18 to 8, that the benefits of reformulated Opana ER (which did not originally gain the labeling describing potential abuse deterrent properties) no longer outweigh its risks. This vote followed an FDA analysis of epidemiological data that indicated that there was a shift in the pattern of Opana ER abuse from the nasal to the injection route after the product was reformulated (*FDA Advisory Committee 2017*). Following the FDA's official withdrawal request, the manufacturer (Endo) announced the voluntary market withdrawal of reformulated Opana ER (*Endo Press Release 2017*).
- On September 20, 2017, the FDA advised clinicians that opioid addiction medications, such as methadone and buprenorphine, should not be withheld from patients receiving concurrent benzodiazepines or other CNS depressants (*FDA Drug Safety Communication 2017*). Even though combination therapy with these agents increases the risk of serious side effects, the harm caused by untreated opioid addiction can outweigh these risks.

DOSING AND ADMINISTRATION

- Certain strengths are appropriate only for patients who are considered treatment-experienced. Please see a detailed description within the prescribing information for each agent regarding when a patient is considered opioid-tolerant and which strengths are appropriate in these patients.
- See prescribing information for detailed conversion recommendations as there are no established conversions from other opioid agents. When converting from one agent to another, it is better to underestimate need and monitor for breakthrough pain.

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Arymo ER, Avinza†, Kadian*, Morphabond, MS Contin (morphine sulfate)	ER capsules and tablets	Oral	Arymo ER, Morphabond, MS Contin: Every 8 to 12 hours Avinza: Once daily Kadian: Once daily	• Renal dose adjustment is required. • Hepatic dose adjustment is required.
Butrans, Belbuca (buprenorphine)	Transdermal system (Butrans) Buccal film (Belbuca)	Topical Oral	Administration every 7 days Every 12 hours	• Not evaluated in patients with severe hepatic impairment and should be administered with caution (Butrans).

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				• The maximum dose is 900 mcg every 12 hours. Do not exceed this dose due to the potential for QTc interval prolongation. If pain is not adequately managed on a 900 mcg dose, consider an alternate analgesic (Belbuca). • For severe hepatic impairment, reduce the starting and incremental dose by half (Belbuca).
Dolophine, Methadose (methadone)	Oral solution, dispersible tablet, tablets	Oral	Every 8 to 12 hours (for management of pain)	• Due to the large variability in half-life (eg, 8 to 59 hours), dose adjustments may vary greatly. Dose increases may be no more frequent than every three to five days; however, some may require up to 12 days. • Due to the metabolism of methadone, patients with liver impairment may be at risk of accumulating methadone after multiple dosing.
Duragesic (fentanyl)	Transdermal system	Topical	Administration every 72 hours (Some patients may not achieve adequate analgesia using this dosing interval and may require systems be applied at 48 hours)	• Avoid use in patients with severe renal impairment. • Avoid use in patients with severe hepatic impairment.
Exalgo (hydromorphone)	ER tablets	Oral	Once daily	• Moderate renal impairment: start 50% of the usual dose. • Severe renal impairment: start 25% of the usual dose. • Moderate hepatic impairment: start 25% of the usual dose.
Hysingla ER Zohydro ER (hydrocodone bitartrate)	ER capsules and tablets	Oral	Hysingla ER: Once daily Zohydro ER: Every 12 hours	• For severe hepatic impairment, reduce the Hysingla ER dose to 1/2 the usual initial dose and start Zohydro ER at the lowest dose of 10 mg every 12 hours. • Hysingla ER: In moderate to severe renal impairment (including end stage renal disease), reduce the initial dose to 1/2 the usual initial dose.
Levorphanol	Tablets	Oral	Every 6 to 8 hours	

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Nucynta ER (tapentadol)	ER tablets	Oral	Twice daily	• Not recommended in patients with severe renal impairment. • Not recommended in patients with severe hepatic impairment.
Opana ER (oxymorphone)‡	ER tablets	Oral	Every 12 hours	• Contraindicated in moderate and severe hepatic impairment.
OxyContin; Xtampza ER (oxycodone)	ER capsules and tablets	Oral	Every 12 hours	• In hepatic impairment, initiate dose at 1/3 to 1/2 the recommended initial dose.
Combination Products				
Embeda (morphine sulfate/ naltrexone)	ER capsules	Oral	Once daily	• Renal dose adjustment may be required in severe renal impairment. • Hepatic dose adjustment may be required in severe hepatic impairment.

*Available only as brand name Kadian
†All Avinza branded products have been removed from the market.
‡Generic products of the pre-reformulated Opana ER are available. The branded versions of Opana ER (pre- and post-reformulation) are no longer available on the market.

CONCLUSION

- Opioids have been the mainstay of pain treatment for a number of years, and there is well-documented evidence of their effectiveness. Oral morphine is the standard for comparison for all other opioid agents currently available. There are several long-acting opioid agents available, which are FDA-approved for the treatment of moderate to severe pain in patients requiring around-the-clock analgesia (*Cohen et al 2016*).
  - Levorphanol is indicated for moderate to severe pain where an opioid analgesic is appropriate; however, the FDA-approved indication does not stipulate that patients require around-the-clock, daily dosing for use.
  - Nucynta ER is the only long-acting agent in this class also indicated for neuropathic pain which requires daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
  - OxyContin has been FDA-approved as an option in pediatric patients, aged ≥ 11 years, for daily, around-the-clock, long term opioid treatment and for which alternative treatment options are inadequate. Unlike adults, pediatric patients must have responded to a minimum opioid daily dose of ≥ 20 mg oxycodone for 5 consecutive days prior to initiating treatment with OxyContin. Although study efficacy and safety data are not rigorous, OxyContin has been prescribed off-label for years within the pediatric population (*FDA Summary: OxyContin 2015*).
- All of the long-acting opioids are classified as Schedule II controlled substances by the FDA, with the exception of transdermal and buccal buprenorphine, which is a Schedule III controlled substance.
- Since 2013, a number of abuse deterrent formulations have come to the market. Although various manufacturers have introduced formulations with properties to deter misuse potential; there are only a few agents that have completed studies supporting the potential to deter abuse and misuse. The only long-acting opioids that meet all requirements and are currently available include OxyContin (oxycodone hydrochloride extended release), Arymo ER (morphine sulfate extended release), Embeda (morphine sulfate/naltrexone), Hysingla ER (hydrocodone bitartrate extended release), Morphabond (morphine sulfate extended release), and Xtampza ER (oxycodone extended release) (*FDA Industry Guidance 2015*).
- Almost all long-acting opioids are part of the REMS program. In general, all of the long-acting opioids are similar in terms of adverse events, warnings, and contraindications. Methadone-containing products warn of the potential for QTc prolongation and risks associated with an interaction with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) is

cited within Duragesic, Hysingla ER, OxyContin, Xtampza ER, and Zohydro ER labeling. The main differences among the individual agents and formulations are due to dosing requirements and generic availability.
  - Several generic long-acting opioids exist, including hydromorphone; oxymorphone; levorphanol; fentanyl transdermal systems; methadone tablets, solution, and concentrate; morphine sulfate ER tablets and capsules; and oxycodone.
- Head-to-head trials demonstrate similar efficacy among the agents in the class. Systematic reviews and treatment guidelines from several professional organizations support and recommend opioids as a potential treatment option for various forms of non-cancer and cancer-related pain. No single opioid is recommended over the others (*Chou et al 2015, Finnerup et al 2015, Mesgarpour et al 2014*). Methadone safety guidelines from the 2014 American Pain Society recommend buprenorphine as an alternative to methadone for the treatment of opioid addiction in patients with risk factors or known QTc prolongation (*Chou et al 2014*).Other current clinical guidelines do not state a preference for the use of one long-acting opioid over another for the use in moderate to severe pain (*Attal et al 2010, Bril et al 2011, Chou et al 2009, Hochberg et al 2012, Manchikanti et al 2012, Qaseem et al 2017*). However, opioid rotation is recommended if a patient experiences adverse effects from one agent (*Chou et al 2009*). A guideline from the CDC has been published that addresses the use of chronic pain outside of active cancer treatment, palliative care, and end-of-life care; this guideline emphasizes the use of nonpharmacologic and nonopioid therapies when possible, and notes that clinicians should consider opioid therapy only if the expected benefits for both pain and function are anticipated to outweigh risks to the patient (*Dowell et al 2016*).

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Therapeutic Class Overview
Fentanyl Immediate Release Products

INTRODUCTION

- Pain is one of the most common symptoms associated with cancer. Patients with cancer experience both chronic and acute pain, and it is important to distinguish the 2 from each other when determining appropriate management strategies. Breakthrough pain (BTP) is commonly defined as a transient increase in pain, occurring either spontaneously or in relation to a trigger, in a patient with relatively stable and adequately controlled background pain (*Zeppetella et al 2014*).
- BTP can broadly be divided into two types: incident BTP (when an obvious trigger precipitates the event) and spontaneous BTP (when no specific triggers are identified) (*Mercadante 2015*).
- On average, a typical duration of untreated BTP is approximately 30 minutes, with a mean time to peak intensity of about 10 minutes. However, BTP is a heterogeneous condition, varying between and within individuals (*Mercadante 2015*).
- Supplemental opioid doses are used to manage episodes of BTP *(National Comprehensive Cancer Network [NCCN] 2018, Portenoy et al 1990).* Any of the available short-acting opioids have the potential to be utilized for the management of BTP; however, immediate-release fentanyl products, due to a fast onset of action, are specifically Food and Drug Administration (FDA) approved for the management of breakthrough cancer pain in patients who are already receiving and who are tolerant to around-the-clock therapy for their underlying persistent cancer pain. Five different dosage forms of immediate-release fentanyl are currently available: a sublingual tablet (Abstral), a transmucosal lozenge (Actiq), a buccal tablet (Fentora), a nasal spray (Lazanda), and a sublingual spray (Subsys). A sixth immediate-release fentanyl product (Onsolis, a buccal film) was approved in the United States but is not currently available; the pharmaceutical company has stated that options for commercializing Onsolis are still being investigated (*BioDelivery Sciences 2017*). Currently, only the fentanyl transmucosal lozenge is available generically.
- Clinical trials have consistently demonstrated the effectiveness of immediate-release fentanyl in the management of BTP in patients with cancer; however, head-to-head trials are limited.
- Medispan class: Immediate-release fentanyl products are classified within the opioid agonist class of medications.

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Abstral (fentanyl sublingual tablet)	-
Actiq (fentanyl oral transmucosal lozenge)	✔
Fentora (fentanyl buccal tablet)	-
Lazanda (fentanyl nasal spray)	-
Onsolis (fentanyl buccal soluble film)*	-
Subsys (fentanyl sublingual spray)	-

*Drug not currently available; the pharmaceutical company has stated that options for commercializing Onsolis are still being investigated.

(*BioDelivery Sciences 2017, Drugs@FDA 2018, Orange Book: Approved drug products with therapeutic equivalence evaluations 2018*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Abstral (fentanyl sublingual tablet)	Actiq (fentanyl oral transmucosal lozenge)	Fentora (fentanyl buccal tablet)	Lazanda (fentanyl nasal spray)	Onsolis (fentanyl buccal soluble film)	Subsys (fentanyl sublingual spray)
Management of breakthrough pain in cancer patients **18 years of age** and older who are already receiving and are tolerant to around-the-clock opioid therapy for underlying persistent cancer pain.	✔		✔	✔	✔	✔
Management of breakthrough pain in cancer patients **16 years of age** and older who are already receiving and are tolerant to around-the-clock opioid therapy for underlying persistent cancer pain.		✔				

(Prescribing information: Abstral 2016, Actiq 2016, Fentora 2016, Lazanda 2017, Onsolis 2016, Subsys 2016)

- 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

- Clinical trials have consistently demonstrated the effectiveness and safety of all available dosage forms of immediate-release fentanyl in the management of BTP in patients with cancer. Several trials have compared the agents to placebo and other short-acting opioids, including oxycodone, morphine, hydrocodone, hydromorphone, and codeine. Due to the nature of the disease in which immediate-release fentanyl is utilized, many of the efficacy clinical trials are open-label, dose titration trials. Patients were typically enrolled in a baseline phase in which the efficacy of their usual BTP medication was assessed and/or the dose of the studied immediate-release fentanyl product was titrated to an effective dose (*Christie et al 1998, Coluzzi et al 2001, Davies et al 2011, Fallon et al 2011, Hanks et al 2004, Jandhyala et al 2013, Kress et al 2009, Masel et al 2017, Mercadante et al 2007, Mercadante et al 2009, Payne et al 2001, Portenoy et al 1999, Portenoy et al 2006, Portenoy et al 2010, Rauck et al 2009, Rauck et al 2010, Rauck et al 2012, Slatkin et al 2007, Ueberall et al 2016, Vissers et al 2010, Zeppetella et al 2010*).
- Trials conducted to compare immediate-release fentanyl to oral short-acting opioids have generally shown immediate-release fentanyl products to improve pain relief shortly after dosing.
  - Two studies demonstrated significantly greater pain intensity difference (PID) scores as early as 10 and 15 minutes after administration of fentanyl nasal spray when compared to immediate-release morphine ($p < 0.05$) (*Davies et al 2011, Fallon et al 2011*).
  - A network meta-analysis of 10 randomized controlled trials evaluating fentanyl in various forms (nasal spray, sublingual tablets, buccal soluble film, buccal tablets, and oral transmucosal lozenge), as well as immediate-release morphine, demonstrated that all tested medications provided pain relief, but the fentanyl products provided greater pain relief in a shorter time frame than oral morphine. It was further noted that the intranasal fentanyl spray provided clinically meaningful pain relief at 15 minutes, whereas other medications did not provide clinically meaningful relief until later time points (*Zeppetella et al 2014*).
  - Another meta-analysis compared fentanyl buccal tablets, sublingual tablets, and transmucosal lozenges to both placebo and immediate-release morphine. Authors of this study found that the probability of each formulation being superior to placebo, in regards to PID over 60 minutes, was 97%, 72%, and 81% for buccal tablets, sublingual tablets, and transmucosal lozenges, respectively. The probability of immediate-release morphine being superior to placebo was 61%. The probabilities of greater pain relief for the fentanyl products compared to immediate-release morphine

were 68%, 57%, and 66% for the buccal tablet, sublingual tablet, and transmucosal lozenge, respectively. Similarly, when the fentanyl preparations were compared with immediate-release morphine over the first 30 minutes post-dosing, the likelihood of superiority estimates were 58%, 56%, and 62% for buccal tablets, sublingual tablets, and transmucosal lozenges, respectively (*Jandhyala et al 2013*).

- In contrast to the studies above, fentanyl transmucosal lozenge demonstrated a slower onset of action when compared to intravenous morphine (*Mercadante et al 2007*).
- There is limited evidence comparing the efficacy among all the various formulations of immediate-release fentanyl products; however, there are data comparing the fentanyl nasal spray to the transmucosal lozenge and to the buccal tablet.
  - One open-label, crossover study evaluated the efficacy of fentanyl nasal spray compared to fentanyl transmucosal lozenge. The primary efficacy endpoint, defined as the time to onset of meaningful pain relief, was 11 minutes for the fentanyl nasal spray group and 16 minutes for the fentanyl transmucosal lozenge group; 65.7% of patients had a faster onset of meaningful pain relief with the intranasal fentanyl spray ($p < 0.001$). Secondary outcomes included PID scores at 10 and 30 minutes (PID_{10}, PID_{30}). The adjusted mean PID_{10} and PID_{30} were significantly greater for the fentanyl nasal spray group compared to the fentanyl lozenge group ($p < 0.001$) (*Mercandante et al 2009*).
  - A meta-analysis by Vissers et al found that differences in PID scores at 15 minutes (PID_{15}) favoring fentanyl nasal spray were 1.2 points better (95% Bayesian credible interval [CrI], 0.8 to 1.5) compared to the buccal tablet and 1.3 points better (95% CrI, 0.9 to 1.6) compared to the transmucosal lozenge. The significant differences in PID scores favoring fentanyl nasal spray were maintained at the 30 minute time point compared to the buccal tablet and at the 30 and 45 minute time points compared to the transmucosal lozenge (*Vissers et al 2010*).

CLINICAL GUIDELINES

- The European Association for Palliative Care (EAPC) guidelines recommend that breakthrough cancer pain be evaluated to ensure that true breakthrough pain is differentiated from uncontrolled background pain. Around-the-clock opioid therapy should be optimized before a rescue opioid is considered. True breakthrough cancer pain can then be treated with immediate-release oral opioids or with oral or intranasal fentanyl formulations (*Caraceni et al 2012*).
- Breakthrough cancer pain should be treated with agents that have a quick onset and short duration in order to mirror the characteristics that define this type of pain. Standard practice is to administer a rescue dose of short-acting opioids equivalent to 10% to 20% of the total daily dose of the maintenance opioid being used to manage the underlying persistent cancer pain. It is preferred to use the same opioid for breakthrough pain that is being used to manage the persistent pain; however, this is not always possible (*Caraceni et al 2012, Caraceni et al 2013, Hagen et al 2007, NCCN 2018*).
- The 2018 NCCN clinical practice guidelines on adult cancer pain state that transmucosal immediate-release fentanyl (TIRF) medications offer rapid onset of analgesic effect and may be considered only for opioid-tolerant patients with breakthrough pain not attributed to inadequate dosing of the maintenance opioid regimen. The NCCN guidelines further indicate that there is no data to support use of one TIRF product over another, only that patients should be started on the lowest dose of the formulation and titrated to effect (*NCCN 2018*).

SAFETY SUMMARY

- Contraindications:
  - Fentanyl immediate-release products are contraindicated in opioid non-tolerant patients, in the management of acute or postoperative pain, in patients with acute or severe bronchial asthma in an unmonitored setting or without access to resuscitative measures, and in patients with suspected gastrointestinal obstruction.
  - Fentanyl immediate-release products are contraindicated in patients with a known intolerance or hypersensitivity to fentanyl or to any of the products' components.

Boxed Warning for Abstral, Actiq, Fentora, Lazanda, Onsolis, and Subsys

WARNING
• Due to the risk of fatal respiratory depression, these medications are contraindicated in opioid non-tolerant patients and in the management of acute or postoperative pain, including headache/migraines. Monitor closely, especially upon initiation or following a dose increase. • Keep out of reach of children. Accidental ingestion can result in a fatal overdose of fentanyl. • Use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) may cause fatal respiratory depression. • Concomitant use with benzodiazepines or other central nervous system (CNS) depressants may result in profound sedation, respiratory depression, or death. • When prescribing, do not convert patients on a mcg per mcg basis from any other oral transmucosal fentanyl product. • When dispensing, do not substitute with any other fentanyl products. • Fentanyl is a Schedule II controlled substance with abuse liability similar to other opioid analgesics. • Available only through a restricted program called the TIRF Risk Evaluation and Mitigation Strategy (REMS) Access program. Outpatients, healthcare professionals who prescribe to outpatients, pharmacies, and distributors are required to enroll in the program. • Prolonged use in pregnant women can result in neonatal opioid withdrawal syndrome (NOWS).

- Key additional warnings and precautions include:
  - Opioid analgesics impair the mental and/or physical ability required for potentially dangerous tasks (eg, driving a car or operating machinery).
  - Respiratory depression is the chief hazard of opioid agonists; it is more likely to occur in patients with underlying respiratory disorders and elderly or debilitated patients.
  - Products contain an amount of medication which can be fatal in children, in individuals for whom they are not prescribed, and in those who are not opioid-tolerant.
  - Products may produce bradycardia; use with caution in patients with bradyarrhythmias.
  - Products are not recommended for use in patients who have received monoamine oxidase inhibitors within 14 days due to the risk of serotonin syndrome.
  - Products may produce adrenal insufficiency, severe hypotension, increased intracranial pressure, and increased seizure frequency in patients with seizure disorders.
  - In clinical trials for Fentora, 10% of patients reported application site reactions which ranged from paresthesia to ulceration and bleeding.
- Common adverse reactions of immediate-release fentanyl products are consistent with the opioid class, including dizziness, somnolence, constipation, nausea, vomiting, and dyspnea.
- Products may cause fetal harm; available data in pregnant women is insufficient to inform a drug-associated risk for major birth defects and miscarriage.
- Fentanyl is excreted in breast milk; breastfeeding is not recommended.
- Reduced fertility may occur in females and males of reproductive potential after chronic use of opioids. It is unknown if these effects are reversible.
- Safety and efficacy have not been established in pediatric patients below 16 years of age for Actiq, and below 18 years of age for all other products.
- Products in this class share a REMS program, the TIRF REMS. The purpose of the TIRF REMS access program is to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors with these agents (*REMS@FDA 2017, TIRF REMS Program*).

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Usual Recommended Frequency	Comments
Abstral (fentanyl)	Sublingual tablet	Once titrated to an effective dose, use 1 tablet at onset of BTP episode. May repeat dose after 30 minutes if adequate analgesia is not obtained. Must wait at least 2 hours before treating another BTP episode. Limit to treatment of 4 or fewer BTP episodes per day.	Administer with caution in patients with renal and hepatic impairment.
Actiq (fentanyl)	Transmucosal lozenge	Once titrated to an effective dose, use 1 lozenge at onset of BTP episode. May repeat dose after 15 minutes if adequate analgesia is not obtained. Must wait at least 4 hours before treating another BTP episode. Limit to use of 4 or fewer units per day.	Administer with caution in patients with renal and hepatic impairment.
Fentora (fentanyl)	Buccal tablet	Once titrated to an effective dose, use 1 tablet at onset of BTP episode. May repeat dose after 30 minutes if adequate analgesia is not obtained. Must wait at least 4 hours before treating another BTP episode.	Administer with caution in patients with renal and hepatic impairment.
Lazanda (fentanyl)	Nasal spray	Once titrated to an effective dose, use 1 dose at onset of BTP episode. Must wait at least 2 hours before treating another BTP episode. Limit treatment to 4 or fewer BTP episodes per day.	Administer with caution in patients with renal and hepatic impairment.
Onsolis (fentanyl)	Buccal soluble film	Once titrated to an effective dose, use 1 unit at onset of BTP episode. Must wait at least 2 hours before treating another BTP episode. Limit to 4 doses per day.	Administer with caution in patients with renal and hepatic impairment.
Subsys (fentanyl)	Sublingual spray	Once titrated to an effective dose, use 1 unit at onset of BTP episode. May repeat dose after 30 minutes if adequate analgesia is not obtained. Must wait at least 4 hours before treating another BTP episode. Limit to 4 or fewer doses per day.	Administer with caution in patients with renal and hepatic impairment. Exposure to Subsys is greater in cancer patients with mucositis leading to an increased risk of respiratory depression and central nervous system depression. Patients with Grade 1 mucositis should be closely monitored. Subsys should be avoided in patients with Grade 2 mucositis or higher unless the benefits outweigh the risks.

See the current prescribing information for full details

CONCLUSION

- Immediate-release fentanyl products are short-acting opioids FDA-approved for the management of breakthrough cancer pain in patients who are already receiving and who are tolerant to around-the-clock therapy for their underlying persistent pain. Five different dosage forms of immediate-release fentanyl are currently available: a sublingual tablet (Abstral), a transmucosal lozenge (Actiq), a buccal tablet (Fentora), a nasal spray (Lazanda), and a sublingual spray (Subsys). A sixth immediate-release fentanyl product (Onsolis, a buccal film) is approved in the United States but is not

currently available; the pharmaceutical company has stated that options for commercializing Onsolis are still being investigated *(BioDelivery Sciences 2017)*. Currently, only the fentanyl transmucosal lozenge is available generically.

- Immediate-release fentanyl has a fast onset of action, making it well-suited for the management of cancer-related BTP as this type of pain is characterized by a rapid onset, severe intensity and a self-limiting course. Currently, these products are the only short-acting opioids specifically FDA-approved for use in the management of cancer pain.
- Current clinical guidelines support the use of immediate-release fentanyl products as an option for the treatment of breakthrough cancer pain in opioid tolerant patients. There is no evidence to support use of one product over another, and patients should be started on the lowest available dose and titrated to effect.
- The effectiveness of these products is well documented in clinical trials. There are limited head-to-head trials comparing efficacy among all dosage forms; however, there is some evidence supporting a faster onset of action for fentanyl nasal spray when compared to the fentanyl lozenge or buccal tablet.
- Bioavailability differs among products and the different formulations are not interchangeable. Appropriate dose titration is important.
- All products share a boxed warning for the risk of life-threatening respiratory depression, accidental ingestion (especially by children), drug interactions, medication errors, abuse potential, REMS, and NOWS.
- Products in this class are only available through a REMS program, the TIRF REMS. The purpose of the TIRF REMS access program is to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors with these agents.

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Board Requested Reports

Opioid Utilization – top prescribers and members

OPTUMRx®

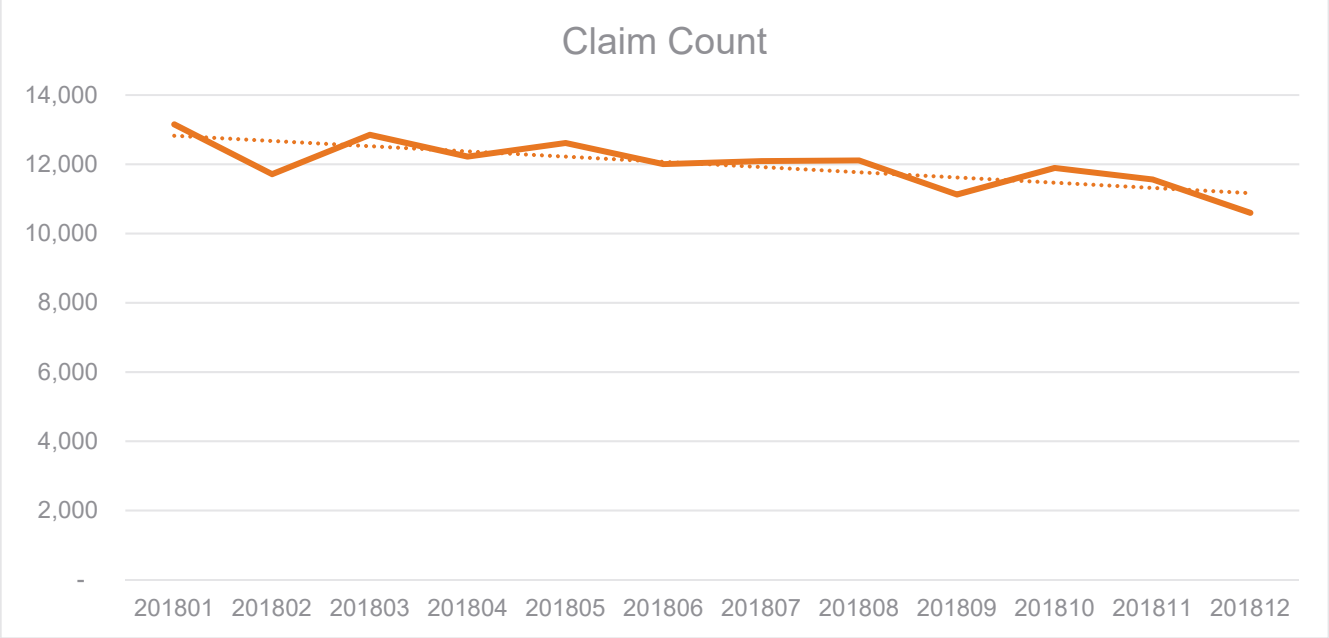
Opioid Utilization

Overall Summary

January 1, 2018 - December 31, 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
201801	9,205	13,154	1.43	245,697	956,196	103.88
201802	8,480	11,714	1.38	223,455	768,592	90.64
201803	8,938	12,854	1.44	242,827	838,459	93.81
201804	8,680	12,225	1.41	232,182	791,869	91.23
201805	8,689	12,618	1.45	233,158	797,275	91.76
201806	8,520	12,005	1.41	223,808	762,625	89.51
201807	8,445	12,092	1.43	221,957	756,930	89.63
201808	8,410	12,114	1.44	223,836	755,283	89.81
201809	8,005	11,130	1.39	206,001	702,850	87.80
201810	8,316	11,895	1.43	216,903	743,457	89.40
201811	8,147	11,561	1.42	216,142	740,513	90.89
201812	7,564	10,598	1.40	197,060	668,408	88.37



Top 10 Opioid Prescribers by Count of Claims

Fee for Service Medicaid

10/1/18 - 12/31/18

Encryped ID	Specialty	Degree	City	Member Count	Claim Count	Sum of Days Supply	Sum of Qty
A	Anesthesiology	DO	Henderson	140	520	14,692	58,008
B	Maxillofacial Surgery	PA	Henderson	171	381	10,970	34,372
C	Pain Management	MD	Carson City	108	371	8,397	21,562
D	Pain Management	PA	Las Vegas	165	327	9,626	29,632
E	Family Practice	NP	Fallon	95	289	6,030	26,279
F		PA	Las Vegas	95	276	7,793	25,812
G	Pain/Anethesiology	MD	Las Vegas	107	268	7,020	23,322
H	Internal Medicine	MD	Las Vegas	42	233	3,303	6,784
I	Orthopedic Surg	PA	Las Vegas	80	221	6,197	21,879
J	Pain Management	MD	Las Vegas	135	218	5,821	17,407

7/1/18 - 9/30/18

Encryped ID	Specialty	Degree	City	Member Count	Claim Count	Sum of Days Supply	Sum of Qty
A	Anesthesiology	DO	Henderson	165	524	14,735	58,133
B	Maxillofacial Surgery	PA	Henderson	191	443	13,142	40,563
C	Pain Management	MD	Carson City	98	362	8,790	22,052
D	Pain Management	PA	Las Vegas	150	257	7,580	23,154
K	Family Practice	NP	Las Vegas	103	255	7,020	22,488
L	Pulmonary	PA	Las Vegas	98	249	7,072	26,017
M	Pain Management	PA	Las Vegas	126	246	7,426	21,696
I	Orthopedic Surg	PA	Las Vegas	87	239	6,917	23,215
J	Pain Management	MD	Las Vegas	141	218	6,137	18,684
H	Internal Medicine	MD	Las Vegas	42	208	3,248	7,169

4/1/18 - 6/30/18

Encryped ID	Specialty	Degree	City	Member Count	Claim Count	Sum of Days Supply	Sum of Qty
A	Anesthesiology	DO	Henderson	154	637	18,610	73,469
F		PA	Las Vegas	99	373	10,072	32,346
C	Pain Management	MD	Carson City	96	369	8,924	22,985
N	Pain Management	MD	Las Vegas	129	337	9,557	32,237
B	Maxillofacial Surgery	PA	Henderson	172	333	9,897	30,356
E	Family Practice	NP	Fallon	126	327	7,040	32,027
O	General Surgery	PA	Las Vegas	80	327	9,559	35,703
D	Pain Management	PA	Las Vegas	193	319	9,240	27,353
P	Pain Management	NP	Las Vegas	129	313	9,325	28,532
J	Pain Management	MD	Las Vegas	195	310	8,453	25,757

Opioid Utilization by Member

Top 10 Members by Claim Count

January 1, 2018 - December 31, 2018

Fee for Service Medicaid

MemberIDEncrypted	Prescriber NPI	Claim Count	Days Supply	Qty Disp
88884905646		156	728	3,934
	II	3	22	86
	KK	139	635	3,564
	LL	6	31	92
	BH	3	9	90
	CB	5	31	102
33333376249		130	720	2,811
	EE	23	131	469
	NN	12	76	210
	BF	4	20	120
	BI	19	87	372
	BJ	46	266	1,010
	BM	1	10	20
	BV	1	10	25
	BY	21	106	505
	CD	3	14	80
66668619978		126	470	2,566
	GG	17	85	384
	OO	1	1	2
	QQ	13	58	247
	VV	82	294	1,670
	WW	2	2	2
	YY	2	10	60
	ZZ	1	1	1
	BM	6	14	180
	CE	2	5	20
33330492333		103	685	1,928
	JJ	4	28	70
	KK	32	263	784
	BO	67	394	1,074
44444458470		102	761	1,988
	EE	20	183	439
	YY	7	57	86
	BF	4	32	104
	BI	1	7	14
	BJ	32	255	650
	BY	23	137	478
	CA	3	15	53
	CD	3	14	50
	CF	9	61	114
29457655656		88	556	2,490
	BB	9	70	330
	PP	22	22	70

MemberIDEncrypted	Prescriber NPI	Claim Count	Days Supply	Qty Disp
	BC	10	90	371
	BP	28	212	1,033
	BR	1	7	14
	BS	17	152	654
	BT	1	3	18
11116193955		83	788	2,631
	CC	8	8	8
	HH	15	430	1,495
	MM	8	240	840
	BD	29	29	49
	BG	12	12	27
	BQ	8	8	25
	L	2	60	185
	BW	1	1	2
88883847895		80	512	1,810
	GG	10	85	270
	BJ	67	412	1,506
	BU	3	15	34
00001004825		80	428	1,508
	BA	9	270	1,080
	BE	68	68	68
	BX	3	90	360
76028922323		75	165	420
	AA	2	2	3
	CC	6	6	7
	DD	1	6	24
	FF	1	2	12
	RR	1	14	30
	SS	2	20	50
	TT	1	5	20
	UU	1	7	15
	WW	22	22	39
	XX	1	3	12
	BD	8	8	11
	BG	14	14	20
	BI	2	6	20
	BK	1	5	10
	BL	5	5	9
	BM	1	5	30
	BN	1	7	21
	BQ	1	1	1
	BZ	1	10	15
	CG	1	7	40
	CH	2	10	32
Grand Total		**1,023**	**5,813**	**22,086**

Opioid Utilization by Member

Top 10 Members by Claim Count
January 1, 2018 - December 31, 2018
Fee for Service Medicaid

Encryped ID	Count of Claims	Day Supply	Quantity
88884905646	**156**	**728**	**3,934**
HYDROMORPHON TAB 2MG	65	189	1,810
HYDROMORPHON TAB 4MG	18	97	486
MORPHINE SUL TAB 15MG	41	194	1,154
MORPHINE SUL TAB 30MG ER	18	140	268
MORPHINE SUL TAB 60MG ER	14	108	216
33333376249	**130**	**720**	**2,811**
HYDROCO/APAP TAB 5-325MG	18	77	458
HYDROCO/APAP TAB 7.5-325	61	282	1,630
MORPHINE SUL TAB 15MG ER	4	29	57
OXYCODONE TAB 20MG ER	11	78	154
OXYCONTIN TAB 20MG CR	36	254	512
66668619978	**126**	**470**	**2,566**
MORPHINE SUL INJ 4MG/ML	1	1	1
MORPHINE SUL TAB 15MG ER	9	78	78
MORPHINE SUL TAB 30MG ER	18	121	235
OXYCOD/APAP TAB 10-325MG	92	256	2,072
OXYCOD/APAP TAB 7.5-325	6	14	180
33330492333	**103**	**685**	**1,928**
HYDROCO/APAP TAB 10-325MG	53	352	1,262
MORPHINE SUL TAB 30MG ER	50	333	666
44444458470	**102**	**761**	**1,988**
HYDROCO/APAP TAB 10-325MG	45	257	1,197
MORPHINE SUL TAB 15MG ER	24	216	216
MORPHINE SUL TAB 30MG ER	33	288	575
29457655656	**88**	**556**	**2,490**
METHADONE TAB 10MG	3	74	222
METHADONE TAB 5MG	30	144	422
MORPHINE SUL TAB 30MG ER	1	7	14
OXYCOD/APAP TAB 10-325MG	3	3	24
OXYCODONE TAB 15MG	16	116	584
OXYCODONE TAB 20MG	32	195	1,178
OXYCODONE TAB 5MG	1	3	18
OXYCONTIN TAB 20MG CR	2	14	28
11116193955	**83**	**788**	**2,631**
HYDROMORPHON TAB 4MG	1	10	50
MORPHINE SUL INJ 4MG/ML	22	22	53
MORPHINE SUL TAB 30MG ER	29	377	739
OXYCOD/APAP TAB 10-325MG	28	376	1,776
OXYCODONE TAB 5MG	2	2	12
TRAMADOL HCL TAB 50MG	1	1	1
88883847895	**80**	**512**	**1,810**
MORPHINE SUL TAB 15MG ER	39	316	634

Encryped ID	Count of Claims	Day Supply	Quantity
OXYCODONE TAB 5MG	41	196	1,176
00001004825	**80**	**428**	**1,508**
DEMEROL INJ 25MG/ML	56	56	56
DEMEROL INJ 50MG/ML	1	1	1
OXYCOD/APAP TAB 10-325MG	12	360	1,440
OXYCOD/APAP TAB 5-325MG	4	4	4
PERCOCET TAB 10-325MG	6	6	6
PERCOCET TAB 7.5-325	1	1	1
76028922323	**75**	**165**	**420**
DILAUDID INJ 1MG/ML	4	4	6
DILAUDID TAB 4MG	1	1	2
HYDROCO/APAP TAB 10-325MG	1	1	1
HYDROCO/APAP TAB 5-325MG	1	1	2
HYDROMORPHON INJ 1MG/ML	14	14	25
HYDROMORPHON INJ 2MG/ML	9	9	15
HYDROMORPHON TAB 2MG	23	84	249
MORPHINE SUL INJ 4MG/ML	10	10	13
MORPHINE SUL TAB 15MG ER	2	17	34
OXYCOD/APAP TAB 10-325MG	4	4	4
OXYCOD/APAP TAB 5-325MG	1	1	1
OXYCOD/APAP TAB 7.5-325	2	10	33
OXYCODONE CAP 5MG	2	8	35
OXYCONTIN TAB 10MG CR	1	1	1
Grand Total	**1,023**	**5,813**	**22,086**

Top 10 Opioid Agents By Claim Count

Overall Summary

January 1, 2018 - December 31, 2018

Anthem Nevada Medicaid

Drug Name	Count of Member	Count of Claims	Sum of Total Quantity	Sum of Total Days of Therapy
1st Quarter 2018	16149	16149	1112656	334162
HYDROCODONE-ACETAMIN 10-325 MG	3686	3686	327543	95553
OXYCODONE-ACETAMINOPHEN 10-325	2019	2019	184168	50744
TRAMADOL HCL 50 MG TABLET	1708	1708	80928	23628
HYDROCODONE-ACETAMIN 5-325 MG	1219	1219	38732	11965
OXYCODONE-ACETAMINOPHEN 5-325	909	909	28542	7909
OXYCODONE HCL 30 MG TABLET	670	670	72698	19155
BUTALB-ACETAMIN-CAFF 50-325-40	652	652	38590	13367
ACETAMINOPHEN-COD #3 TABLET	623	623	14209	3813
HYDROCODONE-ACETAMIN 7.5-325	623	623	36318	11412
OXYCODONE HCL 10 MG TABLET	514	514	47464	12874
2nd Quarter 2018	14944	14944	1048364	318005
HYDROCODONE-ACETAMIN 10-325 MG	3518	3518	314704	92465
OXYCODONE-ACETAMINOPHEN 10-325	1888	1888	176350	48413
TRAMADOL HCL 50 MG TABLET	1564	1564	77978	22937
HYDROCODONE-ACETAMIN 5-325 MG	994	994	32982	10662
OXYCODONE-ACETAMINOPHEN 5-325	815	815	26051	7480
BUTALB-ACETAMIN-CAFF 50-325-40	711	711	39895	14843
OXYCODONE HCL 30 MG TABLET	648	648	70868	18863
HYDROCODONE-ACETAMIN 7.5-325	642	642	36270	11579
ACETAMINOPHEN-COD #3 TABLET	543	543	11963	3625
OXYCODONE HCL 10 MG TABLET	452	452	42732	11730
3rd Quarter 2018	14237	14237	981958	301649
HYDROCODONE-ACETAMIN 10-325 MG	3392	3392	302201	89732
OXYCODONE-ACETAMINOPHEN 10-325	1797	1797	165510	46114
TRAMADOL HCL 50 MG TABLET	1501	1501	71504	20971
HYDROCODONE-ACETAMIN 5-325 MG	1090	1090	32241	10814
OXYCODONE-ACETAMINOPHEN 5-325	772	772	23822	6899

BUTALB-ACETAMIN-CAFF 50-325-40	670	670	38827	14778
OXYCODONE HCL 30 MG TABLET	545	545	58172	15530
HYDROCODONE-ACETAMIN 7.5-325	535	535	28947	9512
OXYCODONE HCL 10 MG TABLET	457	457	42602	11668
ACETAMINOPHEN-COD #3 TABLET	409	409	9209	2686
4th Quarter 2018	13746	13746	946102.4	291665
HYDROCODONE-ACETAMIN 10-325 MG	3350	3350	298358	88399
OXYCODONE-ACETAMINOPHEN 10-325	1738	1738	156869	44204
TRAMADOL HCL 50 MG TABLET	1530	1530	73147	20981
HYDROCODONE-ACETAMIN 5-325 MG	878	878	25362	8350
OXYCODONE-ACETAMINOPHEN 5-325	813	813	25456	7674
BUTALB-ACETAMIN-CAFF 50-325-40	648	648	37602	15090
HYDROCODONE-ACETAMIN 7.5-325	528	528	27912	9251
OXYCODONE HCL 30 MG TABLET	520	520	54471	15018
OXYCODONE HCL 10 MG TABLET	453	453	43154	11740
ACETAMINOPHEN-COD #3 TABLET	410	410	9017	2719

Top 10 Prescribers of Opioid Agents By Claim Count

July 1, 2018 - September 30, 2018

Anthem Nevada Medicaid

Top 10 Opioid Prescribers								
Prescriber ID	**Prescriber Type**	**Physician City**	**Physician State**	**Member Count**	**Claim Count**	**Sum of Days Supply**	**Sum of Quantity**	**Sum of Paid Amount**
*******828	DO	Las Vegas	Nevada	485	485	14073	45665	Anthem confidential
*******700	DO	Reno	Nevada	377	377	10371	34173	Anthem confidential
*******464	NP	Reno	Nevada	305	305	9034	25542	Anthem confidential
*******618	MD	Las Vegas	Nevada	257	257	7473	22123	Anthem confidential
*******850	NP	Lakewood	Colorado	254	254	6641	20624	Anthem confidential
*******881	NP	Las Vegas	Nevada	232	232	6674	19810	Anthem confidential
*******775	NP	Reno	Nevada	229	229	6531	19911	Anthem confidential
*******779	MD	Las Vegas	Nevada	222	222	6612	19998	Anthem confidential
*******117	MD	San Antonio	Texas	214	214	5241	16889	Anthem confidential
*******183	PAC	Reno	Nevada	196	196	5575	17228	Anthem confidential

Top 10 Utilizers of Opioid Agents By Claim Count

July 1, 2018 - September 30, 2018

Anthem Nevada Medicaid

Utilizers	Count of Claims	Sum of Total Days of Therapy	Sum of Total Quantity
******836	13	390	780
******310	12	336	1036
******513	12	360	1200
******405	12	360	960
******325	11	165	535
******255	10	246	842
******073	10	95	210
******628	10	204	612
******173	10	178	459
******725	9	257	600

Top 10 Prescribers of Opioid Agents By Claim Count

October 31, 2018 - December 31, 2018

Anthem Nevada Medicaid

Top 10 Opioid Prescribers

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
*******586	PA	Las Vegas	Nevada	459	459	13086	41997	Anthem confidential
*******525	MD	Henderson	Nevada	323	323	9486	26463	Anthem confidential
*******121	PAC	Las Vegas	Nevada	300	300	8455	26299	Anthem confidential
*******305	PAC	Las Vegas	Nevada	297	297	8129	26295	Anthem confidential
*******050	PAC	Las Vegas	Nevada	258	258	7082	22643	Anthem confidential
*******319	MD	Henderson	Nevada	248	248	6732	21855	Anthem confidential
*******190	NP	Las Vegas	Nevada	238	238	6439	20363	Anthem confidential
*******647	PA	North Las Vegas	Nevada	231	231	6533	20846	Anthem confidential
*******237	NP	Las Vegas	Nevada	229	229	6796	20556	Anthem confidential
*******127	MD	Las Vegas	Nevada	220	220	6365	20105	Anthem confidential

Top 10 Utilizers of Opioid Agents By Claim Count

October 31, 2018 - December 31, 2018

Anthem Nevada Medicaid

Utilizer	Count of Claims	Count of Total Days of Therapy	Count of Total Quantity
******480	12	12	12
******099	12	12	12
******020	12	12	12
******677	10	10	10
******005	10	10	10
******431	10	10	10
******076	10	10	10
******232	10	10	10
******279	10	10	10
******061	9	9	9

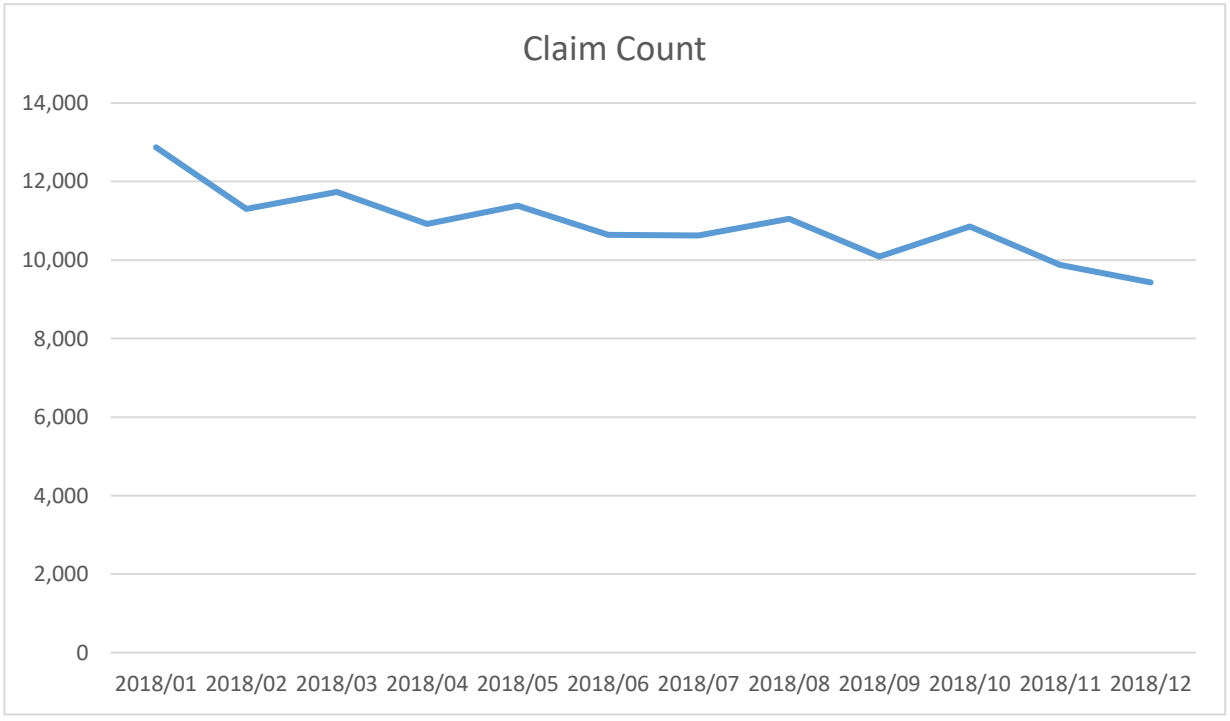
HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Opioid Prescribers/Utilizers

January 1, 2018 - December 31, 2018

Health Plan of Nevada

Opioid Utilization						
Year/Month Filled	Member Count	Claim Count	Claims Per Member	Sum of Days Supply	Sum of Quantity	Sum of Amt Paid
2018/01	10,810	12,872	1.19	288,713	978,757	NA
2018/02	9,755	11,303	1.16	256,794	859,846	NA
2018/03	9,848	11,733	1.19	264,807	888,464	NA
2018/04	9,313	10,918	1.17	245,148	822,394	NA
2018/05	9,440	11,384	1.21	254,968	850,249	NA
2018/06	8,980	10,646	1.19	235,066	791,575	NA
2018/07	8,864	10,627	1.20	233,676	783,145	NA
2018/08	9,077	11,054	1.22	239,958	800,098	NA
2018/09	8,583	10,086	1.18	218,157	724,588	NA
2018/10	8,926	10,856	1.22	236,187	780,702	NA
2018/11	8,309	9,879	1.19	219,752	727,937	NA
2018/12	7,978	9,431	1.18	208,510	690,227	NA



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Opioid Prescribers/Utilizers

January 1,2018 - December 31, 2018

Health Plan of Nevada

Top 10 Opioid Prescribers by Claim Count					Q4 2018 - Current			
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amt
A	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	590	1,398	163	125,192	NA
B	PAIN MANAGEMENT	LAS VEGAS	NEVADA	336	835	157	79,111	NA
C	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	335	632	189	52,354	NA
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	239	567	114	56,184	NA
E	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	178	565	170	63,634	NA
F	PAIN MANAGEMENT	LAS VEGAS	NEVADA	314	516	83	49,067	NA
G	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	266	503	105	45,906	NA
H	PHYSICAL MEDICINE REHAB	LAS VEGAS	NEVADA	188	418	160	35,568	NA
I	GENERAL PRACTICE	LAS VEGAS	NEVADA	117	395	82	37,635	NA
J	PAIN MANAGEMENT & ER MEDICIN	LAS VEGAS	NEVADA	255	347	142	32,426	NA

Top 10 Opioid Prescribers by Claim Count					Q3 2018 - Previous			
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amt
K	PAIN MANAGEMENT	LAS VEGAS	NEVADA	562	1,197	187	104,640	NA
A	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	462	908	193	78,766	NA
B	PAIN MANAGEMENT	LAS VEGAS	NEVADA	340	849	217	77,353	NA
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	256	538	155	51,427	NA
F	PAIN MANAGEMENT	LAS VEGAS	NEVADA	315	511	106	48,564	NA
E	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	189	508	207	57,612	NA
J	PAIN MANAGEMENT & ER MEDICIN	LAS VEGAS	NEVADA	298	446	96	42,453	NA
I	GENERAL PRACTICE	LAS VEGAS	NEVADA	119	416	61	39,504	NA
H	PHYSICAL MEDICINE/REHAB	LAS VEGAS	NEVADA	183	366	200	31,826	NA
C	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	259	363	116	27,575	NA

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Opioid Prescribers/Utilizers

January 1,2018 - December 31, 2018

Health Plan of Nevada

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	Sum of Paid Amt
L	FAMILY PRACTICE & PAIN MGT	HENDERSON	NEVADA	460	1,024	183	90,096	NA
A	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	467	937	200	81,224	NA
F	PAIN MANAGEMENT	LAS VEGAS	NEVADA	375	682	134	66,813	NA
B	PAIN MANAGEMENT	LAS VEGAS	NEVADA	280	650	205	61,076	NA
E	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	196	647	162	75,848	NA
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	579	96	56,370	NA
M	PAIN MANAGEMENT	LAS VEGAS	NEVADA	236	500	177	47,747	NA
J	PAIN MANAGEMENT & ER MEDICIN	LAS VEGAS	NEVADA	320	491	60	46,309	NA
I	GENERAL PRACTICE	LAS VEGAS	NEVADA	128	437	107	42,328	NA
N	PAIN MANAGEMENT	LAS VEGAS	NEVADA	250	386	94	38,493	NA

Top 10 Opioid Prescribers by Claim Count					Q1 2018 - Previous			
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amt
L	FAMILY PRACTICE & PAIN MGT	HENDERSON	NEVADA	530	1,118	244	100,721	NA
O	INTERNAL MED & PAIN MGT	LAS VEGAS	NEVADA	493	1,113	241	87,560	NA
A	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	482	1,024	141	88,126	NA
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	257	634	132	62,181	NA
F	PAIN MANAGEMENT	LAS VEGAS	NEVADA	344	618	85	60,682	NA
E	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	199	592	173	70,538	NA
M	PAIN MANAGEMENT	LAS VEGAS	NEVADA	257	553	149	53,530	NA
J	PAIN MANAGEMENT & ER MEDICIN	LAS VEGAS	NEVADA	337	541	37	51,799	NA
P	PAIN MANAGEMENT	LAS VEGAS	NEVADA	309	457	60	42,734	NA
I	GENERAL PRACTICE	LAS VEGAS	NEVADA	135	444	86	42,270	NA

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

TOP 25 Members by Claim Count

January 1,2018 - December 31, 2018

Health Plan of Nevada

TOP 25 Members and Prescribers

Encrypted Member ID	Encrypted Prescriber ID	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amt
M1	PA	53	299	1,789	NA
	PB	3	20	115	NA
	PC	6	35	210	NA
Total		**62**	**354**	**2,114**	**NA**
M2	PD	1	30	30	NA
	PE	3	21	142	NA
	PF	53	1,014	1,840	NA
	PG	3	18	122	NA
Total		**60**	**1,083**	**2,134**	**NA**
M3	PH	48	322	1,310	NA
	PI	2	6	20	NA
	PJ	2	14	60	NA
Total		**52**	**342**	**1,390**	**NA**
M4	PK	5	35	140	NA
	PL	40	278	1,034	NA
Total		**45**	**313**	**1,174**	**NA**
M5	E	41	1,180	4,720	NA
	PM	1	3	10	NA
Total		**42**	**1,183**	**4,730**	**NA**
M6	PN	3	52	425	NA
	PM	38	769	6,426	NA
Total		**41**	**821**	**6,851**	**NA**
M7	PO	5	150	690	NA
	PP	34	1,020	4,680	NA
Total		**39**	**1,170**	**5,370**	**NA**
M8	PQ	4	56	140	NA
	PR	14	360	900	NA
	C	4	90	225	NA
	B	16	236	582	NA
Total		**38**	**742**	**1,847**	**NA**
M9	PS	1	30	120	NA
	PT	7	210	390	NA
	PU	21	630	1,350	NA
	PV	8	240	540	NA
Total		**37**	**1,110**	**2,400**	**NA**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

TOP 25 Members by Claim Count

January 1,2018 - December 31, 2018

Health Plan of Nevada

TOP 25 Members and Prescribers					
Encrypted Member ID	Encrypted Prescriber ID	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amt
M10	PW	21	540	1,710	NA
	PX	2	60	180	NA
	PY	2	60	180	NA
	PZ	8	180	420	NA
	PPA	2	30	60	NA
	PPB	2	60	120	NA
Total		**37**	**930**	**2,670**	**NA**
M11	PPC	8	130	478	NA
	PPD	1	7	42	NA
	PPE	28	570	3,900	NA
Total		**37**	**707**	**4,420**	**NA**
M12	E	37	1,110	3,085	NA
Total		**37**	**1,110**	**3,085**	**NA**
M13	PPF	36	1,080	6,480	NA
Total		**36**	**1,080**	**6,480**	**NA**
M14	PPI	36	1,080	4,350	NA
Total		**36**	**1,080**	**4,350**	**NA**
M15	E	29	870	1,770	NA
	PPJ	6	180	360	NA
Total		**35**	**1,050**	**2,130**	**NA**
M16	PPK	35	724	4,080	NA
Total		**35**	**724**	**4,080**	**NA**
M17	E	30	900	3,600	NA
	PPJ	5	150	420	NA
Total		**35**	**1,050**	**4,020**	**NA**
M18	PPL	4	88	510	NA
	PPM	31	930	3,060	NA
Total		**35**	**1,018**	**3,570**	**NA**
M19	PPN	2	10	50	NA
	C	19	453	1,326	NA
	B	13	367	1,094	NA
Total		**34**	**830**	**2,470**	**NA**
M20	PPO	32	960	2,040	NA
	PPP	2	60	180	NA
Total		**34**	**1,020**	**2,220**	**NA**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

TOP 25 Members by Claim Count

January 1,2018 - December 31, 2018

Health Plan of Nevada

TOP 25 Members and Prescribers					
Encrypted Member ID	Encrypted Prescriber ID	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amt
M21	PPQ	11	50	627	NA
	PPR	1	3	13	NA
	PPS	1	7	84	NA
	PPT	1	5	10	NA
	PPU	2	8	60	NA
	PPV	12	340	1,464	NA
	PPW	4	11	100	NA
Total		**32**	**424**	**2,358**	**NA**
M22	PPX	32	224	1,302	NA
Total		**32**	**224**	**1,302**	**NA**
M23	PPY	32	960	2,400	NA
Total		**32**	**960**	**2,400**	**NA**
M24	N	2	60	210	NA
	C	17	440	1,380	NA
	B	13	390	1,140	NA
Total		**32**	**890**	**2,730**	**NA**
M25	PPZ	1	21	21	NA
	PPPA	31	315	352	NA
Total		**32**	**336**	**373**	**NA**

Correlation between Top Prescribers and Top Recipients:
Prescriber B - Members M24, M19, M8
Prescriber C - Members M24, M19, M8
Prescriber E - Members M5, M12, M15, M17
Prescriber N - Member M24

Opioid Utilization by Member

Top 25 Members and Prescribers

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Member Enc ID	Enc NPI	Count of Claim	Sum of Qty	Sum of Days		Sum of Due Amt
1		27	792	396	$	6,512.40
	EE	27	792	396	$	6,512.40
2		34	518	260	$	4,182.78
	BB	3	70	35	$	555.18
	DD	31	448	225	$	3,627.60
3		31	572	423	$	2,604.78
	X	31	572	423	$	2,604.78
4		30	2,730	780	$	1,652.27
	F	2	105	30	$	82.64
	J	2	210	60	$	97.14
	V	22	1,995	570	$	1,172.32
	GG	4	420	120	$	300.17
5		29	630	315	$	4,075.83
	I	2	52	26	$	427.05
	EE	24	548	274	$	3,400.10
	OO	3	30	15	$	248.68
6		27	778	404	$	6,385.60
	EE	27	778	404	$	6,385.60
7		27	1,950	745	$	3,696.07
	J	27	1,950	745	$	3,696.07
8		26	2,340	780	$	18,546.72
	A	24	2,160	720	$	17,792.90
	F	2	180	60	$	18,546.72
9		26	1,530	765	$	10,130.52
	R	22	1,290	645	$	8,250.25
	AA	2	120	60	$	936.55
	GG	2	120	60	$	943.72
10		26	1,530	765	$	10,130.52
	J	21	1,960	605	$	6,569.44
	O	5	357	126	$	2,025.32
11		26	780	405	$	6,400.68
	EE	26	780	405	$	6,400.68
12		26	2,280	780	$	5,804.86
	A	2	180	60	$	429.83
	F	20	1,770	600	$	4,420.16
	J	2	180	60	$	442.51
	AA	2	150	60	$	512.36

Opioid Utilization by Member

Top 25 Members and Prescribers
January 1, 2018 - December 31, 2018
Silversummit Healthplan

Member	Enc NPI	Count of	Sum of	Sum of		Sum of Due Amt
13		26	2,108	724	$	2,985.49
	E	10	850	290	$	638.78
	GG	5	480	150	$	248.60
	M	8	600	210	$	1,529.06
	Y	3	178	74	$	569.04
14		26	2,730	780	$	1,779.21
	J	2	240	60	$	308.16
	R	2	240	60	$	251.31
	AA	9	1,080	270	$	1,116.87
	KK	13	1,170	390	$	102.87
15		26	1,560	780	$	1,403.22
	P	14	840	420	$	729.40
	CC	4	240	120	$	245.10
	NN	8	480	240	$	428.72
16		26	2,256	752	$	918.04
	Z	26	2,256	752	$	918.04
17		26	2,340	780	$	917.07
	CC	2	180	60	$	83.47
	L	6	540	180	$	198.82
	FF	16	1,440	480	$	566.87
	II	2	180	60	$	67.91
18		25	2,655	750	$	9,794.09
	Q	1	60	30	$	707.00
	S	5	555	150	$	1,687.35
	LL	19	2,040	570	$	7,399.74
19		25	220	750	$	6,875.98
	A	15	1,320	450	$	4,488.24
	J	10	900	300	$	2,387.74
20		25	750	375	$	6,154.50
	EE	25	750	375	$	6,154.50
21		25	1,611	701	$	4,558.03
	D	8	496	231	$	1,525.38
	JJ	17	1,115	470	$	3,032.65
22		25	3,270	750	$	3,699.99
	A	16	1,530	480	$	2,121.92
	J	9	840	270	$	1,578.07
23		25	1,565	735	$	3,314.67
	D	2	130	60	$	272.76
	H	3	140	90	$	376.09
	JJ	14	905	405	$	1,827.23
	MM	6	390	180	$	838.59

Opioid Utilization by Member

Top 25 Members and Prescribers

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Member Enc ID	Enc NPI	Count of Claim	Sum of Qty	Sum of Days		Sum of Due Amt
24		25	2,244	722	$	920.56
	A	7	660	210	$	356.47
	BB	6	600	180	$	204.66
	KK	2	180	60	$	63.06
	NN	1	30	5	$	14.16
	R	1	120	30	$	40.88
	T	4	360	120	$	142.78
	U	1	60	30	$	20.59
	HH	3	234	87	$	77.96
25		25	216	155	$	719.56
	W	25	216	155	$	719.56

Board Requested Reports

Top claims for member under 18 years-old

Top Claims for Members Under 18 years-old

Fee for Service Medicaid

January 1, 2018 - December 31, 2018

All Medications

Medication Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
Age 0	3,658	4,573	63,079	330,703
2018 Q1	1,234	1,543	20,159	120,695
ALBUTEROL NEB 0.083%	212	294	3,283	40,953
AMOXICILLIN SUS 400/5ML	242	262	2,705	35,938
IBUPROFEN SUS 100/5ML	106	119	487	6,159
NYSTATIN SUS 100000	77	88	1,107	8,191
PREDNISOLONE SOL 15MG/5ML	123	148	942	3,727
PREDNISOLONE SYP 15MG/5ML	95	100	645	2,547
PREVNAR 13 INJ	78	90	90	45
RANITIDINE SYP 75MG/5ML	128	199	6,460	17,332
SYNAGIS INJ 100MG/ML	80	147	3,916	153
TAMIFLU SUS 6MG/ML	93	96	524	5,650
2018 Q2	853	1,026	13,166	77,889
ALBUTEROL NEB 0.083%	91	130	1,501	19,719
AMOXICILLIN SUS 250/5ML	63	67	631	7,554
AMOXICILLIN SUS 400/5ML	184	200	2,036	19,230
IBUPROFEN SUS 100/5ML	78	89	396	5,534
NYSTATIN CRE 100000	60	64	945	2,040
NYSTATIN SUS 100000	71	86	1,154	8,104
POLYMYXIN B/ SOL TRIMETHP	58	59	919	590
PREDNISOLONE SOL 15MG/5ML	70	88	605	2,184
PREVNAR 13 INJ	74	82	82	41
RANITIDINE SYP 75MG/5ML	104	161	4,897	12,893
2018 Q3	723	889	12,611	66,218
ALBUTEROL NEB 0.083%	57	93	1,048	12,726
AMOXICILLIN SUS 400/5ML	138	151	1,540	14,353
COMPOUND	22	47	1,308	4,753
IBUPROFEN SUS 100/5ML	74	81	452	7,801
NYSTATIN CRE 100000	66	72	1,066	2,565
NYSTATIN OIN 100000	57	59	747	1,590
NYSTATIN SUS 100000	80	83	1,213	7,600
PREDNISOLONE SOL 15MG/5ML	52	65	456	2,017
PREVNAR 13 INJ	80	86	86	43
RANITIDINE SYP 75MG/5ML	97	152	4,695	12,771
2018 Q4	848	1,115	17,143	65,901
ALBUTEROL NEB 0.083%	89	126	1,689	16,542
AMOXICILLIN SUS 400/5ML	193	212	2,163	20,025
IBUPROFEN SUS 100/5ML	63	73	374	4,924
NYSTATIN CRE 100000	60	65	796	1,845
NYSTATIN SUS 100000	62	69	977	6,435
PREDNISOLONE SOL 15MG/5ML	111	132	852	3,766
PREVNAR 13 INJ	86	98	98	49
RANITIDINE SYP 75MG/5ML	92	152	4,978	12,159

SYNAGIS	INJ 100MG/ML	57	117	3,253	121
SYNAGIS	INJ 50MG	35	71	1,963	36
Age 1-4		11,272	14,476	185,908	1,839,304
2018 Q1		3,783	4,599	46,204	518,712
ALBUTEROL	NEB 0.083%	524	666	8,652	105,420
AMOXICILLIN	SUS 400/5ML	972	1,058	10,548	152,243
AZITHROMYCIN	SUS 200/5ML	292	312	1,509	6,602
CEFDINIR	SUS 250/5ML	295	318	3,329	20,700
COMPOUND		75	292	5,302	133,840
IBUPROFEN	SUS 100/5ML	492	555	2,252	42,978
MONTELUKAST	CHW 4MG	166	300	9,238	9,238
ONDANSETRON	TAB 4MG ODT	260	322	828	1,510
PREDNISOLONE	SOL 15MG/5ML	349	408	2,344	16,676
TAMIFLU	SUS 6MG/ML	358	368	2,202	29,506
2018 Q2		2,604	3,439	51,086	477,514
ALBUTEROL	NEB 0.083%	291	379	5,430	62,991
AMOXICILLIN	SUS 400/5ML	635	671	6,546	92,372
AZITHROMYCIN	SUS 200/5ML	181	191	957	3,596
CETIRIZINE	SOL 1MG/ML	201	285	8,866	31,193
COMPOUND		73	327	5,403	128,777
IBUPROFEN	SUS 100/5ML	320	360	1,563	29,460
LORATADINE	SOL 5MG/5ML	142	191	5,500	22,130
MONTELUKAST	CHW 4MG	159	279	8,700	8,700
ONDANSETRON	TAB 4MG ODT	237	308	794	1,423
POLYETH GLYC	POW 3350 NF	167	221	5,897	86,854
PREDNISOLONE	SOL 15MG/5ML	198	227	1,430	10,018
2018 Q3		1,914	2,692	42,916	434,599
ALBUTEROL	NEB 0.083%	209	277	3,645	44,280
AMOXICILLIN	SUS 400/5ML	442	473	4,590	62,301
CETIRIZINE	SOL 1MG/ML	177	253	7,983	28,579
COMPOUND		75	316	5,156	123,756
IBUPROFEN	SUS 100/5ML	259	302	1,276	26,092
MONTELUKAST	CHW 4MG	143	247	7,714	7,714
MONTELUKAST	GRA 4MG	84	174	4,921	4,921
ONDANSETRON	TAB 4MG ODT	180	233	710	1,115
POLYETH GLYC	POW 3350 NF	144	183	5,271	124,393
PREDNISOLONE	SOL 15MG/5ML	201	234	1,650	11,449
2018 Q4		2,971	3,746	45,702	408,479
ALBUTEROL	NEB 0.083%	354	484	6,404	78,093
AMOXICILLIN	SUS 250/5ML	201	213	1,973	27,661
AMOXICILLIN	SUS 400/5ML	824	885	8,711	122,010
CEFDINIR	SUS 250/5ML	199	212	2,211	14,030
CETIRIZINE	SOL 1MG/ML	168	252	7,866	28,613
COMPOUND		66	253	5,340	73,384
IBUPROFEN	SUS 100/5ML	334	396	1,835	34,030
MONTELUKAST	CHW 4MG	141	230	7,306	7,307
ONDANSETRON	TAB 4MG ODT	251	310	805	1,469
PREDNISOLONE	SOL 15MG/5ML	433	511	3,251	21,882

Age 5-9	13,345	17,536	359,101	1,829,312
2018 Q1	4,270	5,325	86,298	469,566
ALBUTEROL NEB 0.083%	487	648	8,828	103,773
AMOXICILLIN SUS 400/5ML	852	910	8,830	165,674
AZITHROMYCIN SUS 200/5ML	389	416	2,020	10,832
CETIRIZINE SYP 1MG/ML	195	330	9,403	57,082
FLUTICASONE SPR 50MCG	347	452	16,462	7,310
IBUPROFEN SUS 100/5ML	422	486	2,073	55,389
MONTELUKAST CHW 5MG	354	633	20,025	20,310
ONDANSETRON TAB 4MG ODT	348	433	1,190	2,630
PROVENTIL AER HFA	510	637	15,292	5,206
TAMIFLU SUS 6MG/ML	366	380	2,175	41,360
2018 Q2	3,169	4,280	102,877	488,727
ALBUTEROL NEB 0.083%	317	460	7,208	76,995
AMOXICILLIN SUS 400/5ML	566	588	5,751	106,311
CETIRIZINE SOL 1MG/ML	209	351	10,213	62,324
CLONIDINE TAB 0.1MG	213	273	18,947	26,950
FLUTICASONE SPR 50MCG	354	489	17,735	7,857
IBUPROFEN SUS 100/5ML	304	340	1,532	45,581
MONTELUKAST CHW 5MG	366	657	21,312	21,567
ONDANSETRON TAB 4MG ODT	264	331	893	2,123
POLYETH GLYC POW 3350 NF	220	300	7,958	135,106
PROVENTIL AER HFA	356	491	11,328	3,913
2018 Q3	2,557	3,608	94,551	497,154
ALBUTEROL NEB 0.083%	278	391	6,347	68,967
AMOXICILLIN SUS 400/5ML	389	405	3,945	75,121
CETIRIZINE SOL 1MG/ML	172	301	8,744	55,998
CLONIDINE TAB 0.1MG	186	248	16,322	22,662
FLUTICASONE SPR 50MCG	271	373	13,339	5,966
IBUPROFEN SUS 100/5ML	264	305	1,364	38,188
LEVETIRACETA SOL 100MG/ML	96	242	7,228	86,525
MONTELUKAST CHW 5MG	312	552	17,677	17,953
POLYETH GLYC POW 3350 NF	189	256	7,099	121,433
PROVENTIL AER HFA	400	535	12,486	4,342
2018 Q4	3,349	4,323	75,375	373,865
ALBUTEROL NEB 0.083%	395	515	7,985	91,893
AMOXICILLIN SUS 400/5ML	625	657	6,346	118,185
AZITHROMYCIN SUS 200/5ML	249	266	1,353	6,859
CETIRIZINE SOL 1MG/ML	201	360	10,482	63,608
FLUTICASONE SPR 50MCG	282	401	14,424	6,441
IBUPROFEN SUS 100/5ML	315	367	1,637	42,238
MONTELUKAST CHW 5MG	291	535	17,171	17,222
ONDANSETRON TAB 4MG ODT	260	323	839	1,989
PREDNISOLONE SOL 15MG/5ML	310	355	2,026	20,968
PROVENTIL AER HFA	421	544	13,112	4,462
Age 10-17	16,058	23,248	692,547	967,890
2018 Q1	4,701	6,341	162,110	246,219
ALBUTEROL NEB 0.083%	376	502	7,472	93,477
AMOXICILLIN CAP 500MG	499	517	4,522	12,829

AZITHROMYCIN TAB 250MG	411	445	2,210	2,646
CETIRIZINE TAB 10MG	309	529	17,512	17,752
CLONIDINE TAB 0.1MG	367	480	30,788	51,486
FLUTICASONE SPR 50MCG	568	718	25,110	11,645
LORATADINE TAB 10MG	376	600	18,932	18,948
MONTELUKAST CHW 5MG	377	699	22,407	22,872
ONDANSETRON TAB 4MG ODT	418	521	1,594	3,783
PROVENTIL AER HFA	1,000	1,330	31,563	10,780
2018 Q2	4,156	6,118	190,057	262,120
ALBUTEROL NEB 0.083%	314	408	6,962	76,431
AMOXICILLIN CAP 500MG	405	427	3,639	10,456
CETIRIZINE TAB 10MG	379	603	20,185	20,395
CLONIDINE TAB 0.1MG	344	461	29,022	48,232
FLUTICASONE SPR 50MCG	615	818	28,900	13,275
LORATADINE TAB 10MG	425	680	21,909	21,984
MONTELUKAST CHW 5MG	390	741	23,980	24,340
MONTELUKAST TAB 10MG	286	478	16,525	16,480
PROVENTIL AER HFA	817	1,114	27,044	9,092
RISPERIDONE TAB 1MG	181	388	11,891	21,435
2018 Q3	3,566	5,398	177,166	229,313
ALBUTEROL NEB 0.083%	271	343	5,870	65,145
ARIPIPRAZOLE TAB 5MG	175	344	10,855	13,283
CETIRIZINE TAB 10MG	306	499	17,185	17,315
CLONIDINE TAB 0.1MG	316	436	27,402	46,283
FLUTICASONE SPR 50MCG	491	648	23,041	10,671
LORATADINE TAB 10MG	352	530	17,297	17,327
MONTELUKAST CHW 5MG	361	671	21,730	22,330
MONTELUKAST TAB 10MG	253	423	14,879	14,879
PROVENTIL AER HFA	836	1,113	26,911	9,099
SERTRALINE TAB 50MG	205	391	11,996	12,982
2018 Q4	3,635	5,391	163,214	230,238
ALBUTEROL NEB 0.083%	320	432	6,520	76,392
AMOXICILLIN CAP 500MG	380	391	3,393	9,632
CETIRIZINE TAB 10MG	264	428	14,322	14,427
CLONIDINE TAB 0.1MG	330	442	27,509	45,449
FLUTICASONE SPR 50MCG	444	612	21,197	9,939
LORATADINE TAB 10MG	294	471	14,963	15,023
MONTELUKAST CHW 5MG	341	653	21,225	21,660
MONTELUKAST TAB 10MG	233	428	14,554	14,554
PROVENTIL AER HFA	825	1,128	27,147	9,273
SERTRALINE TAB 50MG	204	406	12,384	13,890
Grand Total	**44,333**	**59,833**	**1,300,635**	**4,967,209**

Top Claims for Members Under 18 years-old

Fee for Service Medicaid

January 1, 2018 - December 31, 2018

Opioids

Medication Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
Age 0	23	38	530	805
2018 Q1	6	10	133	338
HYDROCO/APAP SOL 7.5-325	1	1	4	30
HYDROMORPHON INJ 2MG/ML	1	1	1	5
METHADONE SOL 5MG/5ML	2	6	125	288
MORPHINE SUL SOL 10MG/5ML	1	1	1	5
OXYCODONE SOL 5MG/5ML	1	1	2	10
2018 Q2	12	15	213	291
ALFENTANIL INJ 1000/2ML	1	1	1	2
DURAMORPH INJ 1MG/ML	1	1	1	10
HYDROCO/APAP SOL 7.5-325	5	5	24	170
METHADONE SOL 5MG/5ML	4	7	184	104
MORPHINE SUL SOL 10MG/5ML	1	1	3	5
2018 Q3	4	12	183	174
HYDROCO/APAP SOL 7.5-325	2	2	6	45
METHADONE SOL 5MG/5ML	2	10	177	129
2018 Q4	1	1	1	2
MORPHINE SUL INJ 2MG/ML	1	1	1	2
Age 1-4	165	183	855	10,046
2018 Q1	44	49	203	2,873
APAP/CODEINE SOL 120-12/5	7	7	32	385
APAP/CODEINE TAB 300-30MG	1	1	7	24
DEMEROL INJ 25MG/ML	1	1	1	1
HYDROCO/APAP SOL 7.5-325	25	29	133	2,333
METHADONE SOL 5MG/5ML	1	1	5	15
MORPHINE SUL INJ 2MG/ML	4	4	4	4
MORPHINE SUL INJ 4MG/ML	1	1	1	1
MORPHINE SUL SOL 10MG/5ML	1	1	7	60
OXYCODONE SOL 5MG/5ML	2	3	12	49
ULTIVA INJ 1MG	1	1	1	0
2018 Q2	46	49	212	2,409
APAP/CODEINE SOL 120-12/5	2	2	9	80
HYDROCO/APAP SOL 7.5-325	29	31	142	2,104
HYDROCO/APAP TAB 5-325MG	1	1	1	2
HYDROMORPHON INJ 1MG/ML	1	2	2	1
HYDROMORPHON INJ 2MG/ML	3	3	3	15
METHADONE SOL 10MG/5ML	1	1	1	5
METHADONE SOL 5MG/5ML	3	3	32	70
MORPHINE SUL INJ 4MG/ML	2	2	2	2
MORPHINE SUL SOL 10MG/5ML	2	2	8	60
OXYCODONE SOL 5MG/5ML	2	2	12	70
2018 Q3	29	32	135	1,719

APAP/CODEINE SOL 120-12/5	1	1	14	170
HYDROCO/APAP SOL 7.5-325	12	15	60	1,016
HYDROCO/APAP TAB 5-325MG	2	2	2	2
HYDROMORPHON INJ 1MG/ML	1	1	1	1
METHADONE SOL 10MG/5ML	1	1	30	230
METHADONE SOL 5MG/5ML	1	1	10	250
MORPHINE SUL INJ 2MG/ML	4	4	4	4
MORPHINE SUL INJ 4MG/ML	2	2	2	2
OXYCOD/APAP TAB 5-325MG	1	1	1	3
OXYCODONE SOL 5MG/5ML	4	4	11	41
2018 Q4	46	53	305	3,046
APAP/CODEINE SOL 120-12/5	1	1	1	10
DURAMORPH INJ 1MG/ML	1	1	1	10
HYDROCO/APAP SOL 7.5-325	29	33	160	2,296
HYDROCO/APAP TAB 5-325MG	1	1	1	1
HYDROMORPHON INJ 2MG/ML	1	1	1	1
MEPERIDINE INJ 25MG/ML	1	1	1	1
METHADONE SOL 10MG/5ML	1	3	90	494
METHADONE SOL 5MG/5ML	1	1	23	120
MORPHINE SUL INJ 2MG/ML	1	1	1	1
MORPHINE SUL INJ 4MG/ML	3	3	3	4
MORPHINE SUL SOL 10MG/5ML	1	1	1	5
OXYCODONE SOL 5MG/5ML	4	5	21	103
ULTIVA INJ 1MG	1	1	1	0
Age 5-9	250	268	1,214	21,984
2018 Q1	73	76	355	6,464
APAP/CODEINE SOL 120-12/5	3	3	16	165
APAP/CODEINE TAB 300-30MG	1	1	1	1
HYDROCO/APAP SOL 7.5-325	47	49	242	5,864
HYDROCO/APAP TAB 5-325MG	5	5	44	136
HYDROMORPHON INJ 2MG/ML	1	1	1	1
LORTAB ELX 10-300MG	1	1	5	135
MEPERIDINE SOL 50MG/5ML	1	1	1	3
MORPHINE SUL INJ 10MG/ML	1	1	1	1
MORPHINE SUL INJ 2MG/ML	3	3	3	3
MORPHINE SUL INJ 4MG/ML	3	3	3	3
MORPHINE SUL INJ 5MG/ML	2	2	2	2
MORPHINE SUL SOL 10MG/5ML	3	4	28	121
OXYCOD/APAP TAB 5-325MG	1	1	7	28
TRAMADOL HCL TAB 50MG	1	1	1	1
2018 Q2	61	66	329	5,060
APAP/CODEINE SOL 120-12/5	4	4	34	623
DEMEROL INJ 25MG/0.5	1	1	1	1
HYDROCO/APAP SOL 7.5-325	36	38	185	4,054
HYDROCO/APAP TAB 5-325MG	7	9	66	234
MEPERIDINE INJ 25MG/ML	1	1	1	1
MORPHINE SUL INJ 2MG/ML	6	7	7	8
MORPHINE SUL INJ 4MG/ML	1	1	1	1
MORPHINE SUL INJ 5MG/ML	1	1	1	1

MORPHINE SUL SOL 10MG/5ML	2	2	21	72
OXYCODONE SOL 5MG/5ML	1	1	7	60
TRAMADOL HCL TAB 50MG	1	1	5	5
2018 Q3	61	65	304	5,726
APAP/CODEINE SOL 120-12/5	2	2	2	10
HYDROCO/APAP SOL 7.5-325	41	44	230	5,420
HYDROCO/APAP TAB 5-325MG	1	1	14	45
HYDROMORPHON INJ 1MG/ML	1	1	1	1
MEPERIDINE SOL 50MG/5ML	1	1	1	3
MORPHINE SUL INJ 2MG/ML	3	3	3	3
MORPHINE SUL INJ 4MG/ML	3	3	3	5
MORPHINE SUL SOL 10MG/5ML	1	1	14	28
OXYCODONE SOL 5MG/5ML	7	8	31	202
OXYCODONE TAB 5MG	1	1	5	10
2018 Q4	55	61	226	4,735
APAP/CODEINE SOL 120-12/5	2	2	5	61
APAP/CODEINE TAB 300-30MG	1	1	5	45
DEMEROL INJ 100MG/ML	1	1	1	1
DEMEROL INJ 50MG/ML	1	1	1	1
HYDROCO/APAP SOL 7.5-325	26	27	136	4,254
HYDROCO/APAP TAB 5-325MG	5	9	35	113
HYDROMORPHON INJ 2MG/ML	1	1	1	15
MEPERIDINE INJ 25MG/ML	1	2	2	2
MORPHINE SUL INJ 10MG/ML	1	1	1	1
MORPHINE SUL INJ 2MG/ML	5	5	5	10
MORPHINE SUL INJ 4MG/ML	5	5	5	6
OXYCODONE SOL 5MG/5ML	6	6	29	226
Age 10-17	1,258	1,384	6,281	54,442
2018 Q1	354	388	1,787	14,417
APAP/CODEINE TAB 300-30MG	23	23	88	380
HYDROCO/APAP SOL 7.5-325	26	29	143	7,591
HYDROCO/APAP TAB 10-325MG	19	19	94	555
HYDROCO/APAP TAB 5-325MG	164	183	828	3,404
HYDROCO/APAP TAB 7.5-325	30	30	154	685
MORPHINE SUL INJ 2MG/ML	15	15	15	22
MORPHINE SUL INJ 4MG/ML	22	26	26	33
OXYCOD/APAP TAB 5-325MG	23	25	121	577
OXYCODONE TAB 5MG	11	16	141	539
TRAMADOL HCL TAB 50MG	21	22	177	631
2018 Q2	333	363	1,564	14,047
APAP/CODEINE TAB 300-30MG	15	15	56	236
HYDROCO/APAP SOL 7.5-325	29	30	176	8,506
HYDROCO/APAP TAB 10-325MG	16	16	84	443
HYDROCO/APAP TAB 5-325MG	152	170	788	2,997
HYDROCO/APAP TAB 7.5-325	35	37	196	896
HYDROMORPHON INJ 2MG/ML	14	16	16	37
MORPHINE SUL INJ 2MG/ML	11	12	12	14
MORPHINE SUL INJ 4MG/ML	27	28	28	34
OXYCOD/APAP TAB 5-325MG	21	23	97	449

OXYCODONE TAB 5MG	13	16	111	435
2018 Q3	302	333	1,522	10,690
APAP/CODEINE TAB 300-30MG	5	5	17	69
HYDROCO/APAP SOL 7.5-325	25	25	121	5,336
HYDROCO/APAP TAB 10-325MG	14	14	94	391
HYDROCO/APAP TAB 5-325MG	145	165	808	2,950
HYDROCO/APAP TAB 7.5-325	23	24	118	523
HYDROMORPHON INJ 2MG/ML	15	18	18	37
MEPERIDINE INJ 25MG/ML	5	5	5	7
MORPHINE SUL INJ 2MG/ML	14	14	14	18
MORPHINE SUL INJ 4MG/ML	22	23	23	30
OXYCOD/APAP TAB 10-325MG	3	5	96	556
OXYCOD/APAP TAB 5-325MG	16	16	72	292
OXYCODONE TAB 5MG	15	19	136	482
2018 Q4	269	300	1,408	15,288
HYDROCO/APAP SOL 7.5-325	34	36	193	10,342
HYDROCO/APAP TAB 10-325MG	16	20	164	663
HYDROCO/APAP TAB 5-325MG	130	141	700	2,744
HYDROCO/APAP TAB 7.5-325	13	16	70	302
HYDROMORPHON INJ 2MG/ML	7	9	9	11
MORPHINE SUL INJ 2MG/ML	13	13	13	17
MORPHINE SUL INJ 4MG/ML	27	29	29	33
OXYCOD/APAP TAB 10-325MG	6	9	101	513
OXYCOD/APAP TAB 5-325MG	15	17	57	207
OXYCODONE TAB 5MG	8	10	72	456
Grand Total	**1,696**	**1,873**	**8,880**	**87,277**

Top Claims for Members Under 18 years-old

Fee for Service Medicaid

January 1, 2018 - December 31, 2018

Psychotropics

Medication Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
Age 0	93	151	4,225	19,705
2018 Q1	24	42	1,282	7,123
PHENOBARB SOL 20MG/5ML	5	10	300	2,465
LEVETIRACETA SOL 100MG/ML	4	7	258	1,140
PHENOBARB ELX 20MG/5ML	3	5	136	1,650
ONFI SUS 2.5MG/ML	2	4	152	720
OXCARBAZEPIN TAB 150MG	1	3	90	180
CLONAZEP ODT TAB 0.125MG	1	3	90	270
PHENOBARB TAB 64.8MG	1	2	60	60
DIAZEPAM SOL 1MG/ML	1	2	87	411
DIASTAT PED GEL 2.5M GEL	1	1	30	1
DIAZEPAM GEL 10MG	1	1	2	2
MIDAZOLAM INJ 2MG/2ML	1	1	1	2
VIGABATRIN PAK 500MG	1	1	21	42
HYDROXYZ HCL SYP 10MG/5ML	1	1	25	150
LORAZEPAM CON 2MG/ML	1	1	30	30
2018 Q2	26	47	1,261	5,044
PHENOBARB SOL 20MG/5ML	5	10	259	2,160
LEVETIRACETA SOL 100MG/ML	4	8	240	936
HYDROXYZ HCL SYP 10MG/5ML	3	5	144	790
VIGABATRIN PAK 500MG	1	4	84	168
TOPIRAMATE CAP 15MG	1	3	90	270
DIAZEPAM GEL 2.5MG	1	3	88	3
OXCARBAZEPIN TAB 150MG	1	2	60	120
DIAZEPAM SOL 1MG/ML	1	2	111	175
CLONAZEP ODT TAB 0.125MG	1	2	60	180
PHENOBARB TAB 64.8MG	1	1	30	30
DIAZEPAM GEL 10MG	1	1	2	1
PHENOBARB TAB 32.4MG	1	1	30	60
ONFI TAB 10MG	1	1	30	23
LORAZEPAM INJ 2MG/ML	1	1	1	1
ONFI SUS 2.5MG/ML	1	1	30	120
MIDAZOLAM INJ 2MG/2ML	1	1	1	2
MIDAZOLAM INJ 5MG/5ML	1	1	1	5
2018 Q3	20	28	798	3,138
VIGABATRIN PAK 500MG	3	7	210	780
LEVETIRACETA SOL 100MG/ML	2	3	90	380
TOPIRAMATE TAB 25MG	1	3	90	120
HYDROXYZ HCL SYP 10MG/5ML	2	2	24	338
TOPIRAMATE CAP 15MG	1	2	60	180
PHENOBARB ELX 20MG/5ML	2	2	53	760
ONFI SUS 2.5MG/ML	1	1	30	120
PHENOBARB TAB 32.4MG	1	1	30	60

DIAZEPAM SOL 5MG/5ML	1	1	30	81
SABRIL POW 500MG	1	1	30	106
DIAZEPAM SOL 1MG/ML	1	1	60	81
GABAPENTIN SOL 250/5ML	1	1	30	100
DIAZEPAM GEL 2.5MG	1	1	30	1
MIDAZOLAM INJ 5MG/ML	1	1	1	1
OLANZAPINE TAB 2.5MG	1	1	30	30
2018 Q4	23	34	884	4,400
PHENOBARB SOL 20MG/5ML	7	12	360	2,464
VIGABATRIN PAK 500MG	3	6	180	480
LEVETIRACETA SOL 100MG/ML	3	4	120	582
TOPIRAMATE TAB 25MG	1	3	90	120
HYDROXYZ HCL SYP 10MG/5ML	3	3	66	343
MIDAZOLAM INJ 2MG/2ML	2	2	2	4
ZONEGRAN CAP 25MG	1	1	30	90
PHENOBARB ELX 20MG/5ML	1	1	30	300
LORAZEPAM INJ 2MG/ML	1	1	4	16
DIAZEPAM GEL 10MG	1	1	2	1
Age 1-4	662	1,401	38,833	301,426
2018 Q1	174	345	9,249	70,648
LEVETIRACETA SOL 100MG/ML	67	148	4,520	34,393
HYDROXYZ HCL SYP 10MG/5ML	27	42	849	7,872
OXCARBAZEPIN SUS 300MG/5M	15	30	1,052	9,315
ONFI SUS 2.5MG/ML	11	28	848	5,520
PHENOBARB ELX 20MG/5ML	6	20	418	5,783
TOPIRAMATE TAB 25MG	9	18	511	1,936
DIAZEPAM SOL 1MG/ML	7	15	382	1,534
VALPROIC ACD SOL 250/5ML	6	15	476	4,259
LORAZEPAM INJ 2MG/ML	14	15	15	17
DIAZEPAM GEL 10MG	12	14	178	19
2018 Q2	163	349	10,031	75,621
LEVETIRACETA SOL 100MG/ML	63	146	4,589	33,915
ONFI SUS 2.5MG/ML	15	43	1,140	7,547
OXCARBAZEPIN SUS 300MG/5M	22	39	1,406	12,045
HYDROXYZ HCL SYP 10MG/5ML	18	31	688	4,817
TOPIRAMATE TAB 25MG	8	19	620	1,905
PHENOBARB ELX 20MG/5ML	7	18	381	6,759
LORAZEPAM INJ 2MG/ML	11	16	16	18
VALPROIC ACD SOL 250/5ML	6	12	379	3,649
RISPERIDONE TAB 0.25MG	4	9	330	660
ZONISAMIDE CAP 25MG	4	8	240	660
PHENOBARB SOL 20MG/5ML	5	8	242	3,646
2018 Q3	166	373	10,245	76,695
LEVETIRACETA SOL 100MG/ML	67	171	5,120	38,551
OXCARBAZEPIN SUS 300MG/5M	19	44	1,435	11,395
ONFI SUS 2.5MG/ML	15	38	1,085	7,450
PHENOBARB ELX 20MG/5ML	9	21	575	9,703
DIAZEPAM GEL 10MG	18	21	217	25
HYDROXYZ HCL SYP 10MG/5ML	9	16	438	2,355

LORAZEPAM INJ 2MG/ML	7	16	16	20
VALPROIC ACD SOL 250/5ML	7	14	441	4,411
TOPIRAMATE TAB 25MG	6	14	450	1,140
DIAZEPAM SOL 1MG/ML	5	9	198	805
DIVALPROEX CAP 125MG	4	9	270	840
2018 Q4	159	334	9,308	78,463
LEVETIRACETA SOL 100MG/ML	68	159	4,936	39,574
OXCARBAZEPIN SUS 300MG/5M	16	37	1,245	10,900
HYDROXYZ HCL SYP 10MG/5ML	19	29	710	7,213
PHENOBARB ELX 20MG/5ML	10	21	630	10,640
ONFI SUS 2.5MG/ML	10	18	516	3,870
LORAZEPAM INJ 2MG/ML	7	18	18	18
TOPIRAMATE TAB 25MG	6	14	435	1,425
DIAZEPAM GEL 10MG	10	13	119	19
DIAZEPAM SOL 5MG/5ML	7	13	318	865
VALPROIC ACD SOL 250/5ML	6	12	381	3,939
Age 5-9	2,718	5,479	164,998	521,095
2018 Q1	721	1,412	42,468	129,032
LEVETIRACETA SOL 100MG/ML	105	236	7,184	83,246
RISPERIDONE TAB 0.5MG	90	176	5,225	9,311
GUANFACINE TAB 1MG ER	96	166	4,889	5,242
GUANFACINE TAB 2MG ER	80	160	4,793	4,853
ARIPIPRAZOLE TAB 5MG	65	138	4,110	4,430
GUANFACINE TAB 3MG ER	51	115	3,399	3,399
AMPHET/DEXTR TAB 10MG	57	108	3,295	4,663
RISPERIDONE TAB 1MG	57	107	3,479	6,469
VYVANSE CAP 20MG	54	104	3,065	3,065
AMPHET/DEXTR TAB 5MG	66	102	3,029	4,354
2018 Q2	675	1,388	41,959	135,333
LEVETIRACETA SOL 100MG/ML	97	251	7,496	91,660
GUANFACINE TAB 2MG ER	83	164	5,007	5,067
RISPERIDONE TAB 0.5MG	82	162	4,897	8,147
GUANFACINE TAB 1MG ER	83	144	4,401	5,016
ARIPIPRAZOLE TAB 5MG	68	125	3,808	4,527
RISPERIDONE TAB 1MG	54	120	3,898	7,107
GUANFACINE TAB 3MG ER	48	113	3,177	3,177
AMPHET/DEXTR TAB 5MG	61	104	3,157	4,244
VYVANSE CAP 20MG	54	103	3,058	3,058
METHYLPHENID TAB 36MG ER	45	102	3,060	3,330
2018 Q3	632	1,343	40,355	132,561
LEVETIRACETA SOL 100MG/ML	96	242	7,228	86,525
RISPERIDONE TAB 0.5MG	79	187	5,814	9,975
GUANFACINE TAB 2MG ER	74	155	4,644	4,644
GUANFACINE TAB 1MG ER	71	125	3,694	4,160
RISPERIDONE TAB 0.25MG	64	122	3,821	7,568
AMPHET/DEXTR TAB 5MG	55	106	3,195	4,235
ARIPIPRAZOLE TAB 5MG	55	104	2,947	3,822
GUANFACINE TAB 3MG ER	44	104	3,039	3,039
RISPERIDONE TAB 1MG	47	102	3,107	5,727

VYVANSE CAP 30MG	47	96	2,866	2,866
2018 Q4	690	1,336	40,216	124,169
LEVETIRACETA SOL 100MG/ML	98	224	6,753	78,452
RISPERIDONE TAB 0.5MG	89	182	5,722	10,042
GUANFACINE TAB 2MG ER	87	172	5,112	5,202
GUANFACINE TAB 1MG ER	97	156	4,584	5,400
RISPERIDONE TAB 0.25MG	61	118	3,545	7,049
RISPERIDONE TAB 1MG	53	108	3,420	5,790
AMPHET/DEXTR TAB 5MG	65	104	3,104	4,168
METHYLPHENID TAB 36MG ER	46	94	2,775	2,865
METHYLPHENID TAB 27MG ER	48	91	2,638	2,638
VYVANSE CAP 30MG	46	87	2,563	2,563
Age 10-17	6,106	12,492	380,869	752,700
2018 Q1	1,580	3,134	96,714	123,359
RISPERIDONE TAB 1MG	180	387	12,153	21,212
SERTRALINE TAB 50MG	207	384	11,886	12,932
ARIPIPRAZOLE TAB 5MG	177	356	10,968	12,720
SERTRALINE TAB 100MG	150	305	9,355	12,130
METHYLPHENID TAB 36MG ER	143	304	9,114	11,214
RISPERIDONE TAB 0.5MG	151	302	9,447	16,914
ARIPIPRAZOLE TAB 10MG	148	280	8,300	9,196
GUANFACINE TAB 2MG ER	140	276	8,417	9,004
TRAZODONE TAB 50MG	157	274	8,739	9,642
GUANFACINE TAB 3MG ER	127	266	8,335	8,395
2018 Q2	1,604	3,259	99,116	126,776
RISPERIDONE TAB 1MG	181	388	11,891	21,435
ARIPIPRAZOLE TAB 5MG	206	383	12,035	14,543
SERTRALINE TAB 50MG	199	367	11,306	12,187
SERTRALINE TAB 100MG	153	335	10,331	13,043
GUANFACINE TAB 2MG ER	149	319	9,427	10,043
GUANFACINE TAB 3MG ER	140	307	9,319	9,499
RISPERIDONE TAB 0.5MG	144	306	9,447	17,426
TRAZODONE TAB 50MG	154	300	9,095	9,925
METHYLPHENID TAB 36MG ER	136	285	8,439	9,814
ARIPIPRAZOLE TAB 10MG	142	269	7,826	8,861
2018 Q3	1,441	3,002	91,018	243,832
SERTRALINE TAB 50MG	205	391	11,996	12,982
ARIPIPRAZOLE TAB 5MG	175	344	10,855	13,283
RISPERIDONE TAB 1MG	153	314	9,529	16,815
GUANFACINE TAB 2MG ER	153	303	9,240	9,660
TRAZODONE TAB 50MG	152	300	9,323	10,397
RISPERIDONE TAB 0.5MG	141	289	8,721	16,260
GUANFACINE TAB 3MG ER	133	283	8,642	8,912
SERTRALINE TAB 100MG	128	282	8,463	10,495
LEVETIRACETA SOL 100MG/ML	94	250	7,362	138,128
GUANFACINE TAB 4MG ER	107	246	6,887	6,902
2018 Q4	1,481	3,097	94,021	258,734
SERTRALINE TAB 50MG	204	406	12,384	13,890
ARIPIPRAZOLE TAB 5MG	183	346	10,625	12,692

TRAZODONE	TAB 50MG	161	317	9,808	11,070
GUANFACINE	TAB 2MG ER	158	317	9,562	9,952
RISPERIDONE	TAB 1MG	146	308	9,637	17,777
RISPERIDONE	TAB 0.5MG	144	307	9,084	17,093
GUANFACINE	TAB 3MG ER	132	291	8,892	9,102
SERTRALINE	TAB 100MG	127	281	8,649	10,629
LEVETIRACETA	SOL 100MG/ML	95	267	7,880	148,849
VYVANSE	CAP 40MG	131	257	7,500	7,680
Grand Total		**9,579**	**19,523**	**588,925**	**1,594,926**

Top 10 Claims for Members Under 18

Anthem NV Medicaid

January 1, 2018 - December 31, 2018

All Claims: Members Ages 10 to 18 Years of Age

Drug	Count of Claims
1st Quarter 2018	**31720**
VENTOLIN HFA 90 MCG INHALER	2024
LORATADINE 10 MG TABLET	1718
MONTELUKAST SOD 5 MG TAB CHEW	917
AMOXICILLIN 500 MG CAPSULE	784
AZITHROMYCIN 250 MG TABLET	669
ALBUTEROL SUL 2.5 MG/3 ML SOLN	630
CVS FLUTICASONE PROP 50 MCG	580
MONTELUKAST SOD 10 MG TABLET	544
PROMETHAZINE-DM SOLUTION	503
ONDANSETRON ODT 4 MG TABLET	451
AMOXICILLIN 400 MG/5 ML SUSP	441
2nd Quarter 2018	**29299**
LORATADINE 10 MG TABLET	1961
VENTOLIN HFA 90 MCG INHALER	1759
MONTELUKAST SOD 5 MG TAB CHEW	1067
MONTELUKAST SOD 10 MG TABLET	591
CVS FLUTICASONE PROP 50 MCG	565
AMOXICILLIN 500 MG CAPSULE	516
ALBUTEROL SUL 2.5 MG/3 ML SOLN	442
ONDANSETRON ODT 4 MG TABLET	393
AZITHROMYCIN 250 MG TABLET	391
FLUTICASONE PROP 50 MCG SPRAY	374
3rd Quarter 2018	**28158**
VENTOLIN HFA 90 MCG INHALER	1737
LORATADINE 10 MG TABLET	1520
MONTELUKAST SOD 5 MG TAB CHEW	895
CVS FLUTICASONE PROP 50 MCG	481
AMOXICILLIN 500 MG CAPSULE	478
MONTELUKAST SOD 10 MG TABLET	465
ALBUTEROL SUL 2.5 MG/3 ML SOLN	427
POLYETHYLENE GLYCOL 3350 POWD	350
AZITHROMYCIN 250 MG TABLET	316
ONDANSETRON ODT 4 MG TABLET	303
4th Quarter 2018	**28328**
VENTOLIN HFA 90 MCG INHALER	1804
LORATADINE 10 MG TABLET	1529
MONTELUKAST SOD 5 MG TAB CHEW	951
ALBUTEROL SUL 2.5 MG/3 ML SOLN	563
CVS FLUTICASONE PROP 50 MCG	500
AMOXICILLIN 500 MG CAPSULE	489
MONTELUKAST SOD 10 MG TABLET	467
AZITHROMYCIN 250 MG TABLET	383
ONDANSETRON ODT 4 MG TABLET	353
CLINDAMYCIN PH 1% GEL	340
Grand Total	**117505**

All Claims: Members Ages 5 to 9 Years of Age

Drug Name	Count of Claims
1st Quarter 2018	**25865**
AMOXICILLIN 400 MG/5 ML SUSP	1877
VENTOLIN HFA 90 MCG INHALER	1422
ALBUTEROL SUL 2.5 MG/3 ML SOLN	1417
MONTELUKAST SOD 5 MG TAB CHEW	1264
IBUPROFEN 100 MG/5 ML SUSP	1099
CHILD LORATADINE 5 MG/5 ML SYR	697
PREDNISOLONE 15 MG/5 ML SOLN	694
OSELTAMIVIR 6 MG/ML SUSPENSION	674
AZITHROMYCIN 200 MG/5 ML SUSP	663
AMOXICILLIN 250 MG/5 ML SUSP	661
2nd Quarter 2018	**21115**
MONTELUKAST SOD 5 MG TAB CHEW	1402
AMOXICILLIN 400 MG/5 ML SUSP	1154
VENTOLIN HFA 90 MCG INHALER	1107
CHILD LORATADINE 5 MG/5 ML SOL	919
ALBUTEROL SUL 2.5 MG/3 ML SOLN	851
IBUPROFEN 100 MG/5 ML SUSP	698
LORATADINE 10 MG TABLET	599
CVS FLUTICASONE PROP 50 MCG	507
ONDANSETRON ODT 4 MG TABLET	494
AMOXICILLIN 250 MG/5 ML SUSP	459
3rd Quarter 2018	**17446**
VENTOLIN HFA 90 MCG INHALER	1118
MONTELUKAST SOD 5 MG TAB CHEW	990
AMOXICILLIN 400 MG/5 ML SUSP	849
ALBUTEROL SUL 2.5 MG/3 ML SOLN	735
CHILD LORATADINE 5 MG/5 ML SOL	710
IBUPROFEN 100 MG/5 ML SUSP	562
POLYETHYLENE GLYCOL 3350 POWD	432
LORATADINE 10 MG TABLET	407
PREDNISOLONE 15 MG/5 ML SOLN	405
MONTELUKAST SOD 4 MG TAB CHEW	397
Grand Total	**85957**

All Claims: Members Ages 1 to 4 Years of Age

Drug Name	Count of Claims
1st Quarter 2018	**25574**
AMOXICILLIN 400 MG/5 ML SUSP	2640
ALBUTEROL SUL 2.5 MG/3 ML SOLN	2062
IBUPROFEN 100 MG/5 ML SUSP	1317
PREDNISOLONE 15 MG/5 ML SOLN	1130
OSELTAMIVIR 6 MG/ML SUSPENSION	889
CHILD LORATADINE 5 MG/5 ML SYR	823
AMOXICILLIN 250 MG/5 ML SUSP	784
ONDANSETRON ODT 4 MG TABLET	760
CEFDINIR 250 MG/5 ML SUSP	680
AZITHROMYCIN 200 MG/5 ML SUSP	653
2nd Quarter 2018	**18017**
AMOXICILLIN 400 MG/5 ML SUSP	1464
ALBUTEROL SUL 2.5 MG/3 ML SOLN	907
IBUPROFEN 100 MG/5 ML SUSP	893
CHILD LORATADINE 5 MG/5 ML SOL	884
ONDANSETRON ODT 4 MG TABLET	627
MONTELUKAST SOD 4 MG TAB CHEW	613
PREDNISOLONE 15 MG/5 ML SOLN	565
AMOXICILLIN 250 MG/5 ML SUSP	469
POLYETHYLENE GLYCOL 3350 POWD	433
CEFDINIR 250 MG/5 ML SUSP	416
3rd Quarter 2018	**13488**
AMOXICILLIN 400 MG/5 ML SUSP	1063
ALBUTEROL SUL 2.5 MG/3 ML SOLN	684
IBUPROFEN 100 MG/5 ML SUSP	645
CHILD LORATADINE 5 MG/5 ML SOL	627
PREDNISOLONE 15 MG/5 ML SOLN	492
MONTELUKAST SOD 4 MG TAB CHEW	446
POLYETHYLENE GLYCOL 3350 POWD	389
AMOXICILLIN 250 MG/5 ML SUSP	354
MUPIROCIN 2% OINTMENT	336
ONDANSETRON ODT 4 MG TABLET	324
4th Quarter 2018	**18309**
AMOXICILLIN 400 MG/5 ML SUSP	1783
ALBUTEROL SUL 2.5 MG/3 ML SOLN	1321
PREDNISOLONE 15 MG/5 ML SOLN	1012
CHILD LORATADINE 5 MG/5 ML SOL	996
IBUPROFEN 100 MG/5 ML SUSP	953
AMOXICILLIN 250 MG/5 ML SUSP	519
MONTELUKAST SOD 4 MG TAB CHEW	504
ONDANSETRON ODT 4 MG TABLET	488
POLYETHYLENE GLYCOL 3350 POWD	423
AZITHROMYCIN 200 MG/5 ML SUSP	413
Grand Total	**75388**

All Claims: Members Age < 1 Year of Age

Drug Name	Count of Claims
1st Quarter 2018	**7480**
ALBUTEROL SUL 2.5 MG/3 ML SOLN	728
AMOXICILLIN 400 MG/5 ML SUSP	566
PREDNISOLONE 15 MG/5 ML SOLN	318
RANITIDINE 15 MG/ML SYRUP	305
CHILD PAIN-FEVER 160 MG/5 ML	258
IBUPROFEN 100 MG/5 ML SUSP	246
OSELTAMIVIR 6 MG/ML SUSPENSION	232
NYSTATIN 100,000 UNIT/GM CREAM	223
AMOXICILLIN 250 MG/5 ML SUSP	216
NYSTATIN 100,000 UNIT/ML SUSP	172
2nd Quarter 2018	**5150**
AMOXICILLIN 400 MG/5 ML SUSP	325
ALBUTEROL SUL 2.5 MG/3 ML SOLN	321
RANITIDINE 15 MG/ML SYRUP	269
NYSTATIN 100,000 UNIT/GM CREAM	200
CHILD PAIN-FEVER 160 MG/5 ML	191
NYSTATIN 100,000 UNIT/ML SUSP	190
PREDNISOLONE 15 MG/5 ML SOLN	187
IBUPROFEN 100 MG/5 ML SUSP	165
VITAMIN D3 10 MCG/ML DROP	140
AMOXICILLIN 250 MG/5 ML SUSP	131
3rd Quarter 2018	**4140**
RANITIDINE 15 MG/ML SYRUP	289
AMOXICILLIN 400 MG/5 ML SUSP	249
NYSTATIN 100,000 UNIT/GM CREAM	186
NYSTATIN 100,000 UNIT/ML SUSP	181
VITAMIN D3 10 MCG/ML DROP	159
CHILD PAIN-FEVER 160 MG/5 ML	156
ALBUTEROL SUL 2.5 MG/3 ML SOLN	141
IBUPROFEN 100 MG/5 ML SUSP	132
HYDROCORTISONE 2.5% CREAM	123
MUPIROCIN 2% OINTMENT	105
Grand Total	**22035**

Opioids: Members Ages 10 to 18 Years of Age

Drug Name	Count of Claims
1st Quarter 2018	**14**
OXYCODONE HCL 5 MG TABLET	11
HYDROMORPHONE 2 MG TABLET	2
OXYCODONE HCL 15 MG TABLET	1
2nd Quarter 2018	**19**
OXYCODONE HCL 5 MG TABLET	14
HYDROMORPHONE 2 MG TABLET	2
MORPHINE SULFATE IR 15 MG TAB	1
CODEINE SULFATE 30 MG TABLET	1
MORPHINE SULF ER 15 MG TABLET	1
3rd Quarter 2018	**19**
OXYCODONE HCL 5 MG TABLET	19
4th Quarter 2018	**8**
OXYCODONE HCL 5 MG TABLET	7
OXYCODONE HCL 5 MG CAPSULE	1
Grand Total	**60**

Opioids: Members Ages 5 to 9 Years of Age

Drug	Count of Claims
2nd Quarter 2018	**2**
OXYCODONE HCL 5 MG TABLET	2
3rd Quarter 2018	**2**
OXYCODONE HCL 5 MG TABLET	1
OXYCODONE HCL 5 MG/5 ML SOLN	1
Grand Total	**4**

Opioids: Members Ages 1 to 4 Years of Age

Drug	Count of Claims
2nd Quarter 2018	**1**
OXYCODONE HCL 5 MG/5 ML SOLN	1
Grand Total	**1**

Opioids: Members Ages < 1 Year of Age

Drug	Count of Claims
2nd Quarter 2018	**1**
METHADONE 10 MG/5 ML SOLUTION	1
4th Quarter 2018	**2**
MORPHINE SULF 10 MG/5 ML SOLN	2
Grand Total	**3**

Psychotropic Agents: Members Ages 10 to 18 Years of Age

Drug Name	Count of Claims
1st Quarter 2018	**3027**
CLONIDINE HCL 0.1 MG TABLET	136
DEXTROAMP-AMPHET ER 20 MG CAP	105
GUANFACINE 1 MG TABLET	83
DEXTROAMP-AMPHET ER 15 MG CAP	82
METHYLPHENIDATE ER 36 MG TAB	79
DEXTROAMP-AMPHETAMIN 10 MG TAB	78
ARIPIPRAZOLE 10 MG TABLET	74
ARIPIPRAZOLE 5 MG TABLET	71
TRAZODONE 50 MG TABLET	71
RISPERIDONE 0.5 MG TABLET	64
2nd Quarter 2018	**2945**
CLONIDINE HCL 0.1 MG TABLET	147
DEXTROAMP-AMPHET ER 20 MG CAP	94
ARIPIPRAZOLE 5 MG TABLET	93
TRAZODONE 50 MG TABLET	85
GUANFACINE 1 MG TABLET	78
DEXTROAMP-AMPHETAMIN 10 MG TAB	68
ARIPIPRAZOLE 10 MG TABLET	64
DEXTROAMP-AMPHET ER 15 MG CAP	63
RISPERIDONE 0.5 MG TABLET	60
METHYLPHENIDATE ER 54 MG TAB	58
3rd Quarter 2018	**3228**
CLONIDINE HCL 0.1 MG TABLET	137
TRAZODONE 50 MG TABLET	117
DEXTROAMP-AMPHET ER 20 MG CAP	100
GUANFACINE 1 MG TABLET	90
ARIPIPRAZOLE 5 MG TABLET	84
METHYLPHENIDATE ER 36 MG TAB	72
ARIPIPRAZOLE 10 MG TABLET	70
DEXTROAMP-AMPHET ER 15 MG CAP	66
OXCARBAZEPINE 300 MG TABLET	62
DEXTROAMP-AMPHETAMIN 10 MG TAB	61
4th Quarter 2018	**3265**
CLONIDINE HCL 0.1 MG TABLET	139
TRAZODONE 50 MG TABLET	118
DEXTROAMP-AMPHET ER 20 MG CAP	95
METHYLPHENIDATE ER 36 MG TAB	85
GUANFACINE 1 MG TABLET	79
ARIPIPRAZOLE 5 MG TABLET	78
DEXTROAMP-AMPHETAMIN 10 MG TAB	70
DEXTROAMP-AMPHET ER 10 MG CAP	69
CLONIDINE HCL 0.2 MG TABLET	63
DEXTROAMP-AMPHET ER 15 MG CAP	60
Grand Total	**12465**

Psychotropic Agents: Members Ages 5 to 9 Years of Age

Drug Name	Count of Claims
1st Quarter 2018	**1552**
CLONIDINE HCL 0.1 MG TABLET	156
GUANFACINE 1 MG TABLET	91
DEXTROAMP-AMPHET ER 10 MG CAP	90
DEXTROAMP-AMPHETAMINE 5 MG TAB	87
METHYLPHENIDATE 10 MG TABLET	62
LEVETIRACETAM 100 MG/ML SOLN	61
METHYLPHENIDATE 5 MG TABLET	58
METHYLPHENIDATE ER 27 MG TAB	49
RISPERIDONE 0.5 MG TABLET	47
DEXTROAMP-AMPHET ER 15 MG CAP	47
2nd Quarter 2018	**1375**
CLONIDINE HCL 0.1 MG TABLET	123
GUANFACINE 1 MG TABLET	80
LEVETIRACETAM 100 MG/ML SOLN	72
DEXTROAMP-AMPHET ER 10 MG CAP	69
DEXTROAMP-AMPHETAMINE 5 MG TAB	61
METHYLPHENIDATE 5 MG TABLET	55
METHYLPHENIDATE ER 27 MG TAB	47
METHYLPHENIDATE 10 MG TABLET	47
RISPERIDONE 0.5 MG TABLET	42
DEXTROAMP-AMPHETAMIN 10 MG TAB	41
3rd Quarter 2018	**1511**
CLONIDINE HCL 0.1 MG TABLET	160
GUANFACINE 1 MG TABLET	81
LEVETIRACETAM 100 MG/ML SOLN	71
DEXTROAMP-AMPHETAMINE 5 MG TAB	62
DEXTROAMP-AMPHET ER 10 MG CAP	56
METHYLPHENIDATE 10 MG TABLET	50
RISPERIDONE 0.5 MG TABLET	50
METHYLPHENIDATE ER 27 MG TAB	48
METHYLPHENIDATE 5 MG TABLET	44
DEXTROAMP-AMPHETAMIN 10 MG TAB	41
4th Quarter 2018	**1737**
CLONIDINE HCL 0.1 MG TABLET	172
GUANFACINE 1 MG TABLET	112
LEVETIRACETAM 100 MG/ML SOLN	75
DEXTROAMP-AMPHETAMINE 5 MG TAB	71
RISPERIDONE 0.5 MG TABLET	66
DEXTROAMP-AMPHET ER 10 MG CAP	65
RISPERIDONE 0.25 MG TABLET	54
METHYLPHENIDATE 10 MG TABLET	53
METHYLPHENIDATE ER 18 MG TAB	50
METHYLPHENIDATE 5 MG TABLET	47
Grand Total	**6175**

Psychotropic Agents: Members Ages 1 to 4 Years of Age

Drug Name	Count of Claims
1st Quarter 2018	**154**
LEVETIRACETAM 100 MG/ML SOLN	54
OXCARBAZEPINE 300 MG/5 ML SUSP	24
CLONIDINE HCL 0.1 MG TABLET	16
ONFI 2.5 MG/ML SUSPENSION	8
GUANFACINE 1 MG TABLET	6
TOPIRAMATE 15 MG SPRINKLE CAP	5
DIVALPROEX DR 125 MG CAP SPRNK	5
PHENOBARBITAL 32.4 MG TABLET	4
GABAPENTIN 250 MG/5 ML SOLN	4
ZONISAMIDE 100 MG CAPSULE	3
2nd Quarter 2018	**165**
LEVETIRACETAM 100 MG/ML SOLN	56
OXCARBAZEPINE 300 MG/5 ML SUSP	23
CLONIDINE HCL 0.1 MG TABLET	19
ONFI 2.5 MG/ML SUSPENSION	7
TOPIRAMATE 25 MG SPRINKLE CAP	7
DIVALPROEX DR 125 MG CAP SPRNK	6
GUANFACINE 1 MG TABLET	6
GABAPENTIN 250 MG/5 ML SOLN	5
DIAZEPAM 10 MG RECTAL GEL SYST	4
PHENOBARBITAL 32.4 MG TABLET	4
3rd Quarter 2018	**165**
LEVETIRACETAM 100 MG/ML SOLN	54
CLONIDINE HCL 0.1 MG TABLET	28
OXCARBAZEPINE 300 MG/5 ML SUSP	22
ONFI 2.5 MG/ML SUSPENSION	7
DIAZEPAM 10 MG RECTAL GEL SYST	7
PHENOBARBITAL 20 MG/5 ML ELIX	7
PHENOBARBITAL 32.4 MG TABLET	5
DIAZEPAM 2.5 MG RECTAL GEL SYS	5
DEXTROAMP-AMPHETAMINE 5 MG TAB	4
DIVALPROEX DR 125 MG CAP SPRNK	4
4th Quarter 2018	**153**
LEVETIRACETAM 100 MG/ML SOLN	53
OXCARBAZEPINE 300 MG/5 ML SUSP	15
CLONIDINE HCL 0.1 MG TABLET	12
TOPIRAMATE 15 MG SPRINKLE CAP	7
GUANFACINE 1 MG TABLET	6
VIGADRONE 500 MG POWDER PACKET	6
RISPERIDONE 1 MG/ML SOLUTION	5
DIAZEPAM 5 MG/5 ML SOLUTION	5
CLOBAZAM 2.5 MG/ML SUSPENSION	5
DIAZEPAM 10 MG RECTAL GEL SYST	5
Grand Total	**637**

Psychotropic Agents: Members Age < 1 Year of Age

Drug Name	Count of Claims
1st Quarter 2018	**30**
LEVETIRACETAM 100 MG/ML SOLN	15
PHENOBARBITAL 20 MG/5 ML SOLN	4
TOPIRAMATE 25 MG TABLET	3
PHENOBARBITAL 20 MG/5 ML ELIX	3
PHENOBARBITAL 16.2 MG TABLET	2
TOPIRAMATE 25 MG SPRINKLE CAP	2
LORAZEPAM INTENSOL 2 MG/ML	1
2nd Quarter 2018	**31**
LEVETIRACETAM 100 MG/ML SOLN	12
PHENOBARBITAL 20 MG/5 ML ELIX	7
TOPIRAMATE 15 MG SPRINKLE CAP	4
PHENOBARBITAL 20 MG/5 ML SOLN	3
TOPIRAMATE 25 MG TABLET	2
DIAZEPAM 5 MG/5 ML SOLUTION	2
PHENOBARBITAL 16.2 MG TABLET	1
3rd Quarter 2018	**40**
PHENOBARBITAL 20 MG/5 ML ELIX	18
LEVETIRACETAM 100 MG/ML SOLN	8
TOPIRAMATE 15 MG SPRINKLE CAP	6
PHENOBARBITAL 20 MG/5 ML SOLN	5
PHENOBARBITAL 16.2 MG TABLET	2
VIGADRONE 500 MG POWDER PACKET	1
4th Quarter 2018	**28**
PHENOBARBITAL 20 MG/5 ML ELIX	15
LEVETIRACETAM 100 MG/ML SOLN	8
PHENOBARBITAL 20 MG/5 ML SOLN	4
PHENOBARBITAL 16.2 MG TABLET	1
Grand Total	**129**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

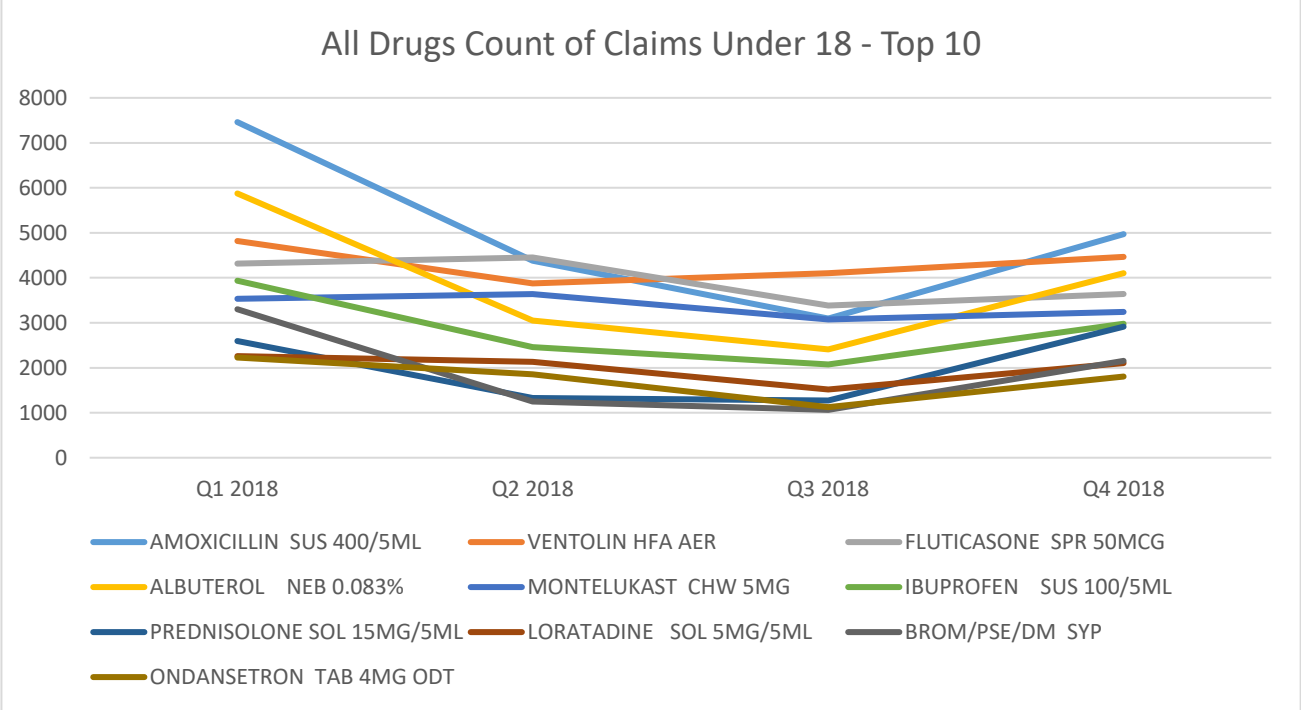
January 1, 2018 - December 31, 2018
Health Plan of Nevada

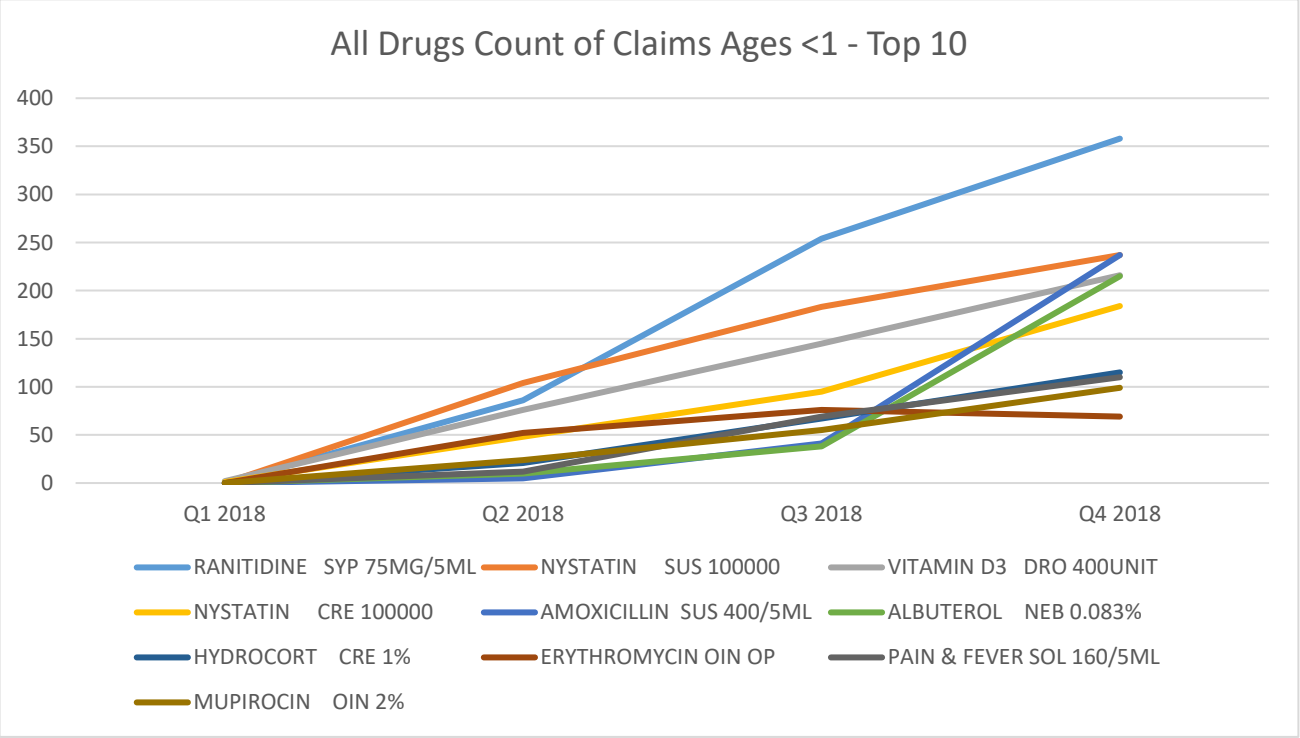
Drug Name	<1	1 - 4 Yrs	5 - 9 Yrs	10 - 17 Yrs	Total
All Drugs Under 18 Count of Claims - Top 35					
AMOXICILLIN SUS 400/5ML	283	9,731	7,453	2,438	19,905
VENTOLIN HFA AER	8	1,185	5,304	10,759	17,256
FLUTICASONE SPR 50MCG	4	1,274	5,967	8,544	15,789
ALBUTEROL NEB 0.083%	263	6,064	5,444	3,662	15,433
MONTELUKAST CHW 5MG	0	34	5,432	8,018	13,484
IBUPROFEN SUS 100/5ML	76	5,175	4,285	1,907	11,443
PREDNISOLONE SOL 15MG/5ML	163	3,998	3,137	805	8,103
LORATADINE SOL 5MG/5ML	25	3,075	3,837	1,073	8,010
BROM/PSE/DM SYP	1	1,619	3,468	2,684	7,772
ONDANSETRON TAB 4MG ODT	31	2,454	2,291	2,232	7,008
LORATADINE TAB 10MG	0	8	815	6,032	6,855
POLYETH GLYC POW 3350 NF	12	1,905	2,299	2,226	6,442
AMOXICILLIN SUS 250/5ML	74	2,741	2,551	935	6,301
CETIRIZINE SOL 1MG/ML	51	2,467	2,219	576	5,313
MONTELUKAST CHW 4MG	2	1,917	2,957	108	4,984
AZITHROMYCIN SUS 200/5ML	26	1,609	2,469	858	4,962
CEFDINIR SUS 250/5ML	20	2,063	2,099	693	4,875
MUPIROCIN OIN 2%	178	2,007	1,245	1,166	4,596
CETIRIZINE TAB 10MG	0	4	562	3,776	4,342
TRIAMCINOLON CRE 0.1%	72	1,330	1,095	1,286	3,783
OSELTAMIVIR SUS 6MG/ML	59	1,767	1,505	327	3,658
CEPHALEXIN SUS 250/5ML	37	1,217	1,436	496	3,186
POLYMYXIN B/ SOL TRIMETHP	77	1,536	1,008	551	3,172
PREDNISOLONE SYP 15MG/5ML	13	1,547	1,095	360	3,015
AMOXICILLIN CAP 500MG	0	0	149	2,739	2,888
RANITIDINE SYP 75MG/5ML	698	1,328	559	295	2,880
TRIAMCINOLON OIN 0.1%	78	1,113	860	779	2,830
NYSTATIN CRE 100000	328	2,039	281	133	2,781
PROMETHAZINE SYP DM	0	324	1,083	1,273	2,680
HYDROCORT CRE 2.5%	148	1,263	597	603	2,611
AMOX/K CLAV SUS 400/5ML	15	971	1,017	487	2,490
CETIRIZINE SOL 5MG/5ML	17	1,048	1,114	284	2,463
MONTELUKAST TAB 10MG	0	2	67	2,298	2,367
PREDNISONE TAB 20MG	0	10	264	1,907	2,181
CETIRIZINE SYP 1MG/ML	0	924	988	249	2,161
Grand Total	**2,759**	**65,749**	**76,952**	**72,559**	**218,019**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

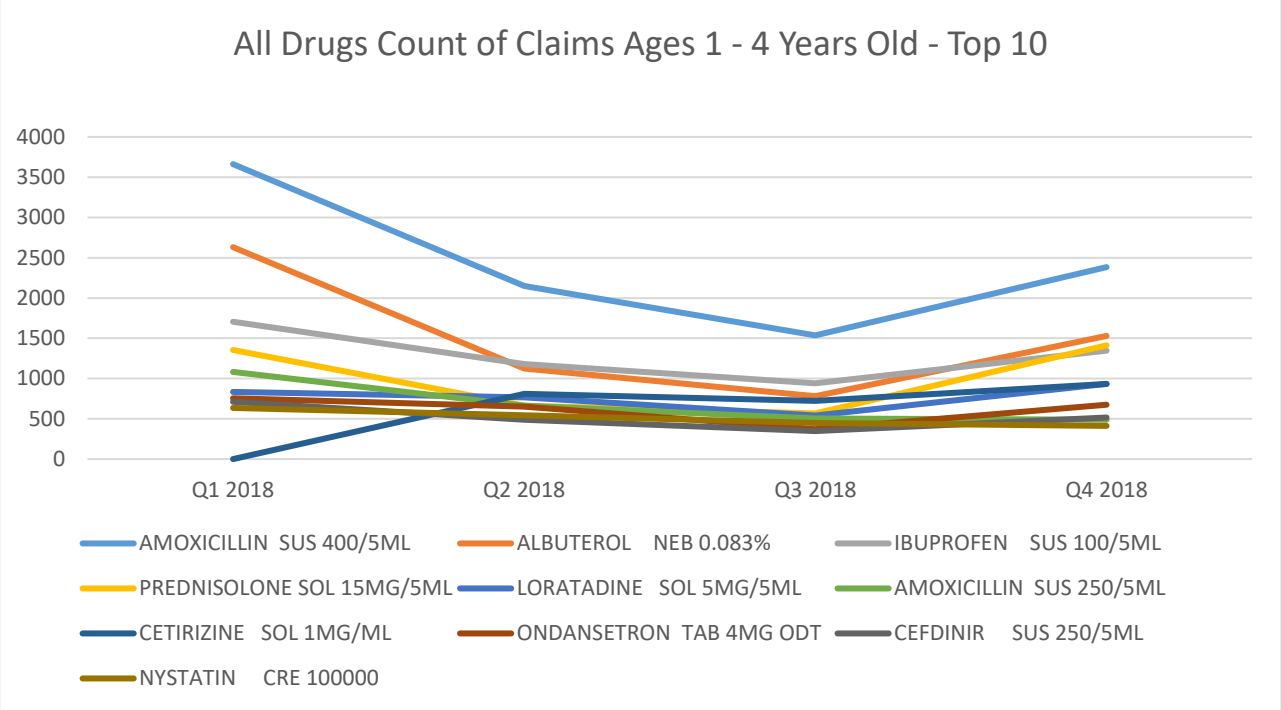


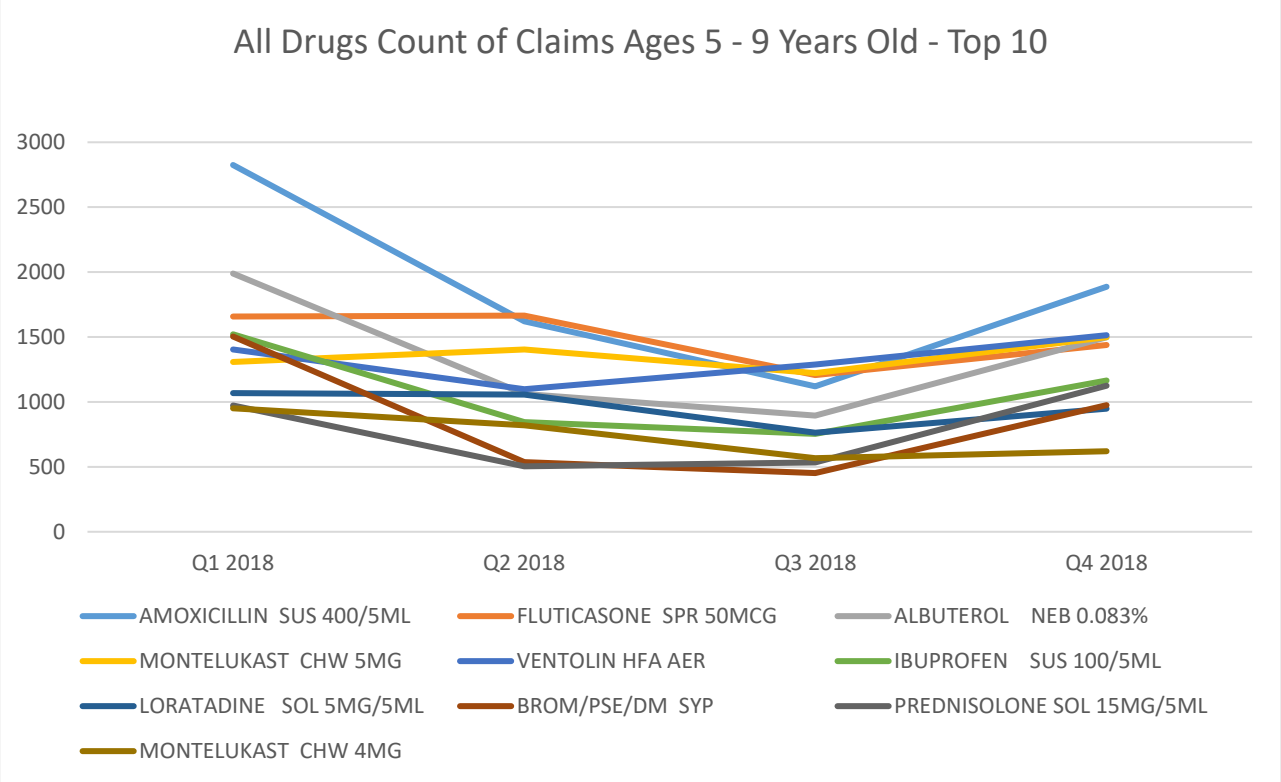


HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

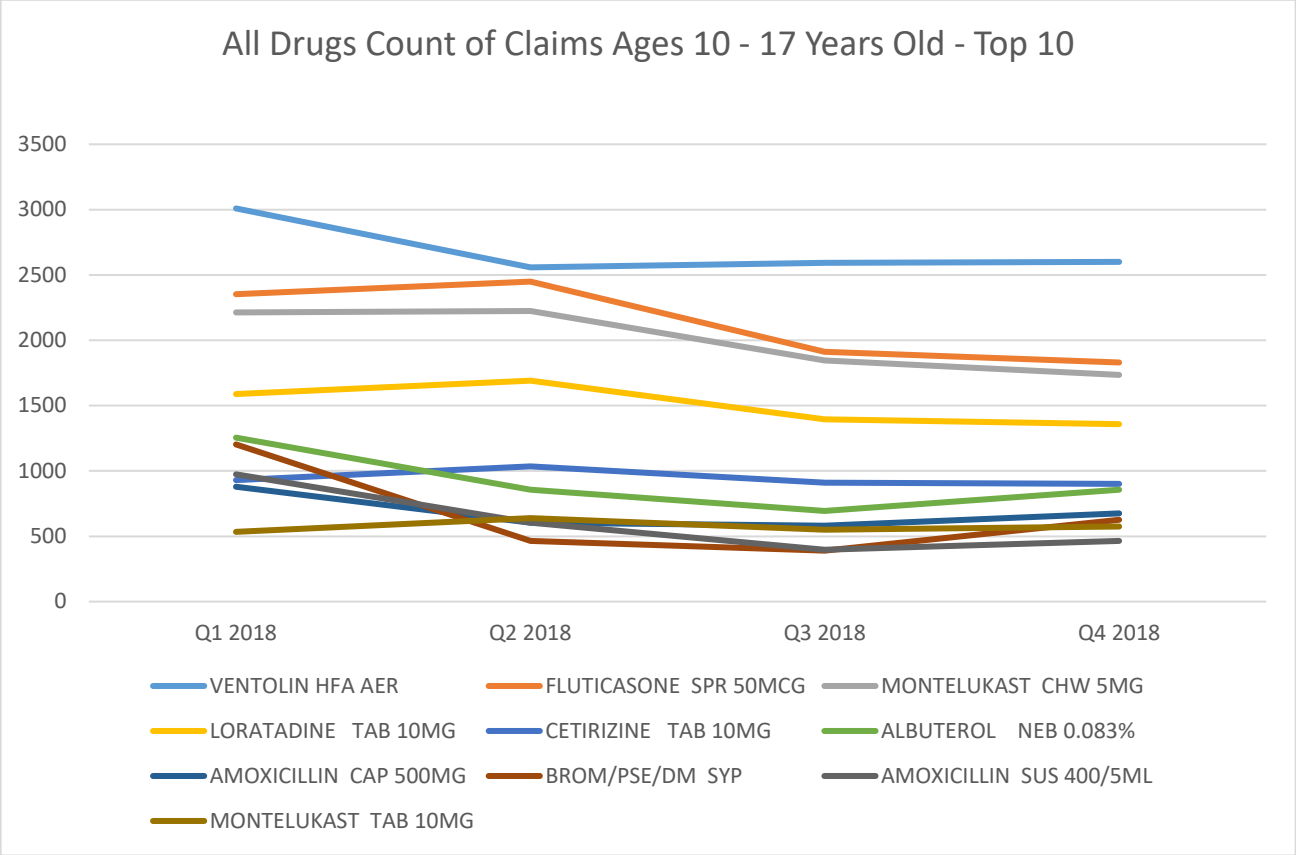




HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

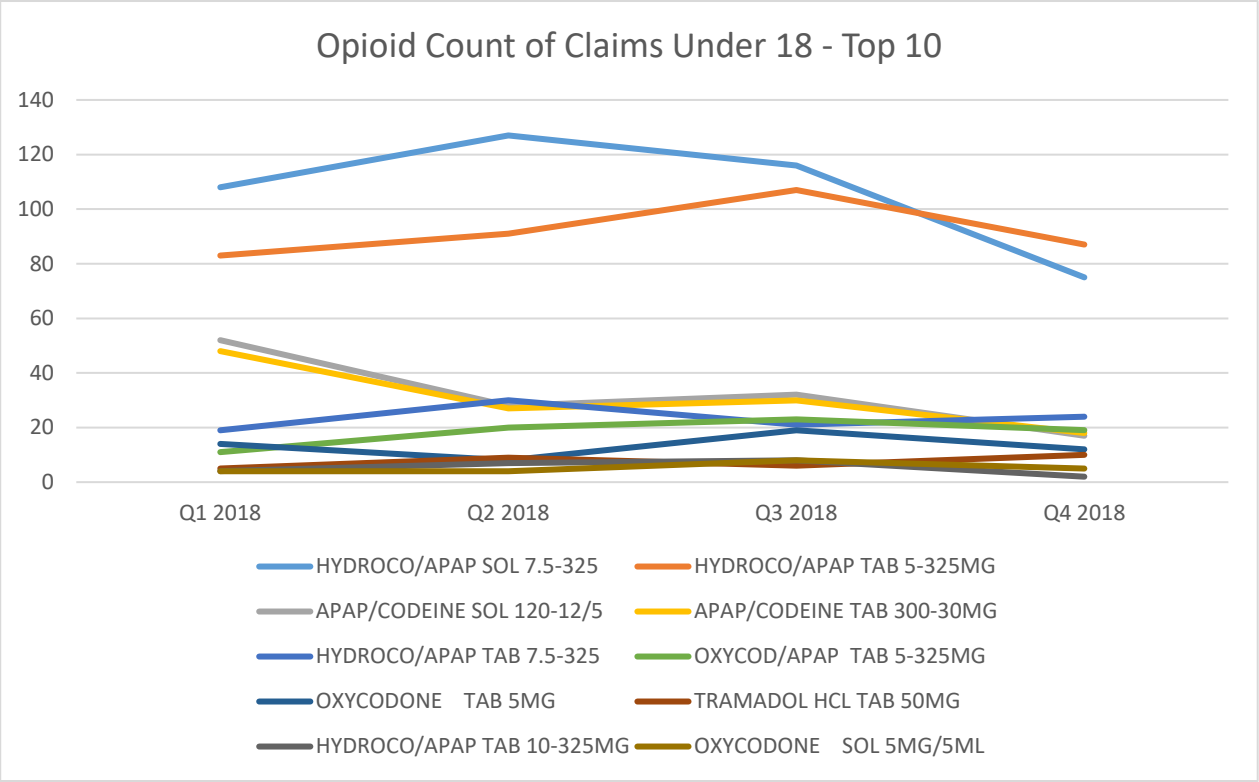
Drug Name	<1	1 - 4 Yrs	5 - 9 Yrs	10 - 17 Yrs	Total
Opioid Under 18 Count of Claims					
HYDROCO/APAP SOL 7.5-325	1	106	180	139	426
HYDROCO/APAP TAB 5-325MG	0	0	11	357	368
APAP/CODEINE SOL 120-12/5	0	25	39	65	129
APAP/CODEINE TAB 300-30MG	0	0	0	123	123
HYDROCO/APAP TAB 7.5-325	1	0	0	93	94
OXYCOD/APAP TAB 5-325MG	0	0	4	69	73
OXYCODONE TAB 5MG	0	0	2	51	53
TRAMADOL HCL TAB 50MG	0	0	1	29	30
HYDROCO/APAP TAB 10-325MG	0	0	0	21	21
OXYCODONE SOL 5MG/5ML	0	10	8	3	21
VIRTUSSIN AC SOL 100-10/5	0	0	2	8	10
PROMETH/COD SYP 6.25-10	0	0	3	5	8
METHADONE SOL 5MG/5ML	4	4	0	0	8
ROBAFEN AC SOL 100-10/5	0	0	1	6	7
GG/CODEINE SOL 100-10/5	0	0	0	5	5
MORPHINE SUL TAB 15MG	0	0	1	4	5
OXYCOD/APAP TAB 7.5-325	0	0	0	4	4
MORPHINE SUL SOL 10MG/5ML	1	0	2	1	4
APAP/CODEINE TAB 300-15MG	0	0	1	2	3
PROMETH/PE/ SYP CODEINE	0	0	1	2	3
MORPHINE SUL TAB 15MG ER	0	0	0	3	3
OXYCOD/APAP TAB 10-325MG	0	0	0	3	3
PROMETH VC/ SYP CODEINE	0	0	0	2	2
LORTAB ELX 10-300MG	0	1	1	0	2
FENTANYL DIS 12MCG/HR	0	1	0	0	1
CODEINE SULF TAB 15MG	0	0	0	1	1
METHADONE SOL 10MG/5ML	1	0	0	0	1
ENDOCET TAB 5-325MG	0	0	0	1	1
MORPHINE SUL INJ 4MG/ML	0	0	0	1	1
LORCET TAB 5-325MG	0	0	0	1	1
APAP/CODEINE TAB 300-60MG	0	0	0	1	1
METHADOSE CON 10MG/ML	1	0	0	0	1
BUT/APAP/CAF CAP CODEINE	0	0	0	1	1
HYD POL/CPM SUS 10-8/5ML	0	0	0	1	1
OXYCONTIN TAB 10MG CR	0	0	0	1	1

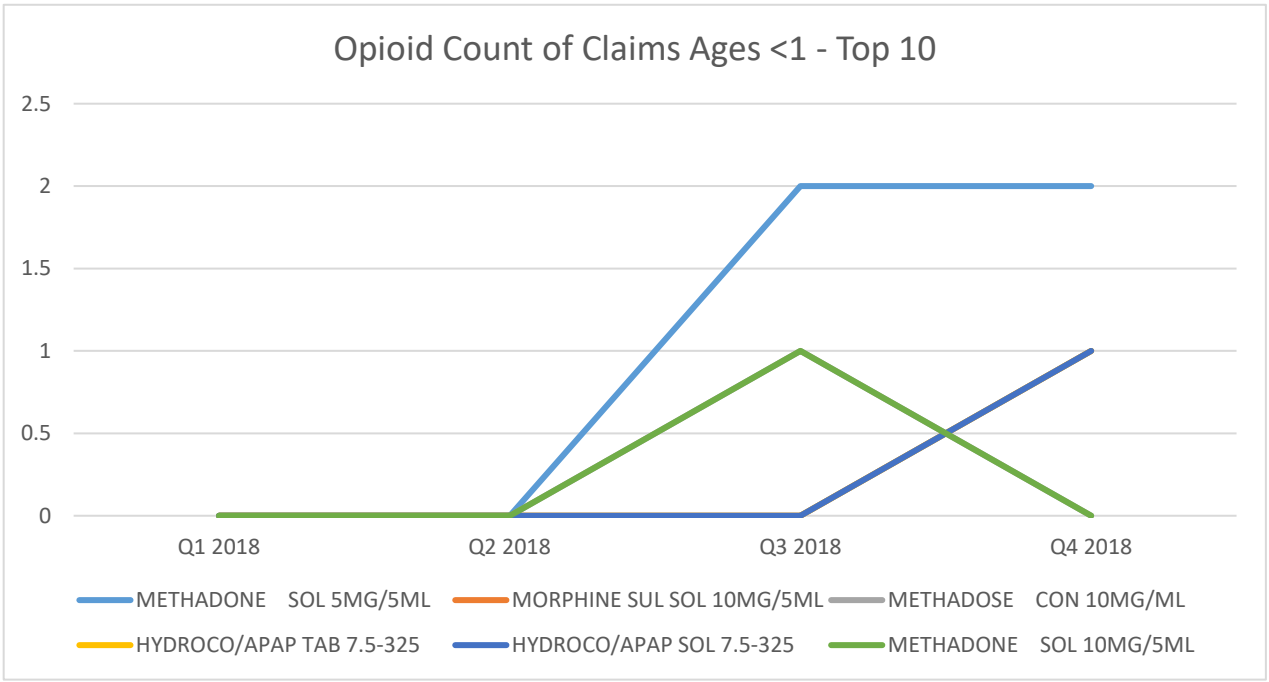
Grand Total	8	147	257	1,000	1,412

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

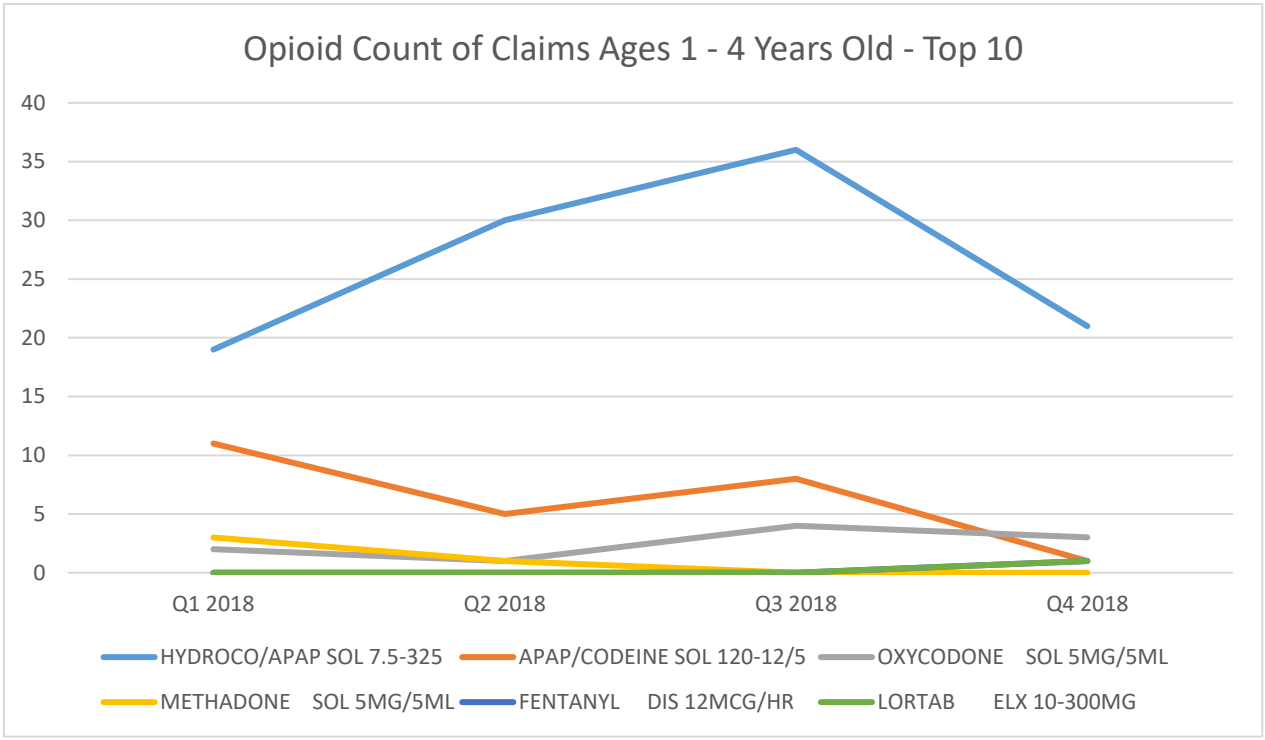


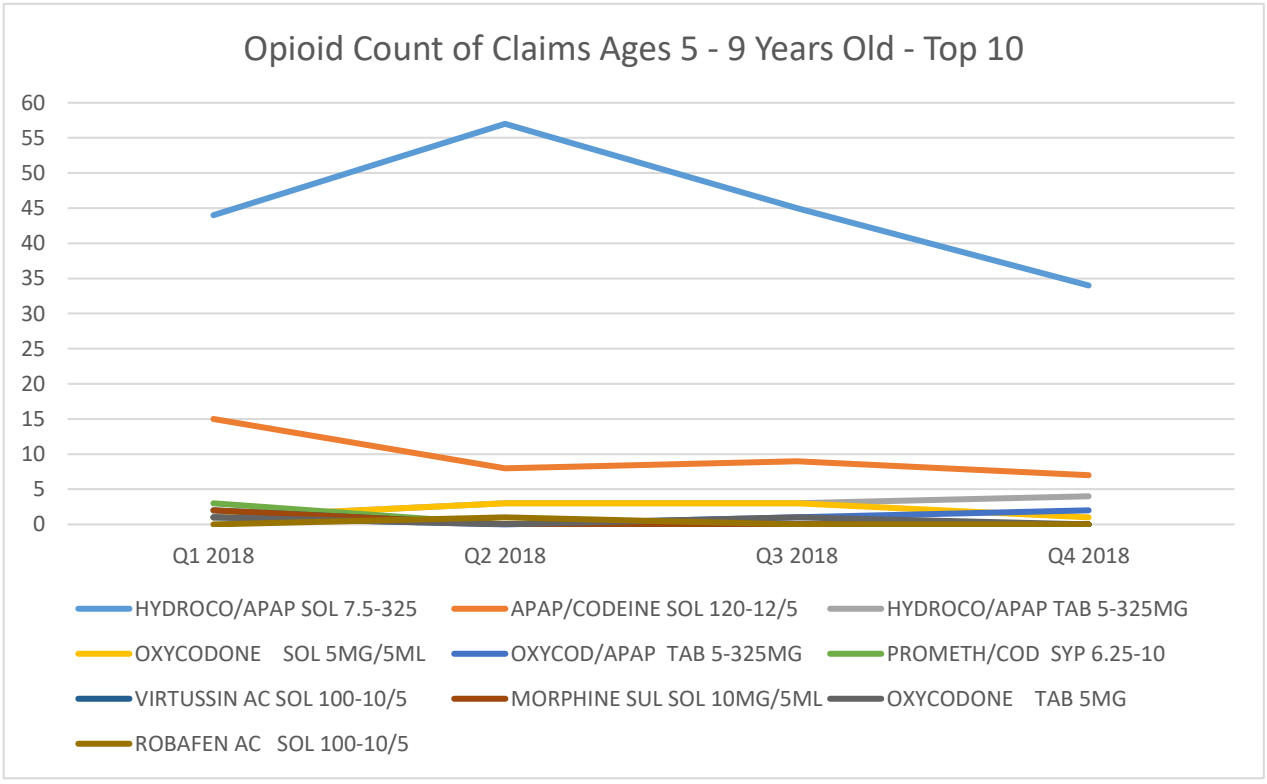


HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

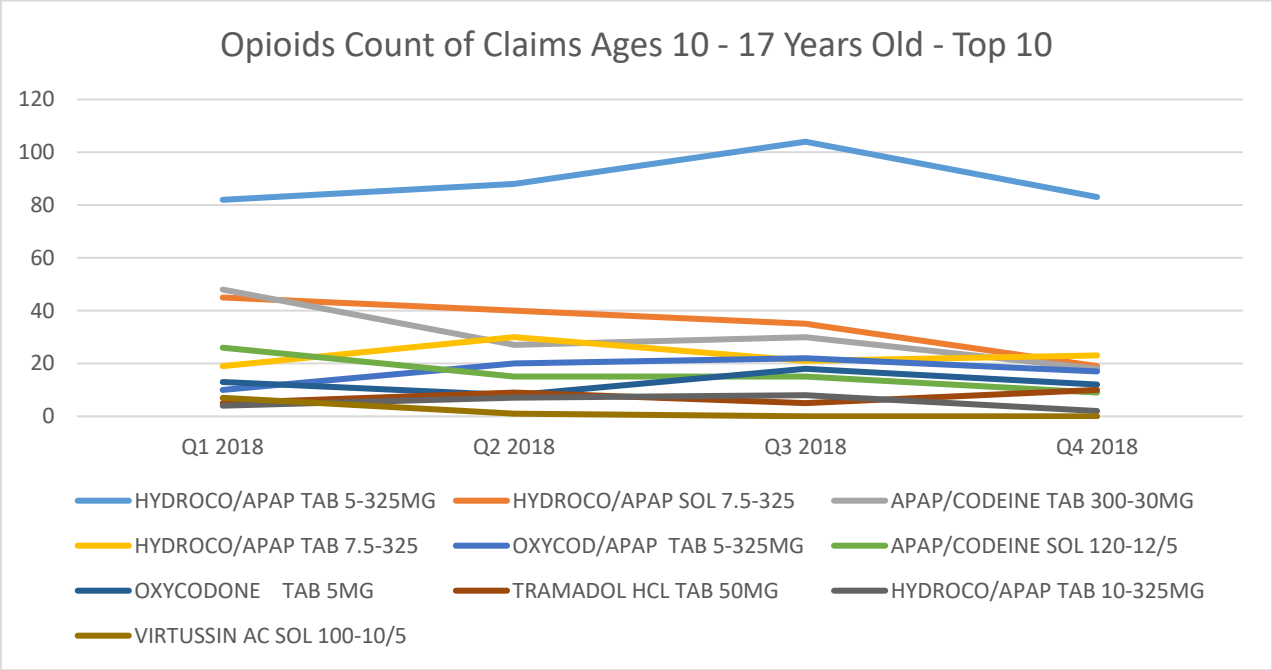




HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

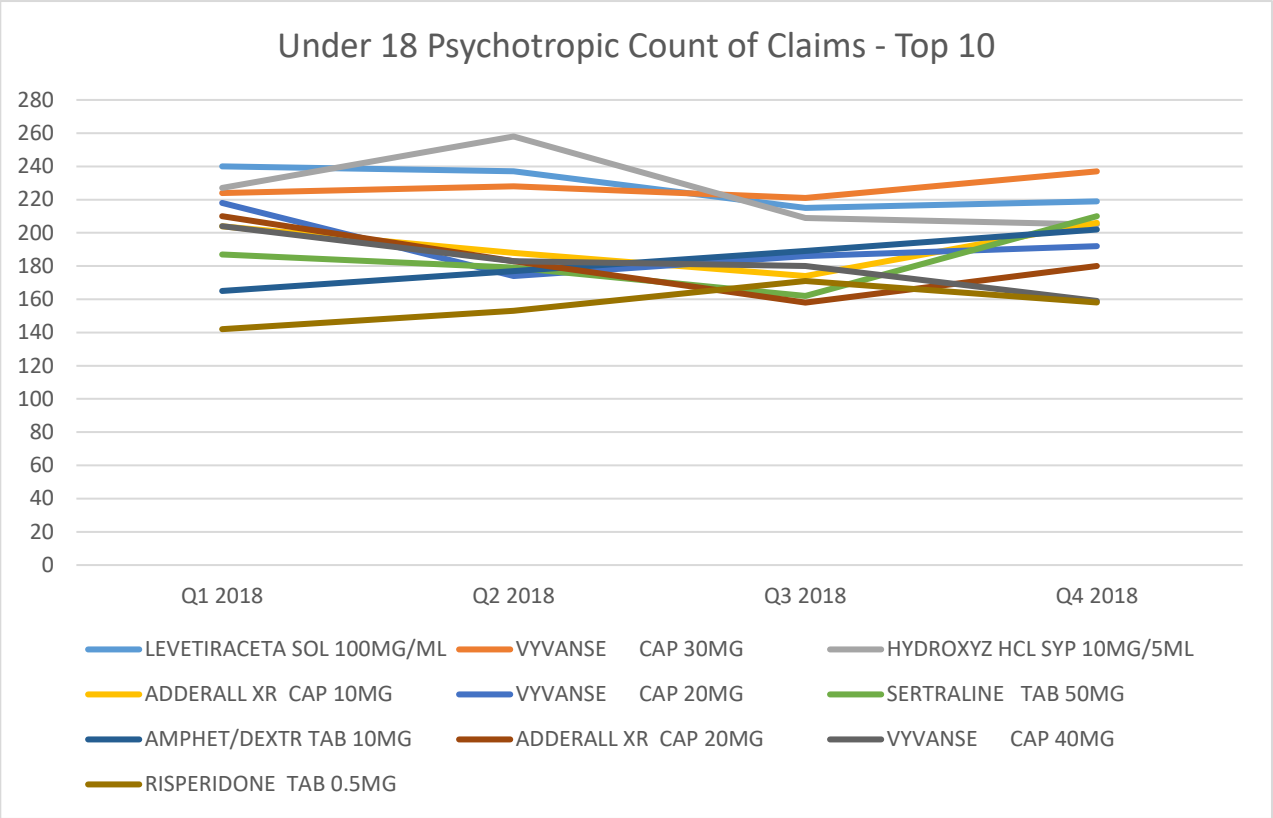
Drug Name	<1	1 - 4 Yrs	5 - 9 Yrs	10 - 17 Yrs	Total
Psychotropic Under 18 Count of Claims - Top 35					
LEVETIRACETA SOL 100MG/ML	14	339	374	184	911
VYVANSE CAP 30MG	0	0	260	650	910
HYDROXYZ HCL SYP 10MG/5ML	17	459	291	132	899
ADDERALL XR CAP 10MG	0	0	348	424	772
VYVANSE CAP 20MG	0	0	374	396	770
SERTRALINE TAB 50MG	0	0	19	719	738
AMPHET/DEXTR TAB 10MG	0	0	208	525	733
ADDERALL XR CAP 20MG	0	0	152	579	731
VYVANSE CAP 40MG	0	0	115	611	726
RISPERIDONE TAB 0.5MG	0	0	223	401	624
ADDERALL XR CAP 15MG	0	0	196	419	615
SERTRALINE TAB 25MG	0	0	40	554	594
AMPHET/DEXTR TAB 5MG	0	6	332	249	587
RISPERIDONE TAB 1MG	0	0	159	418	577
FLUOXETINE CAP 20MG	0	2	7	533	542
METHYLPHENID TAB 10MG	0	1	171	340	512
ADDERALL XR CAP 30MG	0	0	35	468	503
FLUOXETINE CAP 10MG	0	0	18	461	479
METHYLPHENID TAB 36MG ER	0	0	59	398	457
VYVANSE CAP 50MG	0	0	91	358	449
SERTRALINE TAB 100MG	0	0	11	437	448
METHYLPHENID TAB 5MG	0	3	221	219	443
TRAZODONE TAB 50MG	0	0	17	400	417
GUANFACINE TAB 2MG ER	0	0	137	238	375
METHYLPHENID TAB 27MG ER	0	0	129	243	372
HYDROXYZ HCL TAB 25MG	0	0	18	323	341
ESCITALOPRAM TAB 10MG	0	0	5	332	337
RISPERIDONE TAB 0.25MG	0	2	151	182	335
GUANFACINE TAB 3MG ER	0	0	41	249	290
AMPHET/DEXTR TAB 20MG	0	0	33	251	284
METHYLPHENID TAB 54MG ER	0	0	21	261	282
GUANFACINE TAB 1MG ER	0	0	148	119	267
ADDERALL XR CAP 25MG	0	0	29	237	266
OXCARBAZEPIN TAB 300MG	0	0	19	229	248
AMITRIPTYLIN TAB 25MG	0	0	0	244	244

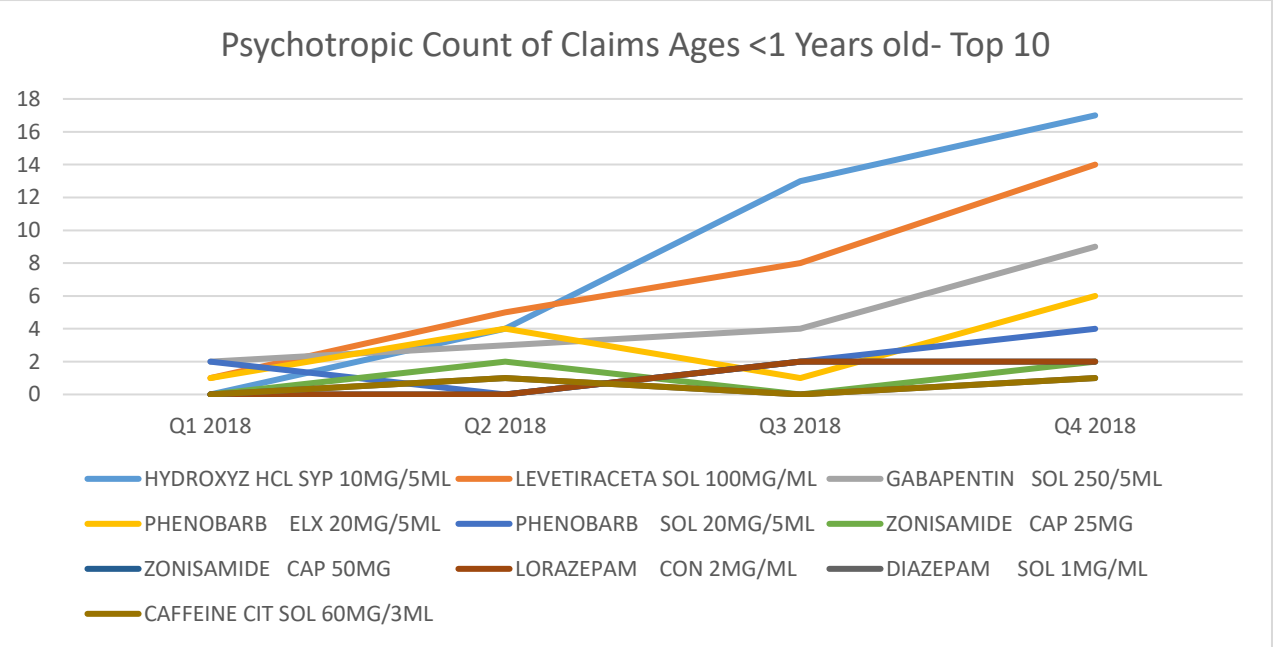
Grand Total	31	812	4,452	12,783	18,078

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

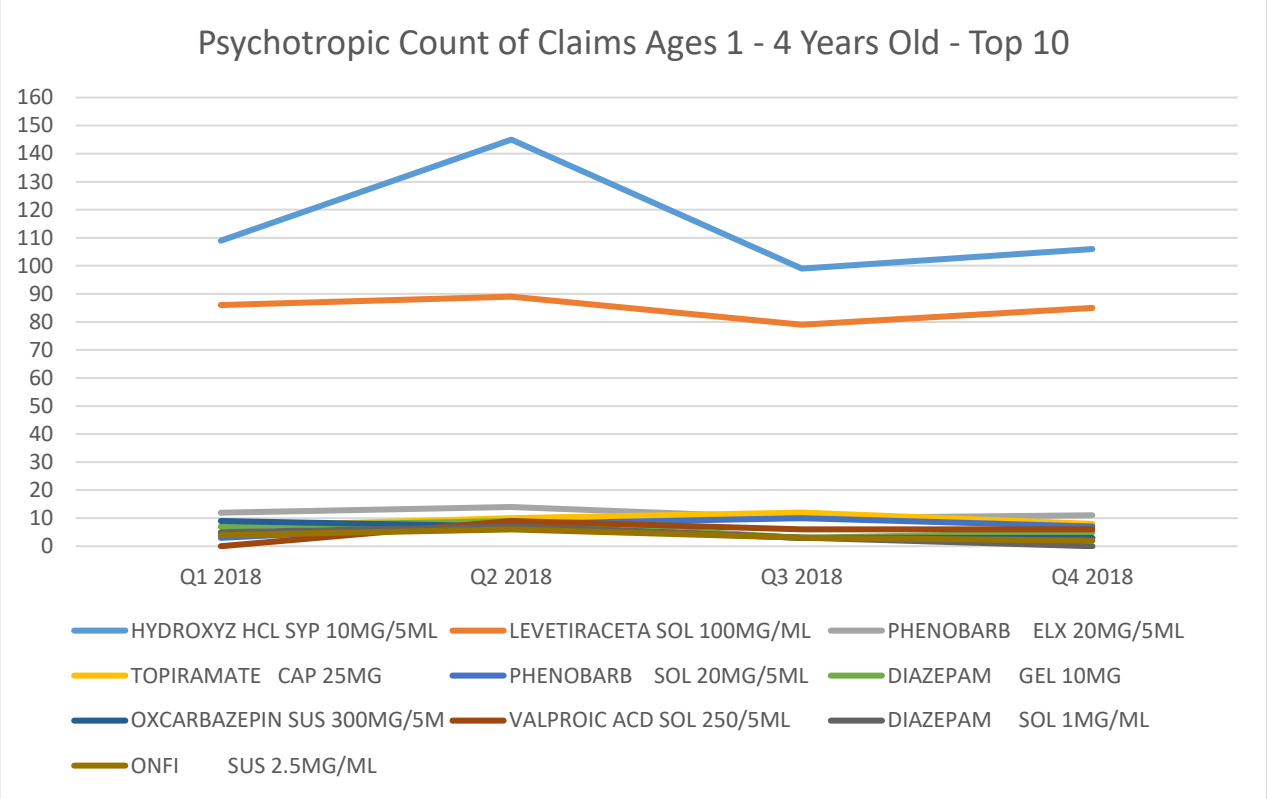


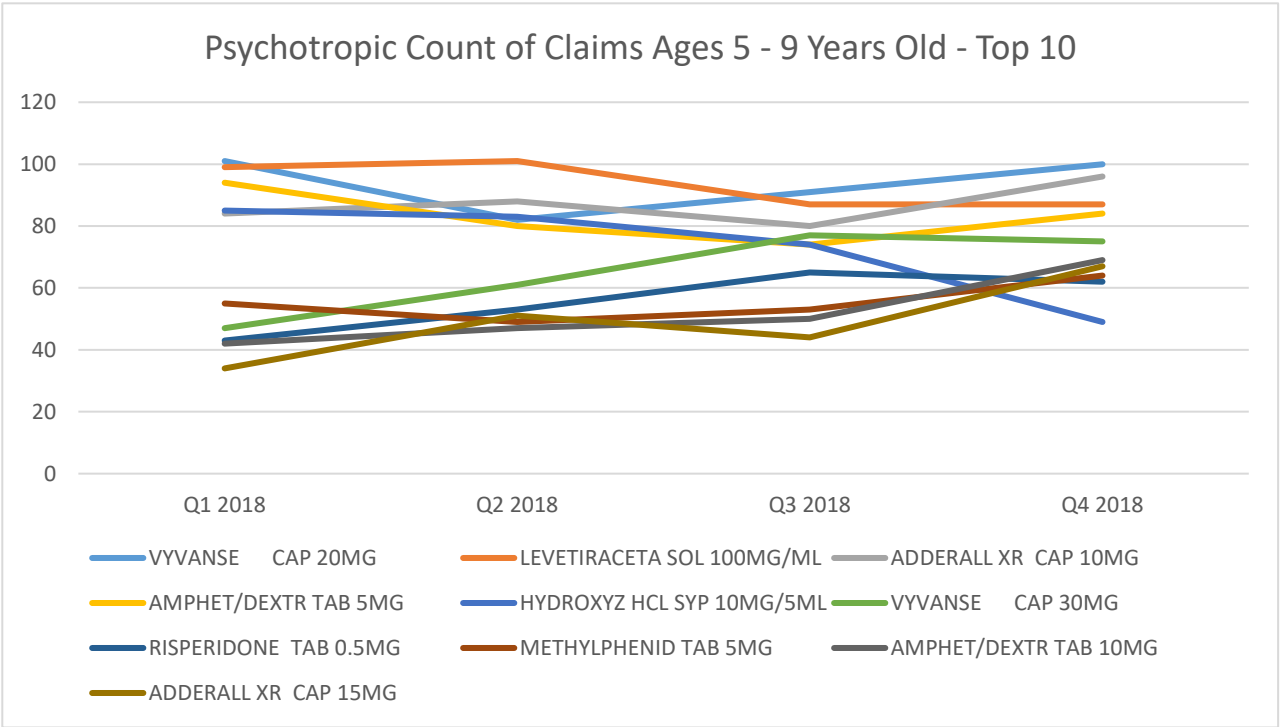


HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada

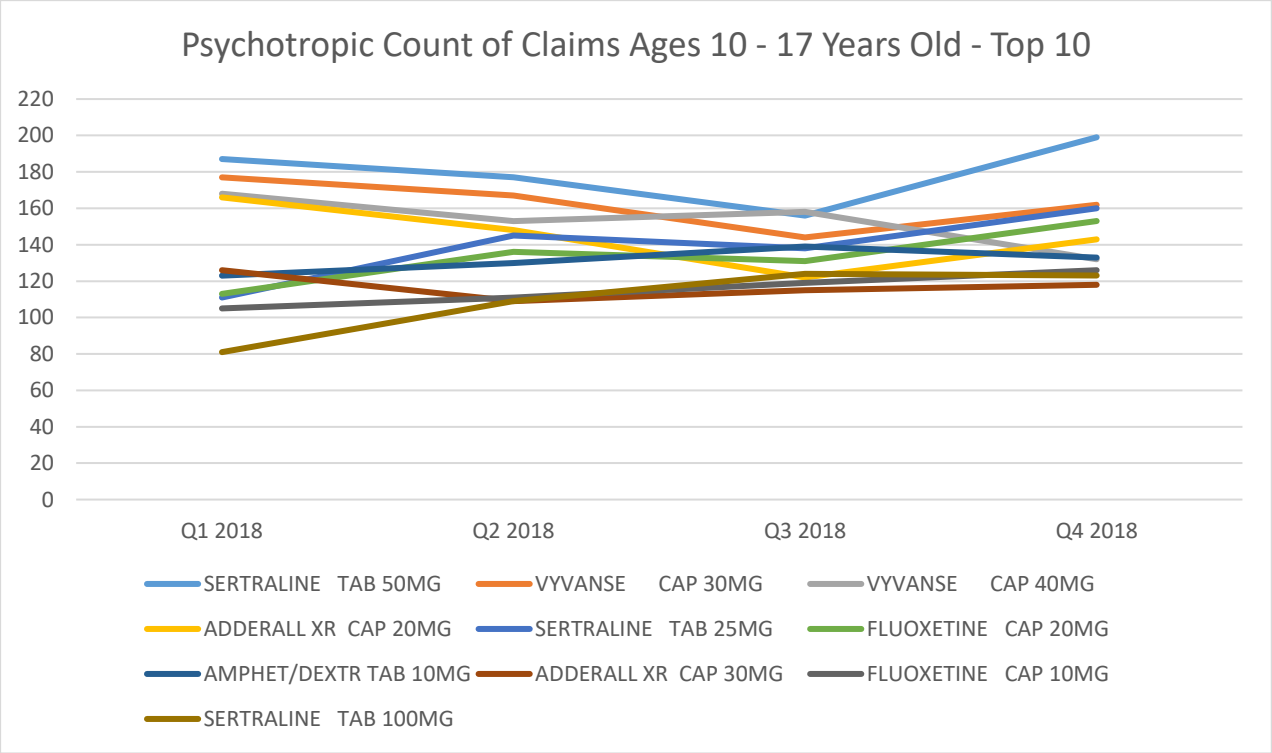




HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top Claims for Under 18 Years Old

January 1, 2018 - December 31, 2018
Health Plan of Nevada



Top 10 Claims Under 18

Summary of Utilization - Less Than 1

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
AMOXICILLIN SUS 400/5ML	213	225	2,249	40,275
ALBUTEROL NEB 0.083%	139	159	2,553	26,055
VENTOLIN HFA AER	125	151	3,037	2,718
BROM/PSE/DM SYP	126	137	1,036	16,836
FLUTICASONE SPR 50MCG	108	120	3,570	1,920
MONTELUKAST CHW 5MG	76	111	3,330	3,330
IBUPROFEN SUS 100/5ML	98	105	689	22,414
AMOXICILLIN SUS 250/5ML	91	95	867	18,000
AZITHROMYCIN SUS 200/5ML	87	90	436	2,108
OSELTAMIVIR SUS 6MG/ML	84	86	468	9,780
April 1, 2018 - June 30, 2018				
RANITIDINE SYP 75MG/5ML	71	96	2,757	5,836
NYSTATIN CRE 100000	71	77	1,105	2,145
AMOXICILLIN SUS 400/5ML	74	76	733	7,400
NYSTATIN SUS 100000	63	72	1,208	6,194
VITAMIN D3 DRO 400UNIT	57	72	2,149	3,633
HYDROCORT CRE 2.5%	49	60	750	1,728
ALBUTEROL NEB 0.083%	47	54	846	8,010
TRIAMCINOLON CRE 0.1%	30	36	481	1,474
MUPIROCIN OIN 2%	33	35	376	770
AMOXICILLIN SUS 250/5ML	35	35	368	3,880
July 1, 2018 - September 30, 2018				
RANITIDINE SYP 75MG/5ML	69	88	2,484	5,420
AMOXICILLIN SUS 400/5ML	65	69	697	7,175
NYSTATIN SUS 100000	52	60	786	4,856
VITAMIN D3 DRO 400UNIT	46	56	1,698	2,745
NYSTATIN CRE 100000	54	54	749	1,455
HYDROCORT CRE 2.5%	36	41	614	1,186
MUPIROCIN OIN 2%	36	40	328	880
IBUPROFEN SUS 100/5ML	33	35	316	4,549
ALBUTEROL NEB 0.083%	33	35	548	5,325
HYDROCORT OIN 2.5%	24	29	697	747
October 1, 2018 - December 31, 2018				
AMOXICILLIN SUS 400/5ML	121	128	1,253	11,955
ALBUTEROL NEB 0.083%	79	87	1,466	13,005
RANITIDINE SYP 75MG/5ML	56	80	2,263	5,562
PREDNISOLONE SOL 15MG/5ML	65	70	494	1,561
NYSTATIN CRE 100000	63	68	980	1,845
VITAMIN D3 DRO 400UNIT	47	67	2,018	3,273
IBUPROFEN SUS 100/5ML	51	57	481	7,953
HYDROCORT CRE 2.5%	39	47	661	1,366
MUPIROCIN OIN 2%	33	42	427	924
HYDROCORT OIN 2.5%	33	38	913	990

Top 10 Claims Under 18

Summary of Utilization - Members 1 to 4

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
AMOXICILLIN SUS 400/5ML	249	257	2,508	36,150
ALBUTEROL NEB 0.083%	158	174	2,485	26,625
IBUPROFEN SUS 100/5ML	123	131	950	21,456
AMOXICILLIN SUS 250/5ML	94	99	951	15,490
PREDNISOLONE SOL 15MG/5ML	76	83	406	2,806
OSELTAMIVIR SUS 6MG/ML	81	81	464	6,480
LORATADINE SOL 5MG/5ML	70	79	1,826	7,909
CEFDINIR SUS 250/5ML	75	78	866	4,840
BROM/PSE/DM SYP	62	64	569	6,057
ONDANSETRON TAB 4MG ODT	61	63	329	575
April 1, 2018 - June 30, 2018				
AMOXICILLIN SUS 400/5ML	195	204	2,012	27,115
ALBUTEROL NEB 0.083%	106	114	1,883	18,150
LORATADINE SOL 5MG/5ML	81	95	2,464	10,510
IBUPROFEN SUS 100/5ML	82	86	638	14,905
MONTELUKAST CHW 4MG	45	66	1,980	1,980
ONDANSETRON TAB 4MG ODT	65	66	389	566
AMOXICILLIN SUS 250/5ML	65	65	628	9,930
CETIRIZINE SOL 1MG/ML	52	61	1,657	5,535
PREDNISOLONE SOL 15MG/5ML	56	58	371	2,121
CEFDINIR SUS 250/5ML	54	56	578	3,520
July 1, 2018 - September 30, 2018				
AMOXICILLIN SUS 400/5ML	143	145	1,451	19,350
IBUPROFEN SUS 100/5ML	93	98	759	16,340
ALBUTEROL NEB 0.083%	75	81	1,328	12,405
PREDNISOLONE SOL 15MG/5ML	59	65	354	2,483
LORATADINE SOL 5MG/5ML	57	62	1,568	6,138
MONTELUKAST CHW 4MG	35	57	1,711	1,711
CETIRIZINE SOL 1MG/ML	42	49	1,303	4,118
AMOXICILLIN SUS 250/5ML	49	49	474	7,940
VENTOLIN HFA AER	37	44	960	792
MUPIROCIN OIN 2%	43	43	520	962
October 1, 2018 - December 31, 2018				
AMOXICILLIN SUS 400/5ML	261	279	2,770	38,645
ALBUTEROL NEB 0.083%	175	193	3,148	29,070
IBUPROFEN SUS 100/5ML	142	154	1,224	24,314
PREDNISOLONE SOL 15MG/5ML	133	146	813	5,435
LORATADINE SOL 5MG/5ML	104	126	3,202	13,420
ONDANSETRON TAB 4MG ODT	78	81	446	753
CETIRIZINE SOL 1MG/ML	61	72	1,848	5,553
VENTOLIN HFA AER	54	64	1,277	1,152
AZITHROMYCIN SUS 200/5ML	60	63	315	1,129
OSELTAMIVIR SUS 6MG/ML	61	61	358	5,160

Top 10 Claims Under 18

Summary of Utilization - Members 5 to 9

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
AMOXICILLIN SUS 400/5ML	213	225	2,249	40,275
ALBUTEROL NEB 0.083%	139	159	2,553	26,055
VENTOLIN HFA AER	125	151	3,037	2,718
BROM/PSE/DM SYP	126	137	1,036	16,836
FLUTICASONE SPR 50MCG	108	120	3,570	1,920
MONTELUKAST CHW 5MG	76	111	3,330	3,330
IBUPROFEN SUS 100/5ML	98	105	689	22,414
AMOXICILLIN SUS 250/5ML	91	95	867	18,000
AZITHROMYCIN SUS 200/5ML	87	90	436	2,108
OSELTAMIVIR SUS 6MG/ML	84	86	468	9,780
April 1, 2018 - June 30, 2018				
AMOXICILLIN SUS 400/5ML	147	152	1,465	27,440
VENTOLIN HFA AER	113	134	2,841	2,410
FLUTICASONE SPR 50MCG	102	120	3,615	1,919
ALBUTEROL NEB 0.083%	97	115	1,944	19,950
MONTELUKAST CHW 5MG	73	110	3,300	3,300
LORATADINE SOL 5MG/5ML	82	99	2,462	15,735
AMOXICILLIN SUS 250/5ML	88	92	849	17,980
IBUPROFEN SUS 100/5ML	71	74	435	14,383
ONDANSETRON TAB 4MG ODT	60	60	357	646
POLYETH GLYC POW 3350 NF	49	56	1,516	22,159
July 1, 2018 - September 30, 2018				
VENTOLIN HFA AER	140	163	3,273	2,934
AMOXICILLIN SUS 400/5ML	114	115	1,145	21,050
ALBUTEROL NEB 0.083%	90	108	1,782	17,385
MONTELUKAST CHW 5MG	66	95	2,850	2,850
IBUPROFEN SUS 100/5ML	84	88	566	18,021
FLUTICASONE SPR 50MCG	70	87	2,613	1,392
AMOXICILLIN SUS 250/5ML	67	70	637	13,040
LORATADINE SOL 5MG/5ML	50	59	1,470	9,110
AZITHROMYCIN SUS 200/5ML	51	55	264	1,275
BROM/PSE/DM SYP	52	54	377	7,079
October 1, 2018 - December 31, 2018				
VENTOLIN HFA AER	157	190	3,957	3,474
AMOXICILLIN SUS 400/5ML	180	186	1,800	32,650
ALBUTEROL NEB 0.083%	146	179	2,800	25,605
MONTELUKAST CHW 5MG	84	141	4,230	4,230
PREDNISOLONE SOL 15MG/5ML	110	123	619	6,480
AZITHROMYCIN SUS 200/5ML	100	103	507	2,438
FLUTICASONE SPR 50MCG	84	103	3,063	1,635
LORATADINE SOL 5MG/5ML	89	103	2,442	16,508
IBUPROFEN SUS 100/5ML	96	101	740	20,727
BROM/PSE/DM SYP	83	86	789	11,206

Top 10 Claims Under 18

Summary of Utilization - Members 10 to Under 18

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
VENTOLIN HFA AER	200	246	5,125	4,428
FLUTICASONE SPR 50MCG	154	182	5,461	2,905
LORATADINE TAB 10MG	117	152	4,266	4,289
AMOXICILLIN CAP 500MG	115	122	1,055	3,070
AZITHROMYCIN TAB 250MG	111	117	569	695
MONTELUKAST CHW 5MG	64	101	3,030	3,030
BROM/PSE/DM SYP	74	79	515	12,380
ALBUTEROL NEB 0.083%	69	76	1,122	11,640
MONTELUKAST TAB 10MG	45	66	1,980	1,965
ONDANSETRON TAB 4MG ODT	62	64	557	855
April 1, 2018 - June 30, 2018				
VENTOLIN HFA AER	206	265	5,312	4,770
FLUTICASONE SPR 50MCG	175	206	6,185	3,295
LORATADINE TAB 10MG	138	185	5,480	5,503
MONTELUKAST CHW 5MG	83	127	3,810	3,810
AMOXICILLIN CAP 500MG	89	97	899	2,517
MONTELUKAST TAB 10MG	61	94	2,804	2,804
AZITHROMYCIN TAB 250MG	77	79	382	470
ONDANSETRON TAB 4MG ODT	70	76	541	1,112
CETIRIZINE TAB 10MG	53	69	2,028	2,028
ALBUTEROL NEB 0.083%	55	63	1,110	10,485
July 1, 2018 - September 30, 2018				
VENTOLIN HFA AER	234	290	5,928	5,228
LORATADINE TAB 10MG	132	175	5,101	5,101
FLUTICASONE SPR 50MCG	126	156	4,646	2,495
AMOXICILLIN CAP 500MG	101	103	864	2,470
MONTELUKAST CHW 5MG	62	95	2,850	2,850
MONTELUKAST TAB 10MG	51	84	2,510	2,510
IBU TAB 600MG	78	80	741	2,436
CEPHALEXIN CAP 500MG	63	69	604	1,825
IBU TAB 800MG	61	66	680	2,136
AZITHROMYCIN TAB 250MG	63	63	312	376
October 1, 2018 - December 31, 2018				
VENTOLIN HFA AER	209	265	5,548	4,788
LORATADINE TAB 10MG	125	164	4,814	4,834
FLUTICASONE SPR 50MCG	123	149	4,429	2,378
AMOXICILLIN CAP 500MG	98	102	885	2,544
AZITHROMYCIN TAB 250MG	89	91	441	531
MONTELUKAST CHW 5MG	47	82	2,460	2,460
MONTELUKAST TAB 10MG	49	81	2,420	2,405
ONDANSETRON TAB 4MG ODT	70	75	663	1,052
IBU TAB 600MG	66	69	692	2,206
ALBUTEROL NEB 0.083%	58	65	1,227	11,505

Opioid Claims Under 18

Summary of Utilization - Members Less Than 1

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
APAP/CODEINE SOL 120-12/5	1	1	3	45
April 1, 2018 - June 30, 2018				
HYDROCO/APAP SOL 7.5-325	1	1	5	55
July 1, 2018 - September 30, 2018				
OXYCODONE SOL 5MG/5ML	1	1	5	15
October 1, 2018 - December 31, 2018				
No Data to report				

Opioid Claims Under 18

Summary of Utilization - Members 1 to 4 Years Old

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
OXYCODONE SOL 5MG/5ML	1	4	20	60
APAP/CODEINE SOL 120-12/5	4	4	28	225
HYDROCO/APAP SOL 7.5-325	2	2	13	90
April 1, 2018 - June 30, 2018				
HYDROCO/APAP SOL 7.5-325	3	3	20	340
APAP/CODEINE SOL 120-12/5	2	2	15	140
July 1, 2018 - September 30, 2018				
HYDROCO/APAP SOL 7.5-325	3	3	13	190
October 1, 2018 - December 31, 2018				
HYDROCO/APAP SOL 7.5-325	7	7	26	380
APAP/CODEINE SOL 120-12/5	1	1	10	150

Opioid Claims Under 18

Summary of Utilization - Members 5 to 9 Years Old

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
HYDROCO/APAP SOL 7.5-325	4	4	20	220
APAP/CODEINE SOL 120-12/5	3	3	17	350
April 1, 2018 - June 30, 2018				
APAP/CODEINE SOL 120-12/5	6	6	45	560
HYDROCO/APAP SOL 7.5-325	4	4	16	365
OXYCODONE SOL 5MG/5ML	1	1	5	60
OXYCODONE TAB 5MG	1	1	2	5
July 1, 2018 - September 30, 2018				
HYDROCO/APAP SOL 7.5-325	6	6	46	1290
October 1, 2018 - December 31, 2018				
HYDROCO/APAP SOL 7.5-325	6	6	40	790

Opioid Claims Under 18

Summary of Utilization - Members 10 to Under 18

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
HYDROCO/APAP TAB 5-325MG	30	33	166	660
APAP/CODEINE TAB 300-30MG	11	12	65	198
HYDROCO/APAP TAB 7.5-325	9	9	55	241
HYDROCO/APAP TAB 10-325MG	1	4	120	360
OXYCOD/APAP TAB 5-325MG	4	4	24	115
OXYCODONE TAB 5MG	3	3	16	80
APAP/CODEINE SOL 120-12/5	3	3	24	520
TRAMADOL HCL TAB 50MG	2	2	11	46
APAP/CODEINE TAB 300-60MG	1	1	6	28
APAP/CODEINE TAB 300-15MG	1	1	10	30

Opioid Claims Under 18

Summary of Utilization - Members 10 to Under 18

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
April 1, 2018 - June 30, 2018				
HYDROCO/APAP TAB 5-325MG	20	20	117	376
APAP/CODEINE TAB 300-30MG	8	9	45	171
HYDROCO/APAP SOL 7.5-325	5	7	39	1075
OXYCOD/APAP TAB 5-325MG	6	6	51	174
HYDROCO/APAP TAB 7.5-325	4	4	19	90
HYDROCO/APAP TAB 10-325MG	2	4	100	310
OXYCOD/APAP TAB 10-325MG	4	4	29	112
APAP/CODEINE SOL 120-12/5	1	1	5	100
MORPHINE SUL TAB 15MG ER	1	1	10	10
TRAMADOL HCL TAB 50MG	1	1	7	30
July 1, 2018 - September 30, 2018				
HYDROCO/APAP TAB 5-325MG	30	31	157	611
HYDROCO/APAP TAB 7.5-325	11	12	64	366
HYDROCO/APAP SOL 7.5-325	6	6	35	1510
OXYCODONE TAB 5MG	5	5	27	124
APAP/CODEINE TAB 300-30MG	4	4	22	63
OXYCOD/APAP TAB 5-325MG	3	3	14	47
OXYCOD/APAP TAB 7.5-325	1	3	74	192
TRAMADOL HCL TAB 50MG	3	3	17	87
HYDROCO/APAP TAB 10-325MG	2	2	10	40
OXYCODONE SOL 5MG/5ML	2	2	13	150
October 1, 2018 - December 31, 2018				
HYDROCO/APAP TAB 5-325MG	31	32	199	741
HYDROCO/APAP TAB 7.5-325	7	7	42	218
OXYCOD/APAP TAB 5-325MG	5	5	36	140
HYDROCO/APAP SOL 7.5-325	3	4	17	660
APAP/CODEINE TAB 300-30MG	4	4	16	60
SUBOXONE MIS 8-2MG	2	2	37	72
TRAMADOL HCL TAB 50MG	2	2	8	32
OXYCOD/APAP TAB 7.5-325	1	1	5	30
APAP/CODEINE SOL 120-12/5	1	1	3	50
HYDROCO/APAP TAB 10-325MG	1	1	4	15

Psychotropic Claims Under 18

Summary of Utilization - Members Less Than 1

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
LEVETIRACETA SOL 100MG/ML	2	4	75	87
PHENOBARB ELX 20MG/5ML	1	2	62	166
HYDROXYZ HCL SYP 10MG/5ML	1	1	30	150
April 1, 2018 - June 30, 2018				
HYDROXYZ HCL SYP 10MG/5ML	8	9	127	760
LEVETIRACETA SOL 100MG/ML	3	4	105	250
CAFFEINE CIT SOL 60MG/3ML	1	3	30	90
PHENOBARB SOL 20MG/5ML	2	2	60	960
PHENOBARB ELX 20MG/5ML	1	1	31	83
TOPIRAMATE TAB 100MG	1	1	14	90
DIAZEPAM SOL 5MG/5ML	1	1	30	240
July 1, 2018 - September 30, 2018				
HYDROXYZ HCL SYP 10MG/5ML	7	7	120	900
PHENOBARB ELX 20MG/5ML	2	3	90	945
PHENOBARB SOL 20MG/5ML	2	2	60	675
DIAZEPAM SOL 5MG/5ML	1	1	30	360
TOPIRAMATE CAP 15MG	1	1	30	120
LEVETIRACETA SOL 100MG/ML	1	1	33	108
TOPIRAMATE TAB 100MG	1	1	14	90
October 1, 2018 - December 31, 2018				
HYDROXYZ HCL SYP 10MG/5ML	6	9	78	855
PHENOBARB ELX 20MG/5ML	2	3	90	900
LEVETIRACETA SOL 100MG/ML	2	3	56	240

Psychotropic Claims Under 18

Summary of Utilization - Members 1 to 4

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
LEVETIRACETA SOL 100MG/ML	3	9	330	1785
HYDROXYZ HCL SYP 10MG/5ML	7	8	185	1224
TOPIRAMATE TAB 25MG	3	8	240	630
GUANFACINE TAB 1MG ER	1	2	60	60
AMPHET/DEXTR TAB 20MG	1	2	60	120
DIAZEPAM GEL 10MG	2	2	35	2
DIAZEPAM SOL 5MG/5ML	1	1	8	5
METHYLPHENID TAB 5MG	1	1	30	60
DIAZEPAM GEL 2.5MG	1	1	30	1
GABAPENTIN SOL 250/5ML	1	1	30	60
April 1, 2018 - June 30, 2018				
LEVETIRACETA SOL 100MG/ML	6	14	532	4177
HYDROXYZ HCL SYP 10MG/5ML	7	9	122	1030
TOPIRAMATE TAB 25MG	2	7	210	660
ONFI SUS 2.5MG/ML	2	6	165	960
IMIPRAM HCL TAB 10MG	1	3	90	90
GUANFACINE TAB 1MG ER	1	3	90	90
AMPHET/DEXTR TAB 20MG	1	2	60	120
DIAZEPAM SOL 5MG/5ML	1	2	60	470
TRAZODONE TAB 50MG	1	2	60	120
AMPHET/DEXTR TAB 30MG	1	1	30	60
July 1, 2018 - September 30, 2018				
LEVETIRACETA SOL 100MG/ML	7	16	557	4255
HYDROXYZ HCL SYP 10MG/5ML	11	11	204	1690
ONFI SUS 2.5MG/ML	2	5	129	720
TOPIRAMATE TAB 25MG	1	3	90	360
AMPHET/DEXTR TAB 30MG	1	3	90	180
IMIPRAM HCL TAB 10MG	1	2	60	90
DEXTROAMPHET CAP 5MG ER	1	1	30	30
CLONAZEPAM TAB 0.5MG	1	1	90	90
RISPERIDONE TAB 1MG	1	1	30	60
TOPIRAMATE CAP 25MG	1	1	30	240
October 1, 2018 - December 31, 2018				
LEVETIRACETA SOL 100MG/ML	8	15	443	2891
HYDROXYZ HCL SYP 10MG/5ML	12	15	311	2259
RISPERIDONE SOL 1MG/ML	2	6	136	180
TOPIRAMATE TAB 25MG	1	4	120	480
CLOBAZAM SUS 2.5MG/ML	1	3	64	360
IMIPRAM HCL TAB 25MG	1	2	60	60
ONFI SUS 2.5MG/ML	1	2	49	240
IMIPRAM HCL TAB 10MG	1	1	30	60
AMPHET/DEXTR CAP 10MG ER	1	1	30	30
METHYLPHENID TAB 5MG	1	1	30	30

Psychotropic Claims Under 18

Summary of Utilization - Members 5 to 9

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
METHYLPHENID TAB 5MG	10	17	487	667
METHYLPHENID TAB 10MG	9	13	367	652
AMPHET/DEXTR TAB 10MG	8	13	374	569
RISPERIDONE TAB 0.5MG	8	12	343	461
LEVETIRACETA SOL 100MG/ML	6	11	300	3133
METHYLPHENID TAB 36MG ER	6	11	291	291
METHYLPHENID TAB 18MG ER	9	11	330	330
AMPHET/DEXTR CAP 10MG ER	8	10	300	300
ARIPIPRAZOLE TAB 5MG	6	10	208	208
SERTRALINE TAB 25MG	5	10	300	285
April 1, 2018 - June 30, 2018				
METHYLPHENID TAB 36MG ER	11	23	690	690
HYDROXYZ HCL SYP 10MG/5ML	17	19	258	3350
AMPHET/DEXTR TAB 10MG	11	18	540	795
GUANFACINE TAB 1MG ER	10	16	437	437
AMPHET/DEXTR TAB 5MG	8	15	450	585
METHYLPHENID TAB 10MG	10	15	450	825
ARIPIPRAZOLE TAB 10MG	7	13	326	326
RISPERIDONE TAB 0.5MG	10	13	390	630
ARIPIPRAZOLE TAB 5MG	7	13	305	305
METHYLPHENID TAB 5MG	9	13	390	570
July 1, 2018 - September 30, 2018				
METHYLPHENID TAB 10MG	14	23	674	1236
RISPERIDONE TAB 0.5MG	9	18	524	944
METHYLPHENID TAB 36MG ER	8	17	510	510
LEVETIRACETA SOL 100MG/ML	8	16	460	4080
METHYLPHENID TAB 5MG	8	15	450	600
ARIPIPRAZOLE TAB 5MG	6	13	312	312
AMPHET/DEXTR CAP 15MG ER	7	13	372	372
GUANFACINE TAB 2MG ER	5	11	330	330
AMPHET/DEXTR CAP 10MG ER	6	11	330	330
AMPHET/DEXTR TAB 10MG	6	10	300	480
October 1, 2018 - December 31, 2018				
METHYLPHENID TAB 5MG	13	22	660	990
METHYLPHENID TAB 36MG ER	10	21	630	630
METHYLPHENID TAB 10MG	11	20	600	900
RISPERIDONE TAB 0.5MG	9	20	600	1050
ARIPIPRAZOLE TAB 5MG	7	16	448	448
AMPHET/DEXTR TAB 5MG	12	16	480	660
AMPHET/DEXTR TAB 10MG	8	14	420	630
METHYLPHENID TAB 18MG ER	9	14	380	365
AMPHET/DEXTR CAP 15MG ER	6	14	415	415
AMPHET/DEXTR CAP 10MG ER	8	13	374	374

Psychotropic Claims Under 18

Summary of Utilization - Members 10 to under 18

January 1, 2018 - December 31, 2018

Silversummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Days	Sum of Qty
January 1, 2018 - March 31, 2018				
SERTRALINE TAB 50MG	26	34	1005	1005
SERTRALINE TAB 25MG	20	33	990	990
TRAZODONE TAB 50MG	20	32	927	1050
METHYLPHENID TAB 36MG ER	16	28	840	1080
ARIPIPRAZOLE TAB 5MG	14	28	819	886
SERTRALINE TAB 100MG	14	24	705	975
AMPHET/DEXTR TAB 10MG	18	24	720	990
FLUOXETINE CAP 20MG	16	23	674	704
RISPERIDONE TAB 0.5MG	13	22	660	990
RISPERIDONE TAB 1MG	14	21	606	831
April 1, 2018 - June 30, 2018				
SERTRALINE TAB 50MG	25	46	1357	1402
SERTRALINE TAB 25MG	24	42	1237	1323
FLUOXETINE CAP 20MG	16	32	960	1200
SERTRALINE TAB 100MG	14	29	855	1185
RISPERIDONE TAB 1MG	14	28	840	1125
TRAZODONE TAB 50MG	18	28	807	817
ARIPIPRAZOLE TAB 5MG	17	27	753	753
RISPERIDONE TAB 0.5MG	15	26	782	992
FLUOXETINE CAP 10MG	16	25	750	750
METHYLPHENID TAB 36MG ER	12	24	720	870
July 1, 2018 - September 30, 2018				
SERTRALINE TAB 50MG	30	56	1607	1729
SERTRALINE TAB 100MG	22	38	1140	1470
METHYLPHENID TAB 36MG ER	19	36	1080	1440
ARIPIPRAZOLE TAB 5MG	19	33	906	971
RISPERIDONE TAB 0.5MG	17	31	930	1200
SERTRALINE TAB 25MG	17	28	844	889
ARIPIPRAZOLE TAB 10MG	17	27	708	708
AMPHET/DEXTR CAP 10MG ER	16	27	795	795
RISPERIDONE TAB 0.25MG	14	25	734	1139
TRAZODONE TAB 50MG	17	25	734	914
October 1, 2018 - December 31, 2018				
SERTRALINE TAB 50MG	36	61	1745	1910
SERTRALINE TAB 100MG	26	57	1587	1811
ARIPIPRAZOLE TAB 10MG	23	50	1294	1414
SERTRALINE TAB 25MG	30	47	1343	1307
TRAZODONE TAB 50MG	23	38	1124	1274
METHYLPHENID TAB 36MG ER	20	36	1080	1320
LAMOTRIGINE TAB 25MG	22	31	809	1897
RISPERIDONE TAB 0.5MG	17	30	884	1154
RISPERIDONE TAB 1MG	13	30	860	1074
ARIPIPRAZOLE TAB 5MG	17	26	725	770

Standard DUR Reports

Nevada Medicaid

Quarterly DUR Report

Health Plan Name: Fee for Service
Health Plan Contact: Carl Jeffery, PharmD
Contact Email: Carl.Jeffery@optum.com
Report Quarter (Calendar Year): Q4 2018
Report Period Start Date: 10/1/2018
Report Period End Date: 12/31/2018
Submission Date of Report:

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)	233,897	61,707	49.51%	50,329	40.38%	12,612	10.12%
Ingredient duplication (ID)	74,503	19,177	26.65%	11,122	15.46%	41,658	57.89%
Late Refill (LR)	42,574	33,776	86.93%	5,079	13.07%	0	0.00%
Total High Dose (HD)	225,505	79,332	56.61%	60,563	43.21%	251	0.18%
Drug-Pregnancy (PG)							
Total Low Dose (LD)							
Drug-Drug (DD)	786,002	144,588	71.61%	51,907	25.71%	5,425	2.69%
Drug-Disease (MC)							
Drug-Allergy (DA)							
Drug-Age (PA)	41	28	68.29%	13	31.71%	0	0.00%

Top 10 Drugs by Therapeutic Problem Type - Overutilization										
ER	**TD**	**ID**	**LR**	**HD**	**PG**	**LD**	**DD**	**MC**	**DA**	**PA**
	MORPHINE SULFATE	ONDANSETRON OD	GABAPENTIN	ONDANSETRON ODT			ONDANSETRON HCL			NITROFURANTOIN
	KETOROLAC TROMETH	PREDNISONE	PROVENTIL HFA	CYCLOBENZAPRINE HYDROCHLORIDE			ALPRAZOLAM			PROMETHAZINE-DM
	HYDROMORPHONE H	HYDROCODONE/AC	GABAPENTIN	IPRATROPIUM BROMIDE/ALBUTEROL SULFATE			ATORVASTATIN CALCIUM			PROMETHAZINE/DEXTROMETHOF
	HYDROCODONE/ACET	PANTOPRAZOLE SO	ATORVASTATIN CAL	FAMOTIDINE			ONDANSETRON HCL			PROMETHAZINE HCL PLAIN
	LORAZEPAM	HYDROCODONE/AC	PROVENTIL HFA	PANTOPRAZOLE SODIUM			ONDANSETRON HCL			PROMETHAZINE/CODEINE
	OXYCODONE/ACETAM	SODIUM CHLORIDE	PROVENTIL HFA	ONDANSETRON HCL			ONDANSETRON HCL			PROMETHAZINE HCL
	LISINOPRIL	ONDANSETRON HCL	ATORVASTATIN CAL	LISINOPRIL			ONDANSETRON HCL			PHENADOZ
	GABAPENTIN	PROVENTIL HFA	GABAPENTIN	HEPARIN SODIUM			ONDANSETRON HCL			VIRTUSSIN A/C
	OXYCODONE HCL	GABAPENTIN	PROVENTIL HFA	AMLODIPINE BESYLATE			ONDANSETRON HCL			ACETAMINOPHEN/CODEINE
	FAMOTIDINE	DEXAMETHASONE S	PROVENTIL HFA	ATORVASTATIN CALCIUM			MORPHINE SULFATE			PROMETHAZINE/DEXTROMETHOF

Retrospective DUR							
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, etc.)
Diabetic with no statin	Physician Letter	Mailing	100	Pending	N/A	Physician	OptumRx
High Potency Steroids/extended tx	Physician Letter	Mailing	zero	N/A	N/A	Physician	OptumRx

Top 10 Drug Classes by Paid Amount - Current Quarter		
Drug Class Name	Count of Claims	Pharmacy Paid
ANTIHEMOPHILIC PRODUCTS	77	$ 66,343,852.12
INSULIN	4,343	$ 21,142,020.90
ANTICONVULSANTS - MISC.	26,382	$ 19,030,246.20
SYMPATHOMIMETICS	21,591	$ 17,561,177.64
ANTIRETROVIRALS	1,881	$ 17,488,092.00
METABOLIC MODIFIERS	2,872	$ 15,970,573.99
ANTINEOPLASTIC - ANTIBODIES	416	$ 15,949,567.48
ANTIPSYCHOTICS - BENZISOXAZOLES	5,694	$ 13,948,875.01
HEPATITIS AGENTS	156	$ 13,867,923.56
ANTIPSYCHOTICS - MISC.	2,610	$ 12,593,525.77

Top 10 Drug Classes by Paid Amount - Previous Quarter		
Drug Class Name	Count of Claims	Pharmacy Paid
ANTIHEMOPHILIC PR	81	$ 71,944,748.47
INSULIN	4,479	$ 21,778,670.34
ANTICONVULSANTS	27,156	$ 18,915,261.12
ANTIRETROVIRALS	1,948	$ 17,834,249.47
SYMPATHOMIMETIC	20,443	$ 17,200,547.05
ANTINEOPLASTIC - A	430	$ 16,812,504.24
METABOLIC MODIFII	2,974	$ 15,925,093.80
ANTIPSYCHOTICS - B	5,836	$ 15,291,829.91
ANTIPSYCHOTICS - M	2,646	$ 12,447,412.88
MULTIPLE SCLEROSIS	242	$ 12,387,624.27

Top 10 Drug Classes by Claim Count - Current Quarter		
Drug Class Name	Count of Claims	Pharmacy Paid
ANTICONVULSANTS - MISC.	26,382	$ 19,030,246.20
SYMPATHOMIMETICS	21,591	$ 17,561,177.64
NSAIDS	18,954	$ 1,947,908.21
OPIOID COMBINATIONS	17,862	$ 2,202,473.50
SSRIS	15,757	$ 1,541,513.40
OPIOID AGONISTS	15,119	$ 4,566,626.96
GLUCOCORTICOSTEROIDS	12,689	$ 2,559,875.76
CENTRAL MUSCLE RELAXANTS	12,399	$ 1,590,017.59
5-HT3 RECEPTOR ANTAGONISTS	11,583	$ 979,195.84
BENZODIAZEPINES	11,362	$ 890,045.59

Top 10 Drug Classes by Claim Count - Previous Quarter		
Drug Class Name	Count of Claims	Pharmacy Paid
ANTICONVULSANTS	27,156	$ 18,915,261.12
SYMPATHOMIMETIC	20,443	$ 17,200,547.05
NSAIDS	19,521	$ 2,029,912.62
OPIOID COMBINATIC	18,312	$ 2,213,953.85
SSRIS	16,154	$ 1,599,368.33
OPIOID AGONISTS	16,040	$ 5,027,879.22
CENTRAL MUSCLE RE	12,621	$ 1,689,640.54
BENZODIAZEPINES	12,221	$ 939,571.85
5-HT3 RECEPTOR AN	11,952	$ 1,136,931.74
GLUCOCORTICOSTEF	11,579	$ 1,946,524.40

Opioid Utilization					
Year/Month Filled	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
October 2018	8,316	11,895	216,903	743,457	$ 467,971.14
November 2018	8,147	11,561	216,142	740,513	$ 479,902.73
December 2018	7,564	10,598	197,060	668,408	$ 437,494.88

Top 10 Opioid Prescribers - Current Quarter								
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
A	Anesthesiology	Henderson	Nevada	140	520	14,692	58,008	$ 54,346.41
B	Maxillofacial Surgery	Henderson	Nevada	171	381	10,970	34,372	$ 20,775.98
C	Pain Management	Carson City	Nevada	108	371	8,397	21,562	$ 138,907.21
D	Pain Management	Las Vegas	Nevada	165	327	9,626	29,632	$ 26,060.60
E	Family Practice	Fallon	Nevada	95	289	6,030	26,279	$ 9,559.94
F		Las Vegas	Nevada	95	276	7,793	25,812	$ 15,406.98
G	Pain/Anethesiology	Las Vegas	Nevada	107	268	7,020	23,322	$ 16,036.79
H	Internal Medicine	Las Vegas	Nevada	42	233	3,303	6,784	$ 43,126.11
I	Orthopedic Surg	Las Vegas	Nevada	80	221	6,197	21,879	$ 33,195.88
J	Pain Management	Las Vegas	Nevada	135	218	5,821	17,407	$ 12,320.96

Top 10 Opioid Prescribers - Previous Quarter								
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
A	Anesthesiology	Henderson	Nevada	165	524	14,735	58,133	$ 47,326.02
B	Maxillofacial Surgery	Henderson	Nevada	191	443	13,142	40,563	$ 25,243.91
C	Pain Management	Carson City	Nevada	98	362	8,790	22,052	$ 154,505.55
D	Pain Management	Las Vegas	Nevada	150	257	7,580	23,154	$ 14,607.48
K	Family Practice	Las Vegas	Nevada	103	255	7,020	22,488	$ 18,285.95
L	Pulmonary	Las Vegas	Nevada	98	249	7,072	26,017	$ 11,289.31
M	Pain Management	Las Vegas	Nevada	126	246	7,426	21,696	$ 19,744.28
I	Orthopedic Surg	Las Vegas	Nevada	87	239	6,917	23,215	$ 40,934.02
J	Pain Management	Las Vegas	Nevada	141	218	6,137	18,684	$ 12,423.75
H	Internal Medicine	Las Vegas	Nevada	42	208	3,248	7,169	$ 10,667.88

Nevada Medicaid

Quarterly DUR Report

Health Plan Name: Anthem
Health Plan Contact: Lisa Todd
Contact Email: lisa.todd@amerigroup.com
Report Quarter (Calendar Year): Q4 2018
Report Period Start Date: 10/1/2018
Report Period End Date: 12/31/2018
Submission Date of Report: 03/06/2019

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)	40,129	39,901	99.43%	n/a	n/a	228	0.57%
Therapeutic duplication (TD)	60,841	32,416	53.28%	n/a	n/a	28,425	46.72%
Ingredient duplication (ID)	8,474	1,192	14.07%	n/a	n/a	7,282	85.93%
Late Refill (LR)	18,669	2,930	15.69%	n/a	n/a	15,739	84.31%
Total High Dose (HD)	22,962	10,559	45.98%	n/a	n/a	12,403	54.02%
Drug-Pregnancy (PG)	379	103	27.18%	n/a	n/a	276	72.82%
Total Low Dose (LD)	5,865	1,270	21.65%	n/a	n/a	4,595	78.35%
Drug-Drug (DD)	0	0	0.00%	n/a	n/a	0	0.00%
Drug-Disease (MC)	15,456	15,376	99.48%	n/a	n/a	80	0.52%
Drug-Allergy (DA)	119	28	23.53%	n/a	n/a	91	76.47%
Drug-Age (PA)	8,829	2,071	23.46%	n/a	n/a	6,758	76.54%

Top 10 Drugs by Therapeutic Problem Type - Overutilization										
ER	**TD**	**ID**	**LR**	**HD**	**PG**	**LD**	**DD**	**MC**	**DA**	**PA**
GABAPENTIN	ALBUTEROL SULFATE	n/a	LISINOPRIL	VENTOLIN HFA	PRENATAL VITAMINS	BUPROPION HCL	n/a	n/a	TRAMADOL HCL	TRIAMCINOLONE ACETONIDE
ATORVASTATIN CALCIUM	VENTOLIN HFA	n/a	GABAPENTIN	ALBUTEROL SULFATE	ASPIRIN EC	MONTELUKAST SODIUM	n/a	n/a	IBU	ONDANSETRON ODT
LISINOPRIL	QUETIAPINE FUMARATE	n/a	METFORMIN HCL	AMOXICILLIN	ALPRAZOLAM	IPRATROPIUM BROMIDE	n/a	n/a	CEPHALEXIN	ALBUTEROL SULFATE
METFORMIN HCL	LEVOTHYROXINE SODIUM	n/a	AMLODIPINE BESYLATE	PREDNISOLONE	MEDROXYPROGESTERONE ACETATE	JANUVIA	n/a	n/a	AMOXICILLIN/CLAVULANATE POTASS	CHILDREN'S LORATADINE
AMLODIPINE BESYLATE	GABAPENTIN	n/a	LEVOTHYROXINE SODIUM	ONDANSETRON ODT	CLONAZEPAM	HYDROXYZINE HCL	n/a	n/a	OXYCODONE-ACETAMINOPHEN	PROMETHAZINE-DM
LEVOTHYROXINE SODIUM	FLUOXETINE HCL	n/a	RANITIDINE HCL	PREDNISOLONE SODIUM PHOSPHATE	ASPIRIN	ACYCLOVIR	n/a	n/a	HYDROCODONE-ACETAMINOPHEN	MOMETASONE FUROATE
VENTOLIN HFA	SERTRALINE HCL	n/a	PREDNISONE	IBUPROFEN	TOPIRAMATE	ATOMOXETINE HCL	n/a	n/a	TRESIBA FLEXTOUCH U-200	GUAIFENESIN
TRAZODONE HCL	TRAZODONE HCL	n/a	METOPROLOL TARTRATE	POLYETHYLENE GLYCOL 3350	PRENATAL	PROPRANOLOL HCL	n/a	n/a	CAYSTON	HYDROXYZINE HCL
SERTRALINE HCL	VENLAFAXINE HCL ER	n/a	TOPIRAMATE	POLYMYXIN B SUL-TRIMETHOPRIM	TRAMADOL HCL	DULOXETINE HCL	n/a	n/a	ADMELOG SOLOSTAR	VENTOLIN HFA
LOSARTAN POTASSIUM	DULOXETINE HCL	n/a	DEXTROAMPHETAMINE-AMPHETAMINE	SUMATRIPTAN SUCCINATE	NICOTINE PATCH	OXYBUTYNIN CHLORIDE	n/a	n/a	NUCYNTA ER	MONTELUKAST SODIUM

Retrospective DUR							
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, etc.)**
Adding Therapy – Gap in Care Asthma	Identifies members that have filled rescue inhalers with no recent claims for a long acting controller. Outreach to provider to recommend adding a long acting controller if clinically appropriate.	Fax/mail	92 Messages	N/A	N/A	Physician	Internal
Adding Therapy-Gap in Care – No Statin	Identifies that are diabetic and not currently on a statin. Outreach to provider to recommend based on clinical guidelines adding a statin.	Fax/mail	166	N/A	N/A	Physician	Internal
Adding Therapy Gap in Care – Post MI No Beta Blocker	Identifies members that had a Myocardial Infarction and no claim for a beta blocker and outreaches to the provider to recommend adding a beta blocker based on clinical guidelines if clinically indicated	Fax/mail	7	N/A	N/A	Physician	Internal
Adding Therapy Gap in Care – Post MI No Statin	Identifies members with a recent MI and no evidence of being on statin therapy. Recommends to the provider the addition of a statin based on clinical guidelines and if clinically appropriate.	Fax/mail	1	N/A	N/A	Physician	Internal

Top 10 Drug Classes by Paid Amount - Current Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
Antiretrovirals	1,903	Anthem confidential
Insulin	4,491	Anthem confidential
Sympathomimetics	17,841	Anthem confidential
Hepatitis Agents	138	Anthem confidential
Antineoplastic Enzyme Inhibito	74	Anthem confidential
Anticonvulsants - Misc.	14,402	Anthem confidential
Anti-TNF-alpha - Monoclonal Antibodies	133	Anthem confidential
Multiple Sclerosis Agents	111	Anthem confidential
Incretin Mimetic Agents (GLP-1 Receptor Agonists)	878	Anthem confidential
Quinolinone Derivatives	1,831	Anthem confidential

Top 10 Drug Classes by Paid Amount - Previous Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
HIV/AIDS THERAPY	1,882	Anthem confidential
MISCELLANEOUS PULMONARY AGENTS	9,768	Anthem confidential
INSULIN THERAPY	4,595	Anthem confidential
ANTIPSYCHOTICS	8,293	Anthem confidential
NON-INSULIN HYPOGLYCEMIC AGENTS	13,502	Anthem confidential
MISCELLANEOUS ANTINEOPLASTIC DRUGS	151	Anthem confidential
MISCELLANEOUS RHEUMATOLOGICAL AGENTS	257	Anthem confidential
ANTICONVULSANTS	17,538	Anthem confidential
MISCELLANEOUS ANTIVIRALS	2,049	Anthem confidential
MISCELLANEOUS NEUROLOGICAL THERAPY	397	Anthem confidential

Top 10 Drug Classes by Claim Count - Current Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
Nonsteroidal Anti-inflammatory	21,455	Anthem confidential
Sympathomimetics	17,841	Anthem confidential
Anticonvulsants - Misc.	14,402	Anthem confidential
HMG CoA Reductase Inhibitors	12,540	Anthem confidential
Selective Serotonin Reuptake I	12,163	Anthem confidential
Opioid Combinations	9,950	Anthem confidential
Central Muscle Relaxants	9,563	Anthem confidential
Aminopenicillins	9,393	Anthem confidential
Antihistamines - Non-Sedating	9,361	Anthem confidential
ACE Inhibitors	8,944	Anthem confidential

Top 10 Drug Classes by Claim Count - Previous Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTIDEPRESSANT AGENTS	25177	Anthem confidential
NSAIDS/COX II INHIBITORS	21282	Anthem confidential
ANTICONVULSANTS	17538	Anthem confidential
VITAMINS & HEMATINICS	14827	Anthem confidential
LIPID/CHOLESTEROL LOWERING AGENTS	14597	Anthem confidential
ANTIHISTAMINES	14478	Anthem confidential
NON-INSULIN HYPOGLYCEMIC AGENTS	13502	Anthem confidential
BETA AGONISTS INHALERS	12363	Anthem confidential
COMBINATION NARCOTIC /ANALGESICS	11025	Anthem confidential
PENICILLINS	10702	Anthem confidential

Opioid Utilization					
Year/Month Filled	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
October 2018	4842	4842	101739	329768	Anthem confidential
November 2018	4572	4572	96864	316068	Anthem confidential
December 2018	4332	4332	93062	300267	Anthem confidential

Top 10 Opioid Prescribers - Current Quarter								
Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
*******586	PA	Las Vegas	Nevada	459	459	13086	41997	Anthem confidential
*******525	MD	Henderson	Nevada	323	323	9486	26463	Anthem confidential
*******121	PAC	Las Vegas	Nevada	300	300	8455	26299	Anthem confidential
*******305	PAC	Las Vegas	Nevada	297	297	8129	26295	Anthem confidential
*******050	PAC	Las Vegas	Nevada	258	258	7082	22643	Anthem confidential
*******319	MD	Henderson	Nevada	248	248	6732	21855	Anthem confidential
*******190	NP	Las Vegas	Nevada	238	238	6439	20363	Anthem confidential
*******647	PA	North Las Vegas	Nevada	231	231	6533	20846	Anthem confidential
*******237	NP	Las Vegas	Nevada	229	229	6796	20556	Anthem confidential
*******127	MD	Las Vegas	Nevada	220	220	6365	20105	Anthem confidential

Top 10 Opioid Prescribers - Previous Quarter								
Prescriber ID	**Prescriber Type**	**Physician City**	**Physician State**	**Member Count**	**Claim Count**	**Sum of Days Supply**	**Sum of Quantity**	**Sum of Paid Amount**
*******828	DO	Las Vegas	Nevada	485	485	14073	45665	Anthem confidential
*******700	DO	Reno	Nevada	377	377	10371	34173	Anthem confidential
*******464	NP	Reno	Nevada	305	305	9034	25542	Anthem confidential
*******618	MD	Las Vegas	Nevada	257	257	7473	22123	Anthem confidential
*******850	NP	Lakewood	Colorado	254	254	6641	20624	Anthem confidential
*******881	NP	Las Vegas	Nevada	232	232	6674	19810	Anthem confidential
*******775	NP	Reno	Nevada	229	229	6531	19911	Anthem confidential
*******779	MD	Las Vegas	Nevada	222	222	6612	19998	Anthem confidential
*******117	MD	San Antonio	Texas	214	214	5241	16889	Anthem confidential
*******183	PAC	Reno	Nevada	196	196	5575	17228	Anthem confidential

Nevada Medicaid

Quarterly DUR Report

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan.Bitton@uhc.com
Report Quarter (Calander Year):	Q4 2018
Report Period Start Date:	10/1/2018
Report Period End Date:	12/31/2018
Submission Date of Report:	

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)	18,362	N/A	N/A	N/A	N/A	18,362	100.00%
Therapeutic duplication (TD)	72,326	49,569	68.50%	15,730	21.70%	7,027	9.70%
Ingredient duplication (ID)	44,346	33	0.10%	38	0.10%	44,275	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)	100,528	69,684	69.30%	20,144	20.00%	10,700	10.60%
Drug-Disease (MC)	198,700	166,125	83.61%	32,575	16.39%	N/A	N/A
Drug-Allergy (DA)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Drug-Age (PA)	30,205	22,917	75.90%	7,288	24.10%	N/A	N/A

Top 10 Drugs by Therapeutic Problem Type - Overutilization

ER	TD	ID	LR	HD	PG	LD	DD	MC	DA	PA
MORPHINE SULFATE ER	AMLODIPINE BESYLATE	MORPHINE SULFATE ER	ATORVASTATIN CALCIUM	OMEPRAZOLE	IBU	COMPOUND CLAIM	ATORVASTATIN CALCIUM	GABAPENTIN	N/A	MONTELUKAST SODIUM
FLUOXETINE HCL	LOSARTAN POTASSIUM	FLUOXETINE HCL	LEVOTHYROXINE SODIUM	DULOXETINE HCL	METRONIDAZOLE	ALBUTEROL SULFATE	LISINOPRIL	HYDROCODONE/ ACETAMINOPHEN	N/A	IBU
HYDROCODONE/ACETAMINOPHEN	ALBUTEROL SULFATE	HYDROCODONE/ACETAMINOPHEN	OMEPRAZOLE	ADDERALL XR	ONDANSETRON ODT	FLUCONAZOLE	HYDROCHLOROTHIAZIDE	ALPRAZOLAM	N/A	CLINDAMYCIN PHOSPHATE
OXYCODONE/ACETAMINOPHEN	LISINOPRIL	OXYCODONE/ACETAMINOPHEN	METFORMIN HCL	SUBOXONE	FLUCONAZOLE	NORETHINDRONE ACETATE/ETHINYL ESTRADIOL	TRAZODONE HYDROCHLORIDE	ATORVASTATIN CALCIUM	N/A	CETIRIZINE HCL
TOUJEO SOLOSTAR	VENTOLIN HFA	TOUJEO SOLOSTAR	LISINOPRIL	ACETAMINOPHEN/CODEINE	NITROFURANTOIN MONOHYDRATE/MACROCRYSTALS	NYSTATIN	FOLIC ACID	FLUTICASONE PROPIONATE	N/A	LORATADINE CHILDRENS
SUBOXONE	HYDROCHLOROTHIAZIDE	SUBOXONE	MONTELUKAST SODIUM	PANTOPRAZOLE SODIUM	VENTOLIN HFA	XULANE	GABAPENTIN	ZOLPIDEM TARTRATE	N/A	ONDANSETRON ODT
SIMVASTATIN	GABAPENTIN	SIMVASTATIN	LOSARTAN POTASSIUM	AMPHETAMINE/DEXTROAMPHETAMINE	TERCONAZOLE	VITAMIN D3	BUSPIRONE HCL	PREDNISONE	N/A	AZITHROMYCIN
ONETOUCH VERIO TEST STRIPS	METOPROLOL TARTRATE	ONETOUCH VERIO TEST STRIPS	PANTOPRAZOLE SODIUM	METHYLPHENIDATE HYDROCHLORIDE ER	FLUTICASONE PROPIONATE	CETIRIZINE HCL	FENOFIBRATE	VENTOLIN HFA	N/A	RANITIDINE HCL
OXYCODONE HCL	CARVEDILOL	OXYCODONE HCL	AMLODIPINE BESYLATE	TEMAZEPAM	SERTRALINE HCL	ONDANSETRON ODT	AMLODIPINE BESYLATE	MONTELUKAST SODIUM	N/A	OSELTAMIVIR PHOSPHATE
ONETOUCH ULTRA BLUE	TRAZODONE HYDROCHLORIDE	ONETOUCH ULTRA BLUE	SERTRALINE HCL	ZOLPIDEM TARTRATE	HYDROCODONE/ACETAMINOPHEN	MICROGESTIN 1.5/30	QUETIAPINE FUMARATE	IBU	N/A	BUDESONIDE

Retrospective DUR

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, etc.)
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	14 (3)	2	66.67%	Prescriber	OptumRx
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	130 (55)	13	23.64%	Prescriber	OptumRx
Drug-Disease Interaction	This is a provider-targeted program designed to minimize the occurrence of clinically significant, patient-specific drug-disease interactions.	Fax/Mail	1222 (716)	102	14.25%	Prescriber	OptumRx
Drug-Drug Interaction	This is a provider-targeted program designed to minimize the occurrence of clinically significant, patient-specific drug-drug interactions.	Fax/Mail	8127 (4953)	1272	25.68%	Prescriber	OptumRx
Duplicate Therapy	This is a provider-targeted program designed to promote awareness of Therapeutic duplication concerns.	Fax/Mail	5169 (3035)	529	17.43%	Prescriber	OptumRx
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	8695 (4922)	460	9.35%	Prescriber	OptumRx
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	2911 (1677)	113	6.74%	Prescriber	OptumRx
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	TBD	TBD	TBD	TBD	TDB

Top 10 Drug Classes by Paid Amount - Q4 2018 - Current Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTIVIRALS	7,206	NA
ANTIDIABETICS	31,974	NA
ANALGESICS - ANTI-INFLAMMATORY	35,576	NA
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	41,678	NA
ANTIPSYCHOTICS/ANTIMANIC AGENTS	11,458	NA
ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	1,644	NA
DERMATOLOGICALS	22,768	NA
PSYCHOTHERAPEUTIC & NEUROLOGICAL AGENTS - MISC.	1,595	NA
ANTICONVULSANTS	28,254	NA
ANALGESICS - OPIOID	30,166	NA

Top 10 Drug Classes by Paid Amount - Q3 2018 - Previous Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTIVIRALS	5,811	NA
ANTIDIABETICS	31,964	NA
ANALGESICS - ANTI-INFLAMMATORY	35,544	NA
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	37,476	NA
ANTIPSYCHOTICS/ANTIMANIC AGENTS	11,810	NA
DERMATOLOGICALS	23,882	NA
ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	1,621	NA
PSYCHOTHERAPEUTIC & NEUROLOGICAL AGENTS - MISC.	5,002	NA
ANTICONVULSANTS	29,036	NA
ANALGESICS - OPIOID	31,768	NA

Top 10 Drug Classes by Claim Count - Q4 2018 - Current Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	41,678	NA
ANTIDEPRESSANTS	40,176	NA
ANALGESICS - ANTI-INFLAMMATORY	35,576	NA
ANTIHYPERTENSIVES	32,586	NA
ANTIDIABETICS	31,974	NA
ANALGESICS - OPIOID	30,166	NA
ANTICONVULSANTS	28,254	NA
ANTIHYPERLIPIDEMICS	23,718	NA
ULCER DRUGS/ANTISPASMODICS/ANTICHOLINERGICS	22,832	NA
DERMATOLOGICALS	22,768	NA

Top 10 Drug Classes by Claim Count - Q3 2018 - Previous Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTIDEPRESSANTS	37,573	NA
ANTIASTHMATIC AND BRONCHODILATOR AGENTS	37,476	NA
ANALGESICS - ANTI-INFLAMMATORY	35,544	NA
ANTIHYPERTENSIVES	33,213	NA
ANTIDIABETICS	31,964	NA
ANALGESICS - OPIOID	31,768	NA
ANTICONVULSANTS	29,036	NA
ANTIHYPERLIPIDEMICS	23,896	NA
DERMATOLOGICALS	23,882	NA
ULCER DRUGS/ANTISPASMODICS/ANTICHOLINERGICS	23,540	NA

Opioid Utilization

Year/Month Filled	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
October 2018	8,926	10,856	236,187	780,702	NA
November 2018	8,309	9,879	219,752	727,937	NA
December 2018	7,978	9,431	208,510	690,227	NA

Top 10 Opioid Prescribers - Q4 2018 - Current Quarter

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
A	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	590	1,398	163	125,192	NA
B	PAIN MANAGEMENT	LAS VEGAS	NEVADA	336	835	157	79,111	NA
C	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	335	632	189	52,354	NA
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	239	567	114	56,184	NA
E	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	178	565	170	63,634	NA
F	PAIN MANAGEMENT	LAS VEGAS	NEVADA	314	516	83	49,067	NA
G	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	266	503	105	45,906	NA
H	PHYSICAL MEDICINE	LAS VEGAS	NEVADA	188	418	160	35,568	NA
I	GENERAL PRACTICE	LAS VEGAS	NEVADA	117	395	82	37,635	NA
J	PAIN MANAGEMENT & ER MED	LAS VEGAS	NEVADA	255	347	142	32,426	NA

Top 10 Opioid Prescribers - Q3 2018 - Previous Quarter

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
K	PAIN MANAGEMENT	LAS VEGAS	NEVADA	562	1,197	187	104,640	NA
A	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	462	908	193	78,766	NA
B	PAIN MANAGEMENT	LAS VEGAS	NEVADA	340	849	217	77,353	NA
D	PAIN MANAGEMENT	LAS VEGAS	NEVADA	256	538	155	51,427	NA
F	PAIN MANAGEMENT	LAS VEGAS	NEVADA	315	511	106	48,564	NA
E	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	189	508	207	57,612	NA
J	PAIN MANAGEMENT & ER MED	LAS VEGAS	NEVADA	298	446	96	42,453	NA
I	GENERAL PRACTICE	LAS VEGAS	NEVADA	119	416	61	39,504	NA
H	PHYSICAL MEDICINE/REHAB	LAS VEGAS	NEVADA	183	366	200	31,826	NA
C	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	259	363	116	27,575	NA

Nevada Medicaid

Quarterly DUR Report

Health Plan Name: Silversummit Healthplan
Health Plan Contact: Tom Beranek, RPh

Contact Email: Thomas.L.Beranek@SilverSummitHealthPlan.com
Report Quarter (Calendar Year): Q4 2018
Report Period Start Date: 10/1/2018
Report Period End Date: 12/31/2018
Submission Date of Report: 3/6/2019

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)	4547	0	0%	0	0%	4547	100%
Therapeutic duplication (TD)	5461	1704	31%	0	0%	3757	69%
Ingredient duplication (ID)	3252	0	0%	0	0%	3252	100%
Late Refill (LR)							
Total High Dose (HD)	544	339	62%	0	0%	205	38%
Drug-Pregnancy (PG)	51	41	80%	0	0%	10	20%
Total Low Dose (LD)	1624	1158	71%	0	0%	466	29%
Drug-Drug (DD)	1738	1256	72%	0	0%	482	28%
Drug-Disease (MC)	872	657	75%	0	0%	215	25%
Drug-Allergy (DA)							
Drug-Age (PA)	5	4	80%	0	0%	1	20%

Silversummit Healthplan

Quarterly DUR Report

10/1/2018 - 12/31/2018

Top 10 Drugs by Therapeutic Problem Type - Overutilization										
ER	**TD**	**ID**	**LR**	**HD**	**PG**	**LD**	**DD**	**MC**	**DA**	**PA**
Albuterol Sulfate	Gabapentin	Albuterol Sulfate		Ibuprofen		Albuterol Sulfate	Quetiapine Fumarate	Bupropion HCl		Guaifenesin - Codeine
Gabapentin	Quetiapine Fumarate	Atrovastatin Calcium		Cefdinir		Ondansetron HCl	Cyclobenzaprine	Amphetamine-Dextroamphetamine		Promethazine -DM
Atrovastatin Calcium	Atorvastatin Calcium	Gabapentin		Oselatmavir Phosphate		Cholecalciferol	Trazadone	Alprazolam		Promethazine HCl
Metformin HCl	Levothyroxine Sodium	Metformin HCl		Dupilumab		Potassium Chloride	Citalopram Hydrobromide	Gabapentin		
Amlodipine Besylate	Lisinopril	Sertraline HCl		Acetaminophen		Fluconazole	Spironolactone	Warfarin		

Retrospective DUR							
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, etc.)**
Oct - 2018, Trifecta/Multiple Opioid Prescribers	Provider outreach for members who are obtaining an opioid, benzo and muscle relaxer combination	Mail	51			Physician	Plan
Nov - 2019, Trifecta/Multiple Opioid Prescribers	Provider outreach for members who are obtaining an opioid, benzo and muscle relaxer combination	Mail	51	4	8%	Physician	Plan
Dec - 2018, Trifecta/Multiple Opioid Prescribers	Provider outreach for members who are obtaining an opioid, benzo and muscle relaxer combination	Mail	51	6	12%	Physician	Plan

Silversummit Healthplan

Quarterly DUR Report

10/1/2018 - 12/31/2018

Top 10 Drug Classes by Paid Amount - Current Quarter

Drug Class Name	Count of Claims	Pharmacy Paid
Anticonvulsants - Misc.	4488	$239,093.15
Antipsychotics - Misc.	271	$251,884.88
Antiretrovirals	682	$1,367,205.09
Hepatitis Agents	34	$422,811.38
Incretin Mimetic Agents (GLP-1 Receptor Agonists)	232	$179,899.84
Insulin	1292	$566,759.99
Multiple Sclerosis Agents	32	$241,546.52
Opioid Combinations	3273	$167,815.51
Opioid Partial Agonists	672	$188,855.39
Sympathomimetics	4108	$365,991.36

Top 10 Drug Classes by Paid Amount - Previous Quarter

Drug Class Na	Count of Claims	Pharmacy Paid
Anti-TNF-alpha	35	$189,933.16
Anticonvulsants - Misc.	4495	$212,924.68
Antipsychotics - Misc.	264	$224,397.39
Antiretrovirals	692	$1,406,085.12
Hepatitis Agents	45	$616,527.55
Incretin	255	$200,180.06
Insulin	1279	$538,338.77
Multiple Sclerosis Agents	34	$245,247.68
Opioid Partial Agonists	597	$182,741.90
Sympathomimetics	3489	$340,782.41

Top 10 Drug Classes by Claim Count - Current Quarter

Drug Class Name	Count of Claims	Pharmacy Paid
ACE Inhibitors	2100	$11,837.02
Aminopenicillins	2092	$14,261.53
Anticonvulsants - Misc.	4488	$239,093.15
Central Muscle Relaxants	2752	$40,769.34
HMG CoA Reductase Inhibitors	3848	$39,722.58
Nonsteroidal Anti-inflammatory Agents	5877	$82,062.52
Opioid Combinations	3273	$167,815.51
Proton Pump Inhibitors	2147	$33,240.79
Selective Serotonin Reuptake Inhibitors	4095	$38,176.18
Sympathomimetics	4108	$365,991.36

Top 10 Drug Classes by Claim Count - Previous Quarter

Drug Class N	Count of Claim	Pharmacy Paid
ACE Inhibitors	2279	$12,925.98
Anticonvulsants - Misc.	4495	$212,924.68
Biguanides	1873	$29,372.60
Central Muscle Relaxants	2775	$36,399.49
HMG CoA	3682	$32,276.86
Nonsteroidal	5890	$57,352.02
Opioid Combinations	3526	$139,260.59
Proton Pump Inhibitors	2146	$32,400.03
Selective	4129	$34,609.68
Sympathomimetics	3489	$340,782.41

Silversummit Healthplan

Quarterly DUR Report

10/1/2018 - 12/31/2018

Opioid Utilization

Year/Month Filled	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
October 2018	1,518	1,835	38,751	120,083	$150,300.69
Novermber 2018	1,471	1,767	37,648	116,806	$157,353.47
December 2018	1,434	1,691	35,641	110,080	$162,064.81

Top 10 Opioid Prescribers - Current Quarter

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
*634	Physician Assistant	LAS VEGAS	NV	31	109	3,202	9,887	$26,895.31
*686	Physician Assistant	LAS VEGAS	NV	68	188	5,422	17,877	$23,902.53
*941	Physician Assistant	LAS VEGAS	NV	128	249	7,390	22,852	$17,915.80
*870	Physician Assistant	LAS VEGAS	NV	94	183	5,400	17,855	$16,315.36
*195	Anesthesiology	LAS VEGAS	NV	52	150	3,613	7,823	$73,280.27
*491	MD- Pain Medicine	LAS VEGAS	NV	43	109	3,254	9,478	$8,394.50
*014	MD- Pain Medicine	LAS VEGAS	NV	103	155	4,425	12,949	$10,431.89
*319	Anesthesiology - Pain	HENDERSON	NV	41	100	2,957	9,643	$4,247.13
*709	MD - Psychiatry	LAS VEGAS	NV	38	168	2,549	4,408	$35,080.71
*730	Physician Assistant	LAS VEGAS	NV	116	246	7,344	22,386	$16,934.62

Top 10 Opioid Prescribers - Previous Quarter

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
*634	Physician Assistant	LAS VEGAS	NV	28	99	2,924	9,372	$15,903.22
*686	Physician Assistant	LAS VEGAS	NV	52	132	3,864	12,626	$13,492.08
*941	Physician Assistant	LAS VEGAS	NV	111	192	5,582	17,823	$11,064.55
*870	Physician Assistant	LAS VEGAS	NV	101	198	5,857	18,884	$14,858.12
*195	Anesthesiology	LAS VEGAS	NV	53	152	3,744	8,188	$77,794.14
*491	MD- Pain Medicine	LAS VEGAS	NV	50	117	3,510	11,010	$5,447.10
*014	MD- Pain Medicine	LAS VEGAS	NV	118	167	4,894	13,417	$11,683.79
*319	Anesthesiology - Pain	HENDERSON	NV	46	98	2,832	8,927	$3,551.81
*709	MD - Psychiatry	LAS VEGAS	NV	33	130	2,013	3,790	$29,382.04
*730	Physician Assistant	LAS VEGAS	NV	138	314	9,407	28,770	$20,679.03