Nevada Medicaid Drug Use Review Board Meeting

July 25, 2019

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NOTICE OF PUBLIC MEETING – DRUG USE REVIEW BOARD

Date of Posting:	June 10, 2019
Date of Revision:	June 11, 2019
Date of Meeting:	July 25, 2019 at 1:00 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 Lane Reno, Nevada 89502 Phone: (775) 826-2500
Webinar Registration:	https://optum.webex.com/optum/onstage/g.php?MTID=7216d936c2a0649eaa70817a5a5762c0 Or go to www.webex.com and enter the Event Number listed below. Once you have registered for the meeting, you will receive an email message confirming your registration. This message will provide the information that you need to join the meeting.
Event Number:	641 465 292 Click "Join Now." Follow the instructions that appear on your screen to join the audio portion of the meeting. Audio will be transmitted over the internet.

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

For Audio Only:

Phone: (763) 957-6300
Event: 641 465 292

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 April 25, 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 growth hormones

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

b. **For Possible Action:** Discussion and possible adoption of prior authorization criteria and/or quantity limits for Spravato® (esketamine)

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 prior authorization criteria and/or quantity limits for gastrointestinal agents used for the treatment of Chronic Idiopathic Constipation (CIC)

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 updated prior authorization criteria and/or quantity limits for anti-migraine medications – Serotonin (5-HT1) Receptor Agonists (triptans)

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

e. **For Possible Action:** Presentation, discussion and possible adoption of updated DUR bylaws

1. Presentation by DHCFP of updates to DUR Bylaws
2. Discussion by Board and review of updates to DUR Bylaws
3. Proposed adoption of updated DUR Bylaws

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. Opioid use disorder and opioid use

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

c. Specialty drug utilization

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

7. Public Comment on any Standard DUR Report

8. Standard DUR Reports

a. Review of prescribing/program trends.

1. Top 10 Therapeutic Classes for Q4 2018 and Q1 2019 (by payment and by claims).

b. Concurrent Drug Utilization Review (ProDUR)

1. Review of Q1 2019.
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 five minutes.

Notice of this public meeting will be available on or after the date of this notice at the DHCFP website at http://dhcfp.nv.gov and at http://notice.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 meeting agendas 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 DHCFP 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

Netochi Adeolokun, Pharm.D.

Mark Canty, MD

Dave England, Pharm D

Mohammad Khan, MD

Brian Le, DO

James Marx, MD

Michael Owens, MD

Jim Tran, Pharm.D.

Jennifer Wheeler, Pharm.D.

Drug Use Review (DUR) Board Meeting Schedule for 2019

Date	Time	Location
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, April 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 2nd St
Reno, NV 89595
Phone: (775) 789-2000

ATTENDEES

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

Board Members Absent
Marta Bunuel, MD
Paul Oesterman, Pharm.D.

DHCFP
Holly Long, Social Services Program Specialist
Beth Slamowitz, Pharm.D.
Andolyn Johnson, DAG

OptumRx
Carl Jeffery, Pharm.D.

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

Lisa Todd – Anthem

Public
Scott Maynard, Genentech
Sandy Sierawski, Pfizer
Georgette Dzwilewski, Indivior
Jennie Feight, MiMedx
Jamie Evins, DHCFP

Public Online:
Rob Bigham, Takeda
Jenna Gianninoto, Abbvie
Jennifer Lauper, BMS

AGENDA

1. Call to Order and Roll Call

Meeting called to order at 5:18 PM

Roll Call

Carl Jeffery
James Marx
Netochi Adeolokun
Jennifer Wheeler
Michael Owens
David England
Andolyn Johnson
Camilla Hauck
Holly Long
Lisa Todd
Thomas Beranek
Ryan Bitton

2. Public Comment on Any Matter on the Agenda

David England opened the floor for public comment and there was none.

3. Administrative

a. **For Possible Action:** Review and Approve Meeting Minutes from January 24, 2019.

Motion to approve the minutes as presented made. Second. Voting: Ayes are unanimous. Minutes approved.

b. Status Update by DHCFP

Holly Long – At the January 24, 2019, DUR meeting, it was asked that we send the letters to the top 10 opioid prescribers replicating what we had done previously. We went ahead and did that. The letters were sent out on March 15. We have not received any feedback on any of those. It is National Drug Take Back Day again. We started posting the information last year. This has been going on for a few years. On the DHCFP Pharmacy Services site, a link can go directly to the DEA site where they have all the information on National Drug Take Back day. You put in your zip code or physical address information and they can direct you to the exact closest location or options of locations for where to go to give your unused drugs. There is an attachment provided along with the agenda for today, which is titled the fact sheet for Nevada's oversight of opioid prescribing and monitoring of opioid use. In an ongoing effort to support Health and Human Services to identify and disseminate effective practices to address the opioid epidemic in the United States. The OIG, or Office of the Inspector General will randomly select and review nine states, using a questionnaire that covers the five categories related to each state's approach to addressing the epidemic including policies and procedures, data analytics programs, outreach, and other efforts. I wanted to provide everyone a copy, so they can see what the decisions that you make here directly affect the information in here, so it is very helpful. Based on the questionnaire and the responses provided, the state fact sheet was produced. It was made public in February 2019. The very last page of this entire document provides the summaries that they have created in an approach to addressing the opioid crisis. In the bottom right-hand corner is Nevada's prescription of opioid death rate compared to the national average. These are different statistics than what I have provided in the past. Once they are done accumulating it they are going to provide to CMS, as well. We worked with Dr. Stephanie Woodard and faculty with DPPH to be able to coordinate the questionnaire. We have not received any feedback as far as recommendations that they are making for changes. I have been in communication with the auditors that did the questionnaire so if you give any feedback, I will be sure to report it here.

James Marx – Holly I think we should point out that the CDC guidelines have been recently updated. They have acknowledged that the guidelines were never intended to be for chronic treatment. They were only for opioid-naive patients for initial use and that's a very big consideration because what a lot of people have done, a lot of organizations, and a lot of institutions have done, have adopted those CDC guidelines for their chronic pain patients which are not appropriate, and I think some of that should be acknowledged. I do not think I saw that in here.

Holly Long – We do have reference to CDC guidelines in many places throughout policy specifically for opioid prescribing, so I can double-check what we reference with policy and see what that aligns with. We did provide specific information where we direct providers for resources and so that would be listed in there. I do not know that it is specific to chronic. There is all those different guidelines that they have. Thank you for adding that.

David England opened the floor for public comment and there was none.

David England – We discussed at our previous meeting last week, and today discussed the annual reports from specific groups, the longer I sit in a meeting, the less attention I spend. Since we are at the first of the meeting, I am more awake right now, and gave everybody some time and go back and review their presentation and discussion of three to five minutes if you

want to go over and review. Not necessarily, re-read it to us, but just go over some content that you want us to look at.

Holly Long – We tried to prepare a little bit to try to ease that. This provides a brief overview. It really focused on the differences that were in there or what you might you want to look at that were different between fee-for service and the MCOs. Regular questions that we get with that opioid questionnaire and other questions that have been asked that might stick out. I really want everyone to take into consideration suggestions that we have one another based off the responses that are provided and maybe that can direct us with the decision-making that goes on here or directs people to suggestions that they have for me that would be very helpful. The handout I provided is a tool. It does not include every question. We just did a full survey online, but this is just a tool to be able to review here today. If we could go through everyone, I asked them to be prepared with a summary and allowing time for questions from Carl and each of the MCO's.

Carl Jeffery – The MCOs are the new ones on the block here, I think they are bringing some fresh ideas to us. We may be kind of stuck in the same process. It is good to have some new ideas and different processes on board, so we can see what is best. As far as prospective DUR criteria, our response was the DUR Board does not really approve that. I think you are available to make suggestions, but you do not have to sign off and approve that before we put it into place. The Pro-DUR is the edits that they get at the point of sale of the pharmacy, so it replies with high dose or early refill or drug-to-drug interaction, and similar things. The same with retrospective. The DUR Board is not required to sign off any of the initiatives that we do, but we are always open for feedback. Our process is a little bit different from what the MCOs do. I think on many cases, we have a pharmacist that sits down manually; it is a very manual process, of running reports, utilization reports, identifying what the issues are for that month and sends the letters out to the doctors. I know there are some more automated processes that I think some of the MCOs use so that is one of our differences there. I highlighted some of the DUR Board activity that was in the attachment; it was in the annual report, so we had four meetings. We had a good job in the fiscal year of meeting all four times; never had a problem meeting a quorum so we all succeeded with that. We added criteria for the opioids for children, rare diseases, hep-C, high dollars, compounds and among others so those are kind of the highlights that we hit last year. The generic drug substitution policy and utilization, our generic dispense rate is almost 82% so we are right up there with most other PBMs, I think even on a commercial side. On Fraud, Waste and Abuse, really our highlighted area, was the lock-in time so approximately 0.44% of the fee for service population is in lock-in, I think it equates to about 700 members. PDMP, one of our struggles is contractors, so I still do not have access to the PDMP. I think Holly does.

Holly Long – We have very limited access. We are only allowed one state employee to have access.

Carl Jeffery – I know that presents a challenge for us because if we do see something funny on our side like some claims, we don't have the ability to just run out and run a report on a PDMP for them. Pain management is something we are still working on, methadone utilization. It is still listed as non-preferred, but it is not use high-use on there, but it still is available. For antipsychotics, remember we went through all this a while ago. We have all the limits under age 18 for antipsychotics and it is in with all the other psychotropics, antidepressants, the

benzodiazepines, and sedative-hypnotics, as well. Stimulants require PA for all ages and I think we are going to talk about those today. Some of the innovative practices that I put on here, something I think we are very proud of, is the antibiotic prior authorization to curb some of the resistance. I think it was a big step and I am proud of the board for taking that step. That was a tough decision to make. It was not very popular, so I think now that it has been implemented; I think we will have some reports back next meeting. The executive summary was provided in here and it just summarized kind of what we just talked about here with adding prior authorizations for over 10,000 dollars to capture some of those rare disease treatments.

Lisa Todd – I kind of went about my overview to kind of talk about some of the things that really stood out that we found that really worked or we found successes. I think that especially since Holly put that compare, and contrast together, that we probably go over that chart. One thing that I wanted to really point out is that I think Anthem really tries to focus on the whole person when they are developing the pharmacy program. We look at medical and pharmacy. We do not just look at a pharmacy drug list or how we are going to limit prescriptions. We look at all kinds of things. Regarding the coverage and such, we looked at the clinical evaluations, we look at the medical outcomes when we are trying to define drugs that are covered or not covered. Our PRODUR and our RETRODUR. Our PRODUR are approved by an internal board. It is not a DUR Board, but we do have a quality board that approves those. Regarding RETRODUR, we do have quite a few clinical programs that we did see some improvements and really feel like they have been worthwhile. We have the diabetic poly-pharmacy program and we identify members that have diabetes and we look at adherence rate and drug safety and gaps in care. We have like comprehensive medication reviews. We monitor for the action on targeting the gaps in care. We do have prescriber faxes that go out if there are any issues regarding those. Behavioral health, we have quite a few little areas that we touch on. We focus on the age-appropriateness of different mental health medications. We have antipsychotic medication adherence. Also, we have poly-pharmacy regarding mental health, high-risk medication for the elderly in mental health, and we have prescriber's faxes. We have ADHD new starts, children who have been started with ADHD medications, that we make sure that they are staying on those. We will make phone calls out to the parents and guardians if there are any questions or concerns. Asthma is another big one that we like to draw attention to and focus on, we look at adherence rates, and safety. We have provider fax. We have new start for that. We also have the controller to make sure the controller's on board. If I rewind back to around the formulary setup, we are very proud of the opioids. I think it is very similar to policy the state has in place. Because we implemented that policy, we have seen almost a 15% reduction of opioids dispensed which is very impressive. Hep-C, one focus that we did last year is that we looked at Harvoni versus Mavyret. The cost savings around different things; we had opioids and hep-C and we did good work for diabetes and COPD.

Ryan Bitton – Thanks for the opportunity to present. I am going to go over the attachments that were given. The first thing is the executive summary. HPN is owned by United Healthcare and United Healthcare Community and State is an arm of United Healthcare that handles Medicaid plans. We have our own DUR meeting, the DUR board for United Healthcare. Prospective DUR, this is to discuss RETRODUR, lock-in program and appropriate clinical criteria. Our DUR Board met twice in the timeframe and did similar things that were done here, took all of those. One of the things also highlighted, it was one of

our perspective DURs that were put in place was a couple drug-inferred health state. It is people who were on opioids and who were also on doxylamine and vitamin b6. Potentially they are pregnant, should they be on this? And, so there is a message to the pharmacy, letting people know that. We really try to focus on opioids like every organization here so that was something we wanted to call out. The innovation attachment talks about pre-check my script, allow prior utilization and looking up formulary coverage in the provider's EMR and so that is something that we have ordered as an organization. Generic utilization summary, we are at 88% generic utilization and some of the things that Holly brought up, the PRODUR and RETRODUR are done by our DUR Board. We also have lock-ins about 0.13% of our population and we do a process in place if we see providers or pharmacies or beneficiaries (beneficiaries are lock-in) for prescribers and pharmacies having issues and we are able to analyze themselves within the company and go to the appropriate board. PDMP access, same story, they do not have access to the PDMP, so we cannot query that, that was one of the questions. We do utilize the DEA registrants file to make sure that people who have their DEA licenses revoked. That is proactive, PRODUR activity. It happens to right at the point of service. It does not really apply to the retro-DUR, because it was in place, so we do not need to go back a second time with that. The last couple of things, the buprenorphine-naloxone, we have similar limits to every other MCO and fee for service as well as antipsychotics and stimulants we manage the appropriate PA from the diagnosis perspective. We have age limits based on the FDA approval and the specific age.

Tom Beranek – Director for Silver Summit, thank you Holly for the comparison. It allowed me to identify a couple areas where I need to update with the Silver Summit Health Plan, one being the lock-ins. When I was submitting the survey, I could not get it to allow me to put a point number less than 1 so I put one survey, but we are at 0.12% in terms of our members that are in lock-in. Prospective DUR and RETRO, Carl covered most of that. The DUR Board activity, the data sets are kind of standard prospective/retrospective DUR. The programs are provided by our pharmacy benefit manager, Envolve pharmacy solutions, utilizing the criteria for possible procedure status by mutually agreement of the Centene Corporate Pharmacy and Therapeutics Committee as well as the health plan of Envolve pharmacy solutions and the importance of applicable state and better requirements and FDA guidelines. The Fraud, Waste and Abuse in our lock-in there and we are at 0.12% and not the 1% that I reported in the survey. We do have documented process in place to identify some possible fraud, waste and abuse with drug pharmacy benefits manager utilized what they call the Special Investigations Unit or the SIU. The SIU and PBM work to ensure pharmacy benefits are properly utilized. The PBM, Envolve, conducts and investigates products of pharmacies within our network and the results of the audits are sent to the SIU by Envolve and investigative next steps. For example, referral to regulatory agencies. Additionally, the SIU analyzes the audit findings and pursues investigations on suspicious activities of members and/or prescribers to identify during the audit. SIU will send the referrals of the pharmacy billing concerns of PBM for additional investigation efforts, as well. The SIU tracks all referrals sent to and from Envolve for investigating long-term reporting purposes. From PBMs standpoint, we do not have access to the PDMP website. I think pain management control, we did apply the DEA to control the substance registrants file. We do verify at the point of sale in real time. Buprenorphine/Naloxone, so that is the other one where we need a modified response, so it has the total amount as per day on buprenorphine and buprenorphine-naloxone combination drugs. I said no to that when I submitted it. My reason for that was for all formulary and MAT therapies, what we have in place is the first fill the seven-day supply

or less is automatically covered at point of sale if the diagnosis is entered for opioid dependence. I need to modify my response there or change it to 24 mg per day same as the other three there because we do have in our PDL the quantity limits of three per day so it's a 24 mg per day there. Antipsychotics and stimulants, Silver Summit Health Plan uses a corporate psychotropic medication utilization review program that interfaces with the PMUR coordinators to monitor the day-to-day activities. There are several triggers for review there like psychotropic medications prescribed without an identified psychiatric diagnosis, prescribing four or more psychotropic medications and many criteria there. I did want to touch on a couple of innovative practices, so in 2018, to express the HEDIS follow-up care for children prescribed ADHD metric the DUR Board partnered with prior-auth team to send a message to prescribers of targeting the ADHD medications for newly-prescribed patients and that just a reminder for prescribers to schedule follow-up visits with the patients. Also, Silver Summit helped to launch a program last October called On-Demand Diabetes Monitoring. It is a monitoring program which allows for (indiscernible) to enable to read the blood glucose levels, provide real-time numbers and results that can be intervened right away instead of waiting on the claims data. The program includes a current education and coaching aspects of standard management for diabetics so if a member does not report a reading for five consecutive days, a compliance call is made to the member and areas of testing of identified and assist the client to eliminate the hurdles, and if they had some barometers with really high readings and low readings 5 days in a row.

David England – Are your groups all working on a transition of care program? When you have patients go in the hospital or go out in the different aspects of treatment and back to the outpatient services. Do you have a transition of care so that med recs and all that are coordinated for review and follow-up? Is that something you are working on or established, transition of care between hospitalizations and outpatient centers?

Ryan Bitton – From an HPN perspective, it doesn't fall within the DUR respectively, but we have a continuity of care department, management team, that has nurses and discharge coordinators within the greater hospitals within Nevada to ensure a smooth transition to home, to a skilled facility. From a pharmacy perspective, we make sure that when you are leaving the hospital, those things get approved and make sure you are not hung up on discharge or hung up at home three days later.

David England – That is a trend that is coming out. There are some surveyors asking about it.

James Marx – One of the things I noticed that is common to all the MCOs and I think even the fee-for service is the 24 mg per day limit on buprenorphine products. I can tell you that our practice only sees your guys failures and all of them fail the 24 mg a day and we give them the 32 mg a day and we have them forever, which is not always forever but we were successful, so that's an arbitrary limit. I think it may be in the PI, that may be an issue, but I can tell you that people that do this commonly go over the 24 mg limit and for patients, the patients that are on high-dose heroin, 24 mg a day is not enough. We see them fail and they call us panicking on Friday nights and the weekends and we end up taking care of them. We are not even a Medicaid provider, so I wish we could do that and then when we call you guys and get prior authorizations and it is like a big deal. We would not call if we did not think it was necessary and then there is a delay. These patients are very, very vulnerable and if you wanted to go back off the street and then what you do is just put in a very arduous prior

authorization program and you will send those people off to the street and they will overdose or whatever or steal your VCR, whatever they do. I think having an arbitrary limit, I think there are other providers that will go over 24 mg a day, mostly addictions and psychiatrists will, people that really do this. There's a big issue, of course, with medication-assisted treatment as only a third of the providers have written a prescription for buprenorphine product and part of it is the prior authorization process, not necessarily with Medicaid but with most of the insurers being so time consuming that they just don't want to do it, that and they don't want the DEA coming through. The DEA process is very, very benign. It is not a turn over your files and we want to look in all your drawers. It is a very, very benign process so unfortunately that is an excuse but anyway, the 24 mg a day I think is something that there needs to be some sort of override available. The overrides are very difficult to get except for HPN is pretty good about overrides, but pretty much everybody else we have a hard time getting overrides and it's very time consuming and very, very frustrating to the patients and the patients that come to us are paying cash because they can't get what they need and they really want to get clean and we try to accommodate them so I think if you could come up with some way of doing a more rapid override process, it's very, very critical and looking at one person in particular, we have a big problem and we really need you guys to address it and it's really a problem.

Lisa Todd – Can I ask Dr. Marx, what milligram dose do you kind of see as more typical instead of the 24 mg?

James Marx – Well, typical and maximum are two different things. Typical, there are patients that we can start on 16 mg. That is not typical. I do not think I have ever had to go over 32 mg; 32 mg basically accommodates everyone we see, and we see the worst of the worst.

Holly Long – If anyone has any suggestions for anything that sticks out that they see for fee-for service, and we are going to be meeting with each of the MCOs in the future regarding this. This will not be submitted until June. So, we have a little time to discuss some of this. If anyone would like to speak to me after the meeting or if they want to send me an email. I can share my contact information if there are any suggestions and if you don't feel comfortable speaking up in the meetings or if you see something that sticks out that would be good for us to address, something that just doesn't align or doesn't look right or isn't in compliance, something like that, or anything, please just let me know. We will be covering that outside of here.

4. Clinical Presentations

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

David England opened the floor for public comment and there was none.

Carl Jeffery – The whole reason we brought this up, the discussion of Lucemyra, which is a new medication specific for the opioid withdrawal mitigation for people who are coming off, and this is really intended for people who have maybe have had hip surgery or some kind of extended injury where they were treated with opioids and then once

they're healed, they're having a hard time getting off the opioids, this is what it's intended to be for, a 14-day supply to help them reduce the symptoms of the opioid withdrawal. We brought up the whole category and I know there was some discussion with this class and I think there was some discussion from the state, as well, about having some of the requirements that we have on this class reduced or removed. I think that it prompted us to bring to the Board a discussion idea of either removing the criteria for the Suboxone-type drugs, the buprenorphine-naloxone and the Vivitrol which we have the criteria on to open access to make this a little bit easier for patients to get this. I think we have a couple suggestions in here. One would be the Board can take no action with buprenorphine-naloxone, up to the Board. We also have the suggested criteria for the Lucemyra which is just simple. There would be a diagnosis of opioid withdrawal with symptoms due to opioid discontinuation and request quantity to be 2.88 mg per day for up to 14 days, so it is simple criteria just to make sure people are using it appropriately.

James Marx – I have a little bit of a problem including Lucemyra and with the other agents because Lucemyra to me is basically for acute withdrawal. It is basically a very expensive clonidine. It is used on label unlike clonidine which is not used on label, so the cost of it is astronomical, I mean thousands of dollars a day, and we do not use it. We were given some samples to use and I have not had an occasion to use it yet, but the bottom line is, I do not think they should be included with medication-assisted treatment drugs. I think it is a separate class; I do not think it really belongs in that same class.

Holly Long – We are proposing a separate policy that would be in a different location because of the behavioral health aspect of it, so part of our goal is to be able to align the chapter 1200 policy along with that proposed policy and that wishes to propose policy. However, that is something if that puts your mind to ease a little bit that will be addressed in the future. While speaking I'll just go ahead and say that the state is recommending that we for one combine and decide on one therapeutic class title for ease of the providers when they're looking at the prior authorization criteria so if there is a way that we can combine the withdrawal agents and opioid dependent agents. Unfortunately, we have located it in a few different parts, it was in the chapter and that is not helpful to the provider. If we can use this time to organize that and decide on a therapeutic class that makes sense for everything to fall under, that would be great. We would also recommend that we remove all the criteria and just require diagnosis.

David England – If Lucemyra is similar in effect to clonidine and the criteria we plugged in was clonidine could have been attempted first and then the secondary failure from clonidine.

Beth Slamowitz – Its off-label.

David England – It is off label, but there is literature to support the use. Even though it is not FDA approved, we still have literature supporting its use, could we implement that? This is a secondary after failure of clonidine.

Holly Long – I don't believe so because it's not FDA approved, but we do have a policy that if they were to provide that, it needs to be FDA approved doesn't it, regardless if the provider were to provide that.

Carl Jeffery – If you were to put it in policy, I would have to check.

David England – Clonidine does have the literature, but because it is generic, no manufacture is going to do the studies to get it approved.

Holly Long – For other drugs that are FDA approved if it's not being used for or prescribed for something it is indicated for and they do have literature then we are able to do that for people, but if it's not FDA approved, then I don't think we can.

James Marx – In fact, I have never seen anyone fail clonidine, so I think it is like you are talking about black swan.

Netochi Adeolokun – Can we wait for some head-to-head trials to see how it compares to clonidine?

Beth Slamowitz – It comes down to really the intent of bringing this forward, can we put this all in one bucket and call them substance-abuse agents or whatever title you want to give them. Then really it would be able to open and have access to these medications and we move forward to look for the medication assistant treatment policy in place so that when we go through this effort and put that in policy in place, restricting providers based on the use of medications to perform that measure. We are really trying to ease accessibility and to allow more providers to be able to use that and provide these services. Taking that into consideration when you look at these drugs that are put forward to make that decision whether we can place them all in one class. And if we do, what criteria do we really want for that class to make sure that there is adequate accessibility as possible while still maintaining the safety in the class.

Holly Long – And not just for that policy, but also a lot of the resources and a lot of the information that's coming out right now, like AMA in support of removing all policies for any substance-abuse treatment drugs right now. The CDC is pushing for that. There are numerous high-level resources that if you are going to do this, you want to be in line with the whole opioid crisis movement, this is part of that. And many states already have this in place where they removed this through criteria to open that access.

James Marx – I am really concerned. These alpha-agonists are rather big. I have been using them for 25 years and I can tell you, I have a lot of respect for them. Yes, we want to have them accessible, but I do not want people handing them out M&M's, either, because you will have problems with them and there will be serious problems. People will fall, break their heads open and do a whole bunch of other things and die. These are not innocuous drugs and just because there is an opioid crisis, we should not be throwing things out like they are innocuous. These are not innocuous and the only advantage of the Lucemyra was if it was packaged in a smaller dose, so it is a little bit harder to really hurt someone than you can with clonidine which is much easier because it is a larger dose. But I am very uncomfortable with just saying, I think the prior

authorization process for those should be a lot more rigorous than just saying, we are not going to have one and that is my concern.

Beth Slamowitz – The option you have is to remove the criteria for this drug in and put it in its own class.

James Marx – It is in a totally different class than these other drugs. These drugs that are either opioid antagonists or they have no relationship to those other drugs that are used in medication assisted treatment or sobriety treatment like the naltrexone. It is a totally different class and I think that there needs to be some sort of imposition. The providers are going to be detailed on these and start passing them out like candy.

Beth Slamowitz – So what would be your recommendations of the Lucemyra, and to what class?

James Marx – I do not know what the answer is. I use them frequently, but I cannot just sit someone down and make them competent in a three- minute call center call.

David England – Since they are in a different class, if you want us to look at how to reclassify things in general, I doubt we are going to have accomplish this in this meeting time. I think for the sake for the PA edits, I would consider going with these criteria and if we are going to the path for the other medications, we remove them as the CDC and AMA recommends. But this one, just consider with Dr. Marx concerns, I would say leave them in the substance abuse class right now and as it progresses, we can pull it out but at the same time, I'm not sold on the fact that it doesn't need criteria. I can see loosening the criteria, but where are we going to go with this?

James Marx – One thing I did not get to point out is if somebody got a prescription for Catapres or clonidine for blood pressure, there is no prior authorization process for that whatsoever. Somebody could start writing those like candy and you would never even know it. Therefore, I am not sure how you would even know how that would even be caught in the Pro-DUR to even capture that to do a prior authorization process. Because when you see that clonidine come through, you do not know if it is coming from blood pressure or for withdrawal treatment, so I do not even know how… The Lucemyra, obviously you're going to know that's an on-label indication and people are going to use it for that but if they're using clonidine, you don't even know it so you're totally ignoring the fact that the reality of the clonidine is used without any sort of prior authorization whatsoever is the same drug basically.

Holly Long – To kind of redirect everyone and provide a little bit more information again. It is at the end of the section within the DUR binder. The buprenorphine, naloxone is currently labeled as a therapeutic narcotic withdrawal therapy and then the Vivitrol or naltrexone is labeled opioid dependence agents. Is there a way to combine those two? Part of my concern is the organization of it.

David England – I see where you're coming from, if you want to consolidate it, I think a quick consolidation would be what we have in there now, substance abuse agents. I think for now we will keep these criteria but look at the other criteria that Carl has for

us that we are going to review for the other products. But at least stick with this for now it is better than nothing even though it is not all that good.

Beth Slamowitz – We still need recommendation that we call it substance abuse agents.

Holly Long – We're going to reorganize it because of the two sections that I listed right now just for the organization piece so that there was section within the chapter that is labeled or titled substance abuse agents. Within that I will keep the two until we make the decision for the buprenorphine and for the Vivitrol and just put that together with substances including several of these in place.

James Marx – First of all, I would put buprenorphine and the naltrexone in the same category. I would not separate them.

Georgette Dzwilewski – You are talking about a new category, I just met with the UCSD and they were saying how MAT, or medication assisted treatment, that terminology kind of going away. And, more terminology like medication in patients with addiction to opioid use disorder is more appropriate or medications to treat opioid use disorder is going to become the new norm rather than MAT.

(Indiscernible speaker)

David England – I think we should stick with substance abuse for now and then look at that in future meetings. Especially as this person commented as this is developing, we can adjust to it but I don't think we're going to be able to come up with it; if we group the categories tonight before we need to go home it would be a success but at least we'll have a starting point, some place to start with and somehow we will get approved again, but I do need to evaluate it at this time.

Carl Jeffery – We had an opportunity because we were adding to this class and it was an opportunity to bring back the whole class and discuss it if the board was for it. The current chapter 1200 criteria in your binder. It starts on page 71 for the buprenorphine-naloxone. Page 73 is where the Vivitrol starts and that is what Holly was talking about. There are two different locations in chapter 1200 and so that was the idea of putting them under one location so when providers are looking for what kind of resources are available, what state covers. There is one location in chapter 1200 that can go and find that resource.

David England – I think the substance abuse drugs would be a good category until the industry and the healthcare field determines a better way of organizing.

Carl Jeffery – There is a push nationwide and within the state and a lot of the stakeholders to remove some of these restrictions and one of the possibilities that we have with the buprenorphine-naloxone product is to only require a diagnosis on the drug. This is what I have up here so we can put a diagnosis requirement on the claim, an ICD-10 of opioid dependence so we can require that diagnosis and remove the remaining restrictions because it gets pretty complex with the information in chapter 1200 right here that they've got to call in, they are limited to age, they had a diagnosis

of opioid dependence, request for diagnosis of chronic pain will not be approved; but all of this would be accomplished with just that same edit within the system, looking for a diagnosis. The other criteria probably not as critical. There is documentation the recipient has honored all their office visits. The prescriber has the X-DEA number and an affidavit saying the recipient will not utilize opioids and the recipient is currently not utilizing opioids so all of that would be forgiven with just that single diagnosis. I think that's consistent with kind of what the State's direction.

Ryan Bitton – From the MCO perspective, we do not have prior authorization on Suboxone. Suboxone is our preferred. It is on formulary, we used to have X-DEA and all that, but we removed that, so there is just the diagnosis touch on Vivitrol.

James Marx – Why we excluding chronic pain for the diagnosis of it, because it is off label?

Carl Jeffery – Yeah, it is off label and you may disagree with me, but I think there are better treatment options.

James Marx – I totally disagree with you because I think buprenorphine is going to be one of the drugs in the future for treating pain and I totally disagree with you. We use it as many, many patients who prefer it to oxycodone to hydromorphone because of the longer duration. Very, very satisfactory results and patients really, really like it and do much better, and I am not the only person that feels that way. There are many people in the pain community that agree. I am not sure that you need to line up with naloxone, and we end up using the Subutex, the single agent, but we use it extensively and very satisfactory and we try and move patients to it because it has much lower propensity for overdose, for respiratory depression, adverse psychiatric effects, so it is really a better choice. I think that excluding it, if all the patients of Medicaid that were on conventional opioids were moved to Suboxone, we would have a lot less overdoses and there would be a lot less overdoses in the street. It would solve a lot of problems, so I totally disagree with what your contention is.

David England – I would entertain a motion if someone comes up with how to address this. My original thing would be to accept these edits as proposed, I seem to agree with Dr. Marx. There are some things we need to keep some criteria, but how do we want to do that with this.

Holly Long – We want to make sure we require the diagnosis.

David England – If we have the diagnosis of opioid dependence.

James Marx – Well why not just take that sufficiently that there is a diagnosis of opioid dependence? That should be sufficiently, and then you do not have to go any further than slicing and dicing.

Netochi Adeolokun – I agree with the diagnosis of opioid dependence.

David England - Now, do we want to still weave these into the category of substance abuse agent, but then the criteria would be opiate dependence. I am getting the sense that is the path you want to go down.

Michael Owens – The opioid dependency includes chronic pain management, correct. This falls under that.

Carl Jeffery – No.

Michael Owens – You are doing what he is saying, this is a great way to treat pain and that is going to be…

James Marx – Yeah, and those patients most of them are opioid dependent because they started, and it was treated early.

David England – Opioid dependence is one thing but other distinction, that is different criteria. So, basically, we will just go with opioid dependence as the criteria for all three of these medications under the new class.

James Marx – I mean, if you want to get technical, if you say what opioid abuse disorder, that really is the issue, not opioid dependence. That is really the crux of the problem. It is an abuse disorder and there are opioid dependents who are not abusive.

Jennifer Wheeler – Is there a way since we require the diagnosis codes with all the controlled substance prescriptions to pull the most commonly used diagnosis codes?

James Marx – They are going to be required for all opioid prescriptions.

Carl Jeffery – Well, yeah, right now and we do not do any edits on that because we require PA on all of them so all of them are going to be opioid use disorder.

Jennifer Wheeler - Just to find out what the most frequent… to make sure that we were covered and that we have it.

Carl Jeffery – Well, yeah, but all of them…

Holly Long – FDA approved indication, as well.

Carl Jeffery - Right now everything requires prior authorization, and all of these require prior authorization, so they should…

Beth Slamowitz – The only way you are going to have a paid claim is if it has a diagnosis of opioid dependence and that would require prior authorization.

(Multiple speakers)

Carl Jeffery – Well, there needs to be an ICD-10 diagnosis on the claim and so I am not….

David England – Using the opioid dependence.

James Marx – Not a DSM diagnosis.

Carl Jeffery – Right, and did the board want to add a max dose? I suggested 16 on there as the starting dose and anything above that would require some additional but context of what Dr. Marx was saying earlier, I do not know if that dose needs to be open for discussion.

David England – I would say let's stick with opioid dependence for right now, we can fine tune the max dosage based on criteria that they have prescribed on the patient before as opposed to a mandatory limit.

Carl Jeffery – So you would not have a max dose at all on it? Is that what you are proposing then?

David England – If we have a maximum of something? I would go with 32 mg.

James Marx – I just go 32.

David England – As opposed to 24. It appears 32 will treat most patients.

Carl Jeffery – So I'm hearing the updated criteria for the buprenorphine-naloxone products would be diagnosis on the claim of opioid dependence, and the max dose if it doesn't exceed 32 mg per day.

Jennifer Wheeler – So the prior authorization is for the 24 mg even though that is the max dose of the manufacturer's studies.

David England – It needs to be FDA approved…

Beth Slamowitz – That is for indication only. You would have to put quantity limits in place if you wanted to be within those guidelines.

Jennifer Wheeler – Prior authorization anything over that?

David England – Yes. Ok, prior authorization anything over 24 mg. Is that acceptable?

James Marx – I still would like to have a 32 mg available but… The problem is that a lot of times the PAs do not get done fast enough and the patients end up with a treatment gap.

David England – Nothing's been said that they can't exceed that, or they should go over, but they need to submit a PA, at least that's the process to get going as opposed to blanking the drug.

James Marx – I think really the crux of the problem is the overrides are so cumbersome that either the pharmacies do not want to do them or whoever issues the overrides does not. If the overrides that were supposed to be there for like a three-day or four-day override, we never seem to be able to get those overrides and that is the problem. If we get the overrides, I would not have a problem, but we cannot get the overrides.

Thomas Beranek – So it takes minimal effort to provide retail pharmacists.

James Marx – Well that may be where the problem is.

Lisa Todd – The retail pharmacists may not be willing to…

James Marx – Well if that is the case, then they should let us know. But they do not say that. They say, well we cannot get an override. We tried, and we cannot do it. That is what they tell us.

Thomas Beranek – Does not even need an override. They just need to put the code in right.

James Marx – No, the go to the 32. So, do we have vote or motion?

David England – We're still using this substance abuse class, but they all have opioid dependence diagnosis for allowing the PA to require dose over 24 mg and then the rest of criteria opioid dependence diagnosis.

James Marx – I'd propose an amendment if that's possible, the proposed increase the 24 mg to 32 mg, and anything above 32 mg would require prior authorization and I don't think you'll ever have to do one.

David England – Is there a second to that amendment? No

A motion to require prior authorization on doses greater than 24 mg per day and a diagnosis of opioid dependence on the claim. Second. Voting: Ayes across the board, the motion carries.

Carl Jeffery – Just for a point of clarification, Dave, Lucemyra…

Holly Long – I believe the suggestion was a different diagnosis wasn't it? The diagnosis of opioid withdrawal syndrome.

David England – You have opioid withdrawal or opioid dependent. This will stay as it is for now.

Carl Jeffery – The motion you just voted on includes the Lucemyra, buprenorphine-naloxone, and the Vivitrol?

David England – Yes.

Holly Long – Just for clarification, have a vote on the Lucemyra, because my understanding the way that they explained it is just for the other…just to make sure we are meeting open meeting law.

David England – Lucemyra add as proposed?

James Marx – Is that going to be an eliminating diagnosis because there are situations where you want to get people off opioids and not necessarily opioid dependence in the negative sense. They may have to do it to comply with a court order. They may have to do it for upcoming, they may be pregnant or if they want to be opioid free in their pregnancy, so there's a lot of situations that might not be an opioid dependence issue. It may be a situation of convenience and for patient comfort.

Holly Long – Carl, do mind just going over reading Optum's proposal for Lucemyra?

Carl Jeffery – Yeah, so on page 59 of your binder is the proposed criteria on here and the approval criteria for the Lucemyra is the diagnosis of an opioid withdrawal with symptoms due to abrupt opioid discontinuation and the requested quantity does not exceed 2.88 mg per day for up to 14 days. For prior authorization to be approved, it would have to have to be treating the acute symptoms of opioid withdrawal and this will be the max dose and it would not be approved for greater than 14 days. So, they would not be able to continue this indefinitely. It would be limited to 14 days.

David England – Is there any need to exceed 14 days?

Carl Jeffery – I am not aware of a study beyond 14 days.

James Marx – I cannot imagine why you would want it.

David England – We put that in line and consider the motion is to accept this as presented. Are there any further questions, comments, or discussions?

Voting: Ayes are unanimous, the motion carries.

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).

David England opened the floor for public comment and there was none.

Carl Jeffery – This was just brought up because it had been a long time since we had last discussed it, the ADD/ADHD medications. On page 89 of your binder is where it starts. The criteria included in the binder and is exactly what is in chapter 1200 currently. This is just the opportunity for the board to review this and make any updates as they see fit with this and to give the MCOs an opportunity to suggest some changes as needed. The only change that really drives me crazy, and you will see on the top of page 91, is the removal of the criteria that says 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, crisis or abuse or neglect. I feel it does not provide any different outcome based on if this is evaluated or not. My suggestion is to have that criteria removed from the current criteria and then the rest of it remain the same but again, it is an opportunity for the board to review the criteria and make any recommended changes. I know some of the MCOs have much more lenient guidelines and I think some of them are kind of open. That was Optum's recommendation for the fee for service side.

David England – How does the board feel about dropping that requirement?

Netochi Adeolokun – I agree.

David England – Does the Board have any questions or comments?

Voting: Ayes are unanimous, the motion passed.

c. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for Androgen/Testosterone Replacement Agents.

David England opened the floor for public comment and there was none.

Carl Jeffery - It does start on page 135 in your binder. There is a new medication here. Xyosted is a self-injected testosterone product so it is once a week. It is kind of like one of those subcutaneous injections. It is something that you do at home, so you do not have to go to the doctor's office anymore. I think it is probably going to be a very popular product. To be consistent with the current testosterone products that we have, we have the topicals and I thought it would be a good idea to include it in other criteria, as well. It has criteria that mirrors what the other products currently have and so they have a diagnosis of hypogonadism. They are a male patient at birth, and one of the following: Low pretreatment levels. And then they have both of the following: The patient had a condition that may cause altered sex hormone binding globulin or one pretreatment with calculated available testosterone, level less than 5 ng/dl or the patient has a history of one of the following: bilateral orchiectomy, or panhypopituitarism, a genetic disorder noted to cause hypogonadism. Or the other criteria for gender dysphoria which is off label but to be consistent with what we've done with the other hormone treatment agents with the GNRH analogs so using hormones to change physical characteristics and diagnosis of gender dysphoria defined by the current DSM and the patient is a female to male transsexual. We have the reauthorization criteria which is similar. It begins on page 139.

David England – So basically, you will be able to pick up from the pharmacy and take home and self-administer. What is the possibility of diversion or misuse, because it is being administered outside the office and even though it's long-acting, the effects go for a week, there is a possibility of a limit of days.

Carl Jeffery – It is no different than the topical testosterones that are currently available like Andro-Gels. The possibilities are the same with those. It is not different.

David England – Does the Board have any questions, concerns, or comments?

Ryan Bitton – It is a 14 days initial approval? I know that is one of the recommendations I made.

Carl Jeffery – On page 136, the initial one is 14 days. I think it is just for the tolerability to make sure that it is tolerated.

Ryan Bitton – HPN's initial authorization for 12 months on the first request.

Carl Jeffery – That would be fine with me.

Ryan Bitton – And we did put the 1% topical as well as in our criteria, a first line generic from there…

Carl Jeffery – From the fee for service standpoint, we usually do not put any kind of step therapy like that into our DUR guidelines.

David England – Does the Board have any questions, comments or concerns?

Carl Jeffery – I like Ryan's idea that approval length of the criteria currently is 14 days is what I put on there as far as a trial, but I think it's worthy of a board discussion if you want that six or 12 months.

Jennifer Wheeler – Do you know how it is packaged? Does it come as a pen or is it an autoinjector?

Carl Jeffery – Yeah.

Jennifer Wheeler – I assume you do not want to make a pharmacy break a box.

Ryan Bitton – They come in cartons of four auto-injectors.

David England – A 28-day supply good for 12 months.

Motion to accept the change to initial approval of 12 months. Second

Voting: Ayes across the board, the motion carries.

David England – Now a vote for the rest of the criteria.

Motion to accept the amended criteria. Second.

Voting: Ayes across the board, the motion carries.

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

David England opened the floor for public comment and there was none.

Carl Jeffery – On page 170 for the criteria, we brought the fentanyl in here and we left it vague because we wanted to talk with the board both about the transdermal fentanyl and the IR lollipop fentanyl. We are seeing quite a few of those that are utilized on here. The criteria for the topical, we will start there, is presented in your binder on page 170. Right now, nothing is presented as being recommended as changes. I think the criteria we have in there is sufficiently. We have the MEQ, the comparison for the dosing and I think that is a good reference for those. No change is recommended on that one and then we get into the prior authorization guidelines for the oral fentanyl products and this is like the Abstral and Actiq and the Fentora and the Lazanda and Subsys. The fentanyl oral either lollipops or sprays and this is the same as what is in chapter 1200 currently, as well. I did not make any recommended changes, but I think you can see the utilization numbers. They start on page 180. This includes all fentanyl products. You can see the Subsys and we have some of the fentanyl lozenges. There is maybe a total of about six members that are on this over the course of the year and they get about 40 claims. We are not seeing a huge number of claims go out for the IR fentanyl products and very limited to just hospice care or palliative care.

David England – On page 170, it talks about the following patients can take the fentanyl patch from any other opioid and one of the following: Morphine equivalent dose of 134 mg a day or less and requested dose of 25 mcg per hour every three days. The last time I was involved, some of these things, the ones I've been working on have been starting on about 25 mcg per hour and 25 mcg the first day; they do an equivalent 60 mg equivalents of morphine a day for a week. This says 24 mg a day or less and start on 25 mcg per hour patch every three days. Is it 134 now, is that the manufacturer's recommendation?

Carl Jeffery – This is just what the current chapter 1200, this is the same criteria that we presented when it was in 2016 or so. I think that was when it was last reviewed. So, the board discussed it at that time and this was the recommendation and I think that we both tried to. I do not remember where we got that reference.

Jennifer Wheeler – On page 170 on number four, we may want to amend that to prescribers encouraged to check the Nevada PDMP. Change that to required?

David England – So number four, change encourage to required? Does the Board have any questions or comments?

Ryan Bitton – We roll our transdermal products into long-acting opioid criteria. We do not have a specific transdermal patch policy, it is the same as like OxyContin.

James Marx – I think a lot of prescribers now have somehow been infected with the idea that patients are dying from prescribed fentanyl products and that is not true. We see this commonly, and as an aside, one of the heads of the comprehensive cancer centers in Las

Vegas, over a quarter of their prescribers will not write opioids whatsoever for any patients with cancer. The pendulum has really swung way too far the other direction.

David England – I think we do need to have appropriate pain management, and at the same time, I think the public needs to have an awareness effective yes you may not be pain free, but you'll have pain that you can bear and live with. As opposed to being treated completely out of the picture because you have so many pain meds you are not coherent. I think as part of that discussion the healthcare providers also educate the public and here is what is practical.

Michael Owens – I have some patients will come and not on an opioid, I have had two patients with severe metastatic malignancy. I will prescribe an opioid I am comfortable with but then our local pain specialists and we will pick them up rapidly. If there and somebody with back pain, they get in the queue and wait their turn but metastatic pain I think is treated appropriately.

David England – For opioid dependence, it is an issue and at the same time, I think we need to education on both sides and in fact, that is what is utilized in a hospital. Yes, you can control your pain, but the thought of possibly being totally pain free is something that we can start with. But there is nothing you can do as a practitioner prescribes this, as well. Does the Board have any questions or comments?

Holly Long – I just wanted to bring up that I had the DHHS pull the data if anyone is interested on the fentanyl overdose in Nevada. That is on page 187. This was a tough one to get. We wanted to try and get it be as accurate as we possibly could. The cause of death and listed those there. Now, of course, we cannot say this is due to prescribed fentanyl, but this is just overdose in general in Nevada.

James Marx – There is a big problem with those numbers, though, because one of the issues we have in Clark County is that there is an accreditation agency for forensic pathologists and their standards for accreditation state that forensic pathologists should not do more than 250 forensic autopsies a year. In Clark County, the typical forensic pathologist does between 750 to 1000 and as a result, a lot of deaths are written off as overdoses. If there is presence of a drug and the patient died, it is written off as an overdose death and obviously there is not sufficiently oversight that is really taking place there. It's a really serious problem and really skews the figures tremendously so I think you look at those numbers with a little bit of skepticism because there really isn't adequate time to really work that out.

Holly Long – Just something to be aware of. I was also recently provided a rather interesting report that included information about Homeland Security considering labeling it as a weapon of mass destruction considering how bad it is nationally.

David England – The fentanyl they are talking about is not coming out of pharmacies. I think that sometimes, when we are talking with patients who make that distinction. The stuff that is on the street is a whole different ball game than what we are dealing with a prescription.

Holly Long – I think we do, considering and comparing what we have for prior authorization material and fentanyl compared to other states. We have structured…The only question that I have on here was the quantity limit; what is their quantity limit on each of those?

Carl Jeffery – It is on a different list, but I want to say it is one every 48 hours. I will double-check that.

David England – On the third page of the prior authorization, it says when the patient…

Carl Jeffery - Currently, lozenges like the Actiq 120 lozenges for 30 days, Fentora 120. The Duragesic is one patch every two days if failure to achieve pain relief is documented and clinical notes were provided to the clinical call center. Otherwise, there would be one patch for three days.

David England – One patch every two days, every 48 hours or 15 per month.

James Marx – I have some patients on four patches every two days. If it does happen…

Motion to accept the edits as presented. Second. Voting: Ayes across the board. The motion carries.

5. Public Comment on any DUR Board Requested Report

David England opened the floor for public comment and there was none.

6. DUR Board Requested Reports

a. Opioid Utilization – Top Prescribers and Members

Carl Jeffery – On page 215 starts the fee for service overall summary for the opioid utilization. Similar trends to what we have seen in the past. Still a downward trend. If you look at our last month, we reported December 2018, 7500 members and just over 10,000 claims. This trend from January 2018 we're seeing almost 13,000 claims so it's going down quite a bit and the seven-day supply is also there and just a quantity per member. On the next page on 216, is the top 10 opioid prescribers by claim count so we broke these down by quarters, as well, so you can see the last quarter. We have had that anesthesiologist from Henderson, as our number one now. We had that nurse practitioner that was our number one for a long time. I think he has completely fallen off the top ten, so I do not know if it was either effective or scared the wits out of him and now he is not prescribing anything for Medicaid patients or anything, so I do not know if that is a good thing or bad thing. We have another the oral surgeons, number two has been on there for a while, and then the rest are pretty much the same for pain management in Carson City, but still the numbers are holding consistent quarter per quarter. If anything, maybe a downward trend except for maybe the last quarter that starts in July. Moving on the opioid utilization by member of the top 10 members by claim count, so looking at the whole year here. There are a couple highlighted

prescriber NPIs that correlate so when we get down to page 218, you can see there's that one encrypted ID has that prescriber L, that corresponds to the other prescriber in the top 10 list. Otherwise, they do not correspond with those. You can see the number of claims they are getting from each prescriber. I think this is the last one we have in here, it's the breakdown of exactly what our top 10 members are taking and the therapy that they're on, so on page 219 it's where that starts. Still, I do not think we are seeing any real alarming numbers that I can notice easily. Any questions from the board on this?

David England – These are the claims throughout the year?

Carl Jeffery – All of 2018. You can see the middle column that has the day's supply in here, you can see if you add it up. There are some members on here that have 720 days of opioids during the year so that means they're on concurrent therapy, which would make sense like the one I'm looking at is on page 219 and ends in 6249, they're on an OxyContin-ER, extended release product with a short-acting product for rescue and I think that therapy makes sense.

Lisa Todd – We have seen a decrease in our opioids. If you compare quarter to quarter, it looks like it is the same drugs or the same offenders as far as what is being prescribed. There is not much change. Our numbers are decreasing. As far as our top 10 prescribers, we did this time which we had before was the physicians city also, I do think that one of them is the top 10 providers in Texas.

Carl Jeffery – Well, in Lakewood, Colorado. We sometimes see this, too, but that is just where the billing office is and so sometimes our address is screwed up.

Lisa Todd – It would also be we are the secondary payer. So, if the member has primary insurance and Medicaid second, then it might be primary insurance that are allowing these providers.

Carl Jeffery – You would hope those providers would not show up in the top 10 though.

David England – With the fee for service, even though we are seeing decreases in the use of opioids, how are these patients describing their pain management. Are they still happy with or do they just grin and bear it? Are we seeing patients with the decrease in opiate use, and with the pain management, are we still seeing congruence with that?

James Marx – That is the question that no one ever asks. Not only satisfaction but function I think is even more important and that quotient never gets really expressed. We can cut down on everybody's opioids; there is no problem in doing that but what is going to happen to those patients.

David England – How would we know? Yes, we are decreasing opiates but are our patients still comfortable? Are they still comfortable and are they still functional with the decreased opiates or are we also adding alternative therapies? Are we still getting good patient satisfaction? I think that is the question we want to ask ourselves. Are we are doing our part by decreasing the opiate use but are we still taking care of…

Lisa Todd – And how do we measure it?

Carl Jeffery – I wonder if we can look at some levels of disability claims for the Medicaid population. I do not know if we have access to that data but like the disability claims because someone who has so much pain they cannot come back to work.

Holly Long – Currently Medicaid does cover chiropractic services to a point, but I believe it is only for children. We do not cover for adults. And, that's something that comes up annually to change and is looked at, but we haven't been able to justify that so that remains the same. We do not pay for any acupuncture. I am trying to think of other examples. We do have therapy services but most of it is for children and not for adults. That is for physical therapy type of services.

Beth Slamowitz – I think you look at it from both sides, it's very difficult to look at data to tell us whether the patients are still receiving a certain follow-up with pain management. But it is also very difficult to look at the data and say, why were they given pain medications to begin with and was it appropriate to begin with. Which is why they are putting that criteria or policy in place, are we putting something appropriate in place. Are the patients still being taken care of, but we are also looking at it from a safety and efficacy standpoint and do we see a decrease based on policies that we put in place, hopefully that policy is appropriate, and that decrease is appropriate as well?

James Marx – I can tell you that we get 10 to 15 calls a week from patients who have been involuntarily tapered and I don't know if it's inappropriate or not. But they are seeking some sort of correction in that situation, so I suspect that is a very, very small percentage of the patients who are impacted, but I think there is a lot of patients.

David England –I do not think this is something we can measure easily, but we should keep in the back of our minds. Even though we are doing something appropriate, how does it impact the patients?

Lisa Todd – So, then the top 10 utilizers, I did not look at disease states for these members. I do not know if anything really stands out too much.

David England – I think for myself, I like numbers but at the same time they get numbing after a while. Let us cut to the chase, is there a number that stands out.

Lisa Todd – I think there's always more to the story when you're talking opioids and even when we were talking about fentanyl earlier and different things, there are a lot of our members on that do have cancer. Nothing really stood out too much to me.

David England – I think all in all, I think we are taking good care of our patients. I just want to make sure our data is leading down the right path as opposed to just numbers but there is really some benefit here.

Ryan Bitton - I did not figure out the actual slope of the lines. The trend looks about the same. From our perspective, I think it is probably in line with everybody. If you look at the top prescribers, we had a prescriber L and O kind of dropped off. One of those was pain management so now we see that pain management at the top for prescriber perspective. Seems relatively consistent. Then, the top 25 members. There are eight members who I think four of the top prescribers and two of those prescribers are in the same clinic, I think B and C because those are seeing the same members. That is kind of the summary from HPN perspective.

James Marx – I have an idea that we could possibly do, and I hope that Holly does not take offence. But I think that the point you make is that we have these patients… we know who these opioid patients are. Why don't we send them questionnaires and say, have you been impacted by any change in your prescribing and how does it affect your life. I think that would be very valuable and I think that really would be far more valuable than maybe talking about and getting my opinion, which is just one guy's idea. I think it would really be valuable to go to the patients and see what they really are saying and see how they're impacted because that really would give us some information. This stuff is just like, raw statistics.

David England – So Holly what were you talking about other states, have they done that? Have they may be questioned, like our top 10's here, or just a sample of our patients and maybe ask that type of question. Would be that something we could do or what would work?

Holly Long – That's something that I think you could work on and be encouraging and supporting on that aspect of it but that's really something that would have to come from the providers and not from us, and it can't be with the Medicaid sponsored.

James Marx – The CMS does all kinds of surveys and all kinds of situations and providers and institutions…

Beth Slamowitz – CMS does not usually contact patients directly.

James Marx – They do surveys of hospitalized patients; that's part of the patient quality survey so I mean it is being done.

Holly Long – Right, but that does not mean that the prescribers are. There are other avenues to investigate.

David England – Even if the prescribers did not want to do it with the patients, how does that give us any good feedback and what we are doing.

James Marx – Prescribers are already overloaded with the compliances with AB474, 459, 259, 630 – all of these – the prescribers are totally overwhelmed right now and that's a big impact on the prescribing load and how many are willing to prescribe so it's not going to come from the prescribers. It is nice to think but it is not going to happen.

David England – Along the same lines, Medicaid has a website, though. Do we get comments or feedback from patients?

Holly Long – We do have a general pharmacy email address. We do get information sometimes.

David England – Could that be presented to us?

Holly Long – I think the best information would not be coming from this email address. I think the PA data would be more valuable.

David England – Would that be able to be presented?

Holly Long – The emails I get are so broad and all over the place. I do not think there is anything consistent there. As far as raw data, the HPM's or other information around PA's. The only feedback we get that are not numbers.

David England – Would the MCO's be able to present something like that too?

Holly Long – HPM's are hearing prep meetings. It is an avenue for members or providers to appeal the prior authorization decision. I think the MCO's have a similar process, is that right?

Ryan Bitton – Yes, we have appeals and then to state fair hearing after that. But we have not surveyed people.

Beth Slamowitz – I do not think we are going to get to what you are looking for with this data. The only thing we could do is a patient satisfaction survey that would go to providers.

David England – I think this information would be valuable.

Holly Long – I have not heard of anything from other DUR programs.

Thomas Beranek – The data reads a little different. Our membership was growing over last year, so our graphs look different as the utilization goes up. It is because we were adding more members each month. There is not anything glaring in this data.

b. Top Claims for Member Under 18 Years-Old

Carl Jeffery – This is a Board-requested report from last meeting. I broke it down, we have the first one that starts on page 237 is for all medications and then the subsequent pages indicate with different classes here. It has broken down by quarter and by age and so the first page here, it says ages zero to one- year old. I do not think there is anything that is weird here. With Albuterol and amoxicillin, what you are seeing as your top claims on there. I do not think that is anything unusual. Age one to four is the next category. Again, albuterol and amoxicillin and then we get into the five to nine and then we start throwing in some cetirizine, the fluticasone sprays and some of the other…

David England – And some clonidine.

Carl Jeffery – Clonidine? Likely it is used for ADHD. We still see the regular release to clonidine. In the last category, there is the 10 to 17 so then we get into the teenagers and still I do not see anything that I would find very weird on these. The next category here is your opioids and so again, this starts on page 241, your ages zero to one- year old, it is under one-year-old. You have short course opioids as your number 1 and I am guessing either that or methadone which I am guessing are your babies born to mothers who are also using opioids. It continues with one to four. There is nothing, I do not know who is writing a Demerol shot for under four- year old. So, there is a couple of things that are a little concerning on here. The five to nine, continues to be on here. Still not a whole lot of utilization on these so we're still looking at a small number of claims until we get into the 10 to 17 and now you're talking into getting the teenagers with sports-related injuries and more ER visits and jumping off monkey bars. They are a little bit crazier. The last category here is the psychotropics, and it's just I think a good overview of what we we've been looking at with the other psychotropics and it's probably good to review these but under one.

David England – Most of these appear to be for seizure.

Carl Jeffery – Yeah, so you get the phenobarbital and Onfi. That is not unexpected. One to four, again ties into this and then they will start throwing in some hydroxyzine maybe for some sleep or anxiety. I am not quite sure exactly what they are using that one for. Then when you get into the five to nine, then you start seeing more of the risperidone and the guanfacine and the ADHD medications and in the 10 to 17, then you're getting more into the Risperdal and the antidepressants, as well, and antipsychotics. Nothing that I would really be concerned about with any of these numbers.

Lisa Todd – From an Anthem perspective, I do not really see anything that really stands out. We just look at all claims. It looks to be typical for the kids under 18, and it's kind of interesting and typical that when you do drop it off and work from five to nine, that's when you start seeing a lot more suspensions and chewable tablets, and similar formulations. But, as far as the regular claims, nothing alarming. The opioids, I did kind of look at these numbers a little closer and it didn't look like there were a lot of repeat customers or repeat kind of fills, so kind of maybe the jumping off the monkey bars kind of thing. It's the short-term use compared to the long-term use. So as far as opioids, it does not really stand out anything more. As far as psychotropic, I think there is a lot of ADD medications and some of the antipsychotics. I always want to look closely at some of the very young kids receiving some of those medications. I think I looked at some of these members and just verified and there were some of our kids under, 0 to 1, receiving these medications and I just do not…, still kind of mind baffling, you know what I mean? But, it is the real deal.

David England – As long as we are monitoring it, that is the important thing and be sure our policies are appropriate.

Ryan Bitton – From an HPN perspective, I am not sure there is anything we want to add. Reviewing these, I do not see anything, it is inappropriate in age and inappropriate from a trend perspective, to make it different. We have periodic discussions within our health plan, the behavioral health organizations about inappropriate anti-psychotics in youth so we have age-appropriate use but some of those things will slip through like risperidone. We're going to sit down to see if the medical plans back up what we got from a pharmacy perspective to see if that's an appropriate use there, but I don't think the reports are anything alarming from my perspective.

Thomas Beranek – For Silver Summit, I was going through our reports while Carl was discussing fee for service and pretty much mirrored exactly what he was saying on his reports that he has had less claims. Really nothing to call out, for the case of one claim or zero claims but all the other ones, under one and one to four and then the top 10 and so on, pretty much mirrored exactly what Carl said for fee for service.

David England – So we are not seeing anything out of line, sounds good.

7. Public Comment on any Standard DUR Report

David England opened the floor for public comment and there was none.

8. Standard DUR Reports

Carl Jeffery – Page 282 starts the Standard DUR reports. Here we have used the standard format and the different programs should look the same here.

David England – Anything that stands out from the time before? I do not see a whole lot jumping out at me.

Carl Jeffery - It's kind of interesting when they're all put together and all the different programs; you can see our different Pro DUR programs work and how they identify even though they're similar edits, they put them in different buckets just a little bit different in that perspective but otherwise, we've watched the Pro DUR's every month. We report these and anything that is very weird then we will look more into those on a case by case basis. We are working on, there was some new legislation or a rule that came down adding opioid edits, something that we talked about at ADURS was using opioids with anti-psychotics, atypical antipsychotics. Not sure where this came from at ADURS, but it is a CMS requirement that we have an edit that identifies members who are on opioids and atypical antipsychotics, so we will be working on adding a Pro DUR edit on that. It will be in place by October first, so we will be ahead of that, but that is something that is coming down that is a requirement.

David England – Nothing really stands out or?

Carl Jeffery – We're looking at the top 10 drugs by paid amount in the previous and current quarters still have the hemophilia drugs. We have some criteria that is going to go in I think in June that will add the Board-approved for the anti-hemophilia

medications. So, those will be added soon. I think that will have an impact where maybe we will be able to get a handle on some of this stockpiling that maybe some of these members are doing.

David England – On page 286, it says top 10 drugs by therapeutic problem type, over utilization, what do those abbreviations mean, ER, TD?

James Marx – Look at the page before?

Carl Jeffery – If you look at the page before, they're all spelled out, so ER is like early refill, TD is therapeutic duplication…There's nothing else that I need to call out for fee for service on there.

Lisa Todd – For Anthem, I really do not see anything that really stood out regarding our Pro DUR. Nothing really stood out very much. Did we go over the retrospectives?

Carl Jeffery – It was included in there.

Lisa Todd – I think that might be and I think maybe those are kind of going to be different for all of us, so I do not know if you wanted to review those at all. Like our chart of the retrospective DUR, I think we were instructed to put like examples of some of our clinical programs that we are doing. We may all have different programs. I do not know if you want us to go over those at all or? They are self-explanatory.

David England – I guess what I'm looking for is there anything in your group that stood out, this is where we go down this path as opposed to the numbers looks like what we expect, we look at this area or this view.

Lisa Todd – No alarm bells here.

Ryan Bitton – I think from an HPN perspective, similar, no alarms. We are somewhat consistent with the drug class names, jump quarter to quarter, claims count as well as drug classes by claim count for antidepressants and asthma are swapping. Pain also up there so it's consistent quarter to quarter and the last two quarters reviewed. We have already reviewed the opioid utilization going down as well as the top prescribers in the previous report. Nothing else to add.

Thomas Beranek – For SilverSummit, there are not any outliers. I got the top 10 and alphabetically rather than by pharmacy pay amount, so I want to make sure I fix that for next time so it's top to bottom but other than, not a lot here.

9. Closing Discussion

a. Public comments on any subject.

David England opened the floor for public comment and there was none.

b. Date and location of the next meeting.

   i. Discussion of the time of the next meeting.

      Carl Jeffery – We will be back next time July 25. The first one we will be doing at 1 p.m. instead of our 5:15 so it will be in the afternoon. And we will back at the Hyatt.

c. Adjournment.

Meeting adjourned at 7:43 PM

Growth Hormones

Prior Authorization Guideline

Guideline Name Growth Hormones

1 . Indications

Drug Name: Genotropin, Humatrope, Norditropin Flexpro, Nutropin AQ NuSpin, Omnitrope, Saizen, and Zomacton **Indications** **Pediatric Growth Hormone Deficiency** Indicated for the long-term treatment of pediatric patients who have growth failure due to inadequate secretion of normal endogenous growth hormone.
Drug Name: Genotropin and Omnitrope **Indications** **Prader-Willi Syndrome (PWS)** Indicated for the treatment of pediatric patients who have growth failure due to Prader-Willi Syndrome (PWS). The diagnosis of PWS should be confirmed by appropriate genetic testing. **Small for Gestational Age (SGA)** Indicated for the treatment of growth failure in children born small for gestational age (SGA) who fail to manifest catch-up growth by age 2.
Drug Name: Norditropin Flexpro, Humatrope and Zomacton **Indications** **Small for Gestational Age (SGA)** Indicated for the treatment of children with short stature born small for gestational age (SGA) with no catch-up growth by age 2-4 years.
Drug Name: Genotropin, Humatrope, Norditropin Flexpro, Nutropin AQ NuSpin, Omnitrope and Zomacton **Indications**

Turner Syndrome Indicated for the treatment of short stature associated with Turner syndrome.

Drug Name: Humatrope, Zomacton

Indications

SHOX Deficiency Indicated for the treatment of short stature or growth failure in children with short stature homeobox-containing gene (SHOX) deficiency.

Drug Name: Nutropin AQ NuSpin

Indications

Chronic Renal Insufficiency Indicated for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation. Therapy should be used in conjunction with optimal management of chronic renal insufficiency.

Drug Name: Genotropin, Humatrope, Nutropin AQ NuSpin, and Omnitrope

Indications

[Non-Approvable Use] Idiopathic Short Stature (ISS) [E] Indicated for the long-term treatment of idiopathic short stature, also called non-growth hormone-deficient short stature, defined by height SDS less than or equal to -2.25, and associated with growth rates unlikely to permit attainment of adult height in the normal range, in pediatric patients whose epiphyses are not closed and for whom diagnostic evaluation excludes other causes associated with short stature that should be observed or treated by other means. **Please Note: The request for growth hormone (GH) injections to treat idiopathic short stature (ISS) is not authorized. There is no consensus in current peer-reviewed medical literature regarding the indications, efficacy, safety, or long-term consequences of GH therapy in children with ISS who are otherwise healthy.

Drug Name: Norditropin Flexpro

Indications

Noonan Syndrome Indicated for the treatment of pediatric patients with short stature associated with Noonan Syndrome.

Prader-Willi Syndrome Indicated for growth failure due to Prader-Willi syndrome (PWS).

[Non-Approvable Use] Idiopathic Short Stature (ISS) [E] Indicated for Idiopathic Short Stature (ISS), height standard deviation score (SDS) <-2.25, and associated with growth rates unlikely to permit attainment of adult height in the normal range. **Please Note: The request for growth hormone (GH) injections to treat idiopathic short stature (ISS) is not authorized. There is no consensus in current peer-reviewed medical literature regarding the indications, efficacy, safety, or long-term consequences of GH therapy in children with ISS who are otherwise healthy.

Drug Name: Genotropin, Humatrope, Norditropin Flexpro, Nutropin AQ NuSpin, Omnitrope, and Saizen

Indications

Adult Growth Hormone Deficiency Indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency who meet either of the following two criteria: Adult-Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation, or trauma; Childhood-Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes. In general, confirmation of the diagnosis of adult growth hormone deficiency in both groups usually requires an appropriate growth hormone stimulation test. However, confirmatory growth hormone stimulation testing may not be required in patients with congenital/genetic growth hormone deficiency or multiple other pituitary hormone deficiencies due to organic disease.

Drug Name: Serostim

Indications

AIDS Wasting or Cachexia Indicated for the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

Drug Name: Zorbtive

Indications

Short Bowel Syndrome Indicated for the treatment of short Bowel Syndrome in patients receiving specialized nutritional support. Zorbtive therapy should be used in conjunction with optimal management of Short Bowel Syndrome. Specialized nutritional support may consist of a high carbohydrate, low-fat diet, adjusted for individual patient requirements and preferences. Nutritional supplements may be added according to the discretion of the treating physician. Optimal management of Short Bowel Syndrome may include dietary adjustments, enteral feedings, parenteral nutrition, fluid and micronutrient supplements, as needed.

Drug Name: Norditropin Flexpro, Zomacton

Indications

Adult Growth Hormone Deficiency Indicated for the replacement of endogenous GH in adults with GH deficiency.

Drug Name: Zomacton

Indications

[Non-Approvable Use] Idiopathic Short Stature (ISS) [E] Indicated for Idiopathic Short Stature (ISS), height standard deviation score (SDS) <-2.25, and associated with growth rates unlikely to permit attainment of adult height in the normal range. **Please Note: The request for growth hormone (GH) injections to treat idiopathic short stature (ISS) is not authorized. There is no consensus in current peer-reviewed medical literature regarding the indications, efficacy, safety, or long-term consequences of GH therapy in children with ISS who are otherwise healthy.

2 . Criteria

Product Name: Genotropin® (somatropin); Humatrope® (somatropin); Norditropin® (somatropin); Nutropin® (somatropin); Omnitrope® (somatropin); Saizen® (somatropin); Tev-Tropin® (somatropin)

Approval Length	6 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

1. Children (up to age 21, with open epiphyses and with remaining growth potential) must meet all of the following:
    a. The recipient has had an evaluation by a pediatric endocrinologist or pediatric nephrologist with a recommendation for growth hormone therapy; and
    b. The recipient has had an evaluation ruling out all other causes for short stature; and
    c. The recipient is receiving adequate replacement therapy for any other pituitary hormone deficiencies, such as thyroid, glucocorticoids or gonadotropic hormones.

    The recipient must then meet one of the following:
    1. The recipient has a diagnosis of Noonan Syndrome, their height is as least two standard deviations below the mean or below the fifth percentile for the patient's age and gender and the bone age is < 16 years for male and <14 years for female; or
    2. The recipient has a diagnosis of Prader-Willi Syndrome; or
    3. The recipient has a diagnosis of Turner Syndrome, is female, and has a bone age of < 14 years; or
    4. The recipient has a diagnosis of chronic renal insufficiency (<75 mL/minute) and their bone age is < 16 years for male and < 14 years for female; or
    5. The recipient has a diagnosis of being small for gestational age, the recipient is two years of age or older, and their height is at least two standard deviations below the mean or below the third percentile for the recipient's age and gender; or
    6. The recipient is a newborn infant with evidence of hypoglycemia, and has low growth hormone level (<20ng/mL), low for age insulin like growth factor (IGF)-1 or IGF binding protein (BP) 3 (no stimulation test required for infants); or

7. The recipient has a diagnosis of growth hormone deficiency or hypothalamic pituitary disease (e.g., hypopituitarism due to structure lesions/trauma to the pituitary including pituitary tumor, pituitary surgical damage, trauma or cranial irradiation), their height is at least two standard deviations below the mean or below the third percentile for the patient's age and gender and their bone age is < 16 years for male and < 14 years for female.

   And recipient must meet one of the following:
   a. The recipient has failed two growth hormone stimulation tests (<10 ng/mL); or
   b. The recipient has failed one growth hormone stimulation test (<10 ng/mL) and one IGF-1 or IGFBP-3 test; or
   c. The recipient has failed one growth hormone stimulation test (<10 ng/mL) or IGF-1 or IGFBP-3 test and they have deficiencies in three or more pituitary axes (e.g., thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH), adrenocorticotropic hormone (ACTH) or antidiuretic hormone (ADH).

2. Adults (age 21 years and older, with closed epiphyses, and no remaining growth potential) must meet all of the following:
   a. The recipient is being evaluated by an endocrinologist; and
   b. The recipient is receiving adequate replacement therapy for any other pituitary hormone deficiencies, such as thyroid, glucocorticoids or gonadotropic hormones; and
   c. The recipient has a diagnosis of growth hormone deficiency or hypothalamic pituitary disease (e.g., hypopituitarism due to structure lesions/trauma to the pituitary including pituitary tumor, pituitary surgical damage, trauma or cranial irradiation); and

   The recipient must then meet one of the following:
   1. The recipient has failed two growth hormone stimulation tests (<5 ng/mL); or
   2. The recipient has failed one growth hormone stimulation test (<5 ng/mL) and one IGF-1 or IGFBP-3 test; or
   3. The recipient has failed one growth hormone stimulation test (<5 ng/mL) or IGFBP-3 test and has deficiencies in three or more pituitary axes (i.e., TSH, LH, FSH, ACTH, ADH), and has severe clinical manifestations of growth hormone deficiency as evident by alterations in body composition (e.g., decreased lean body mass, increased body fat), cardiovascular function (e.g., reduced cardiac output, lipid abnormalities) or bone mineral density.

Product Name: Genotropin® (somatropin); Humatrope® (somatropin); Norditropin® (somatropin); Nutropin® (somatropin); Omnitrope® (somatropin); Saizen® (somatropin); Tev-Tropin® (somatropin)

Approval Length	12 Months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

1. Continued authorization will be given for recipients (up to age 21, with remaining growth potential) who meet all of the following:
    a. The recipient has a diagnosis of chronic renal insufficiency, growth hormone deficiency, hypothalamic pituitary disease, newborn infant with evidence of hypoglycemia, Noonan Syndrome, Prader-Willi Syndrome, small for gestational age or Turner Syndrome; and
    b. The recipient's epiphyses are open; and
    c. The recipient's growth rate on treatment is at least 2.5 cm/year; and
    d. The recipient does not have evidence of an expanding lesion or tumor formation; and
    e. The recipient has not undergone a renal transplant.

2. Continued authorization will be given for recipients (age 21 years and older, with closed epiphyses and no remaining growth potential) who meet all of the following:
    a. The recipient has a diagnosis of growth hormone deficiency or hypothalamic pituitary disease; and
    b. There is documentation of improvement in clinical manifestations associated with growth hormone deficiency.

Product Name: Serostim® (somatropin)

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

Recipients must meet all of the following:
1. The recipient has a diagnosis of Human Immune Deficiency Virus (HIV) with wasting or cachexia; and
2. The medication is indicated to increase lean body mass, body weight and physical endurance; and
3. The recipient is receiving and is compliant with antiretroviral therapy; and
4. The recipient has experienced an involuntary weight loss of >10% pre-illness baseline or they have a body mass index of <20 kg/m^2; and
5. The recipient has experienced an adverse event, allergy or inadequate response to megestrol acetate, or the recipient has a contraindication to treatment with this agent; and
6. The recipient has experienced an adverse event, allergy or inadequate response to an anabolic steroid (e.g., testosterone, oxandrolone, nandrolone) or the recipient has a contraindication to treatment with these agents.

Product Name: Zorbtive® (somatropin)

Approval Length	6 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Recipients must meet all of the following:

1. The recipient has a diagnosis of short bowel syndrome; and
2. The recipient is age 18 years or older; and
3. The medication is being prescribed by or following a consultation with a gastroenterologist; and
4. The recipient is receiving specialized nutritional support (e.g., high carbohydrate, low-fat diets via enteral or parenteral nutrition).

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: July 25, 2019

Prior Authorization Criteria being reviewed: Growth Hormone

Managed Care Organization name: Choose an item.

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.

Suggested changes:

1a Remove Tev-Tropin (no longer available)

Add Nutopin AQ, Nutropin AQ NuSpin, Saizenprep, Zomacton

1a1c. Add Short Stature Homeobox (SHOX) gene

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: _____*L Todd*_____

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: July 25, 2019

Prior Authorization Criteria being reviewed: Growth Hormone

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

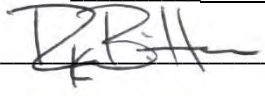
I recommend the following changes to the criteria as presented. Please be brief and identify the section of the proposed criteria. If you feel you need more space for proposed changes, you may attach a word document, with only the suggested changes to criteria being presented.

HPN agrees with the intent of the policy. The UHC Community Plan criteria used by HPN is much more comprehensive and detailed and in addition, separates out the different indications for ease of review, but the intent seems similar.

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: July 25, 2019

Prior Authorization Criteria being reviewed: Growth Hormone

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.

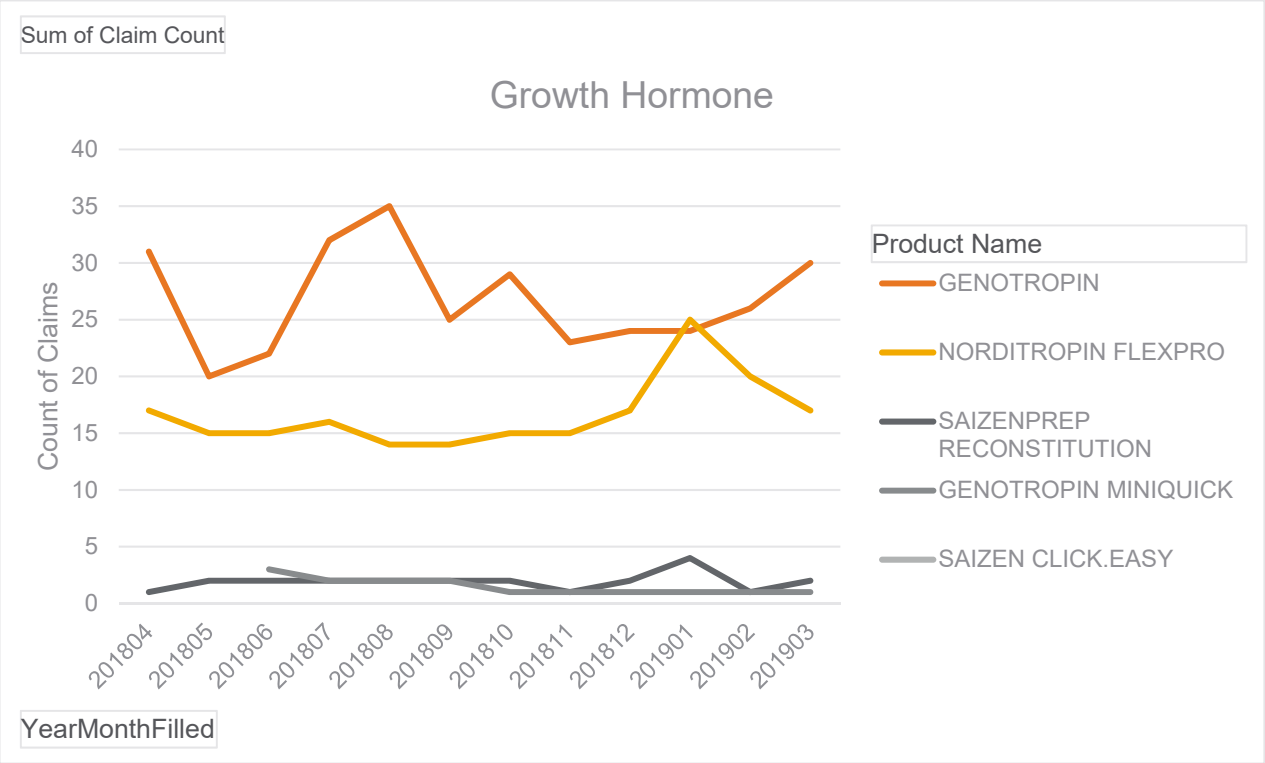
Please print the name of the individual completing this form: Tom Beranek

Signature of individual completing this form: Tom Beranek

Growth Hormone Products

Summary of Utilization
April 1, 2018 - March 31, 2019
Fee for Service Medicaid

Product Name	Member Count	Claim Count	Days Supply	Sum of Qty
GENOTROPIN	47	321	9,381	1,664
GENOTROPIN MINIQUICK	4	17	656	686
NORDITROPIN FLEXPRO	32	200	5,473	939
SAIZEN CLICK.EASY	1	1	29	4
SAIZENPREP RECONSTITUTION	2	23	671	96
Total	**86**	**562**	**16,210**	**3,389**



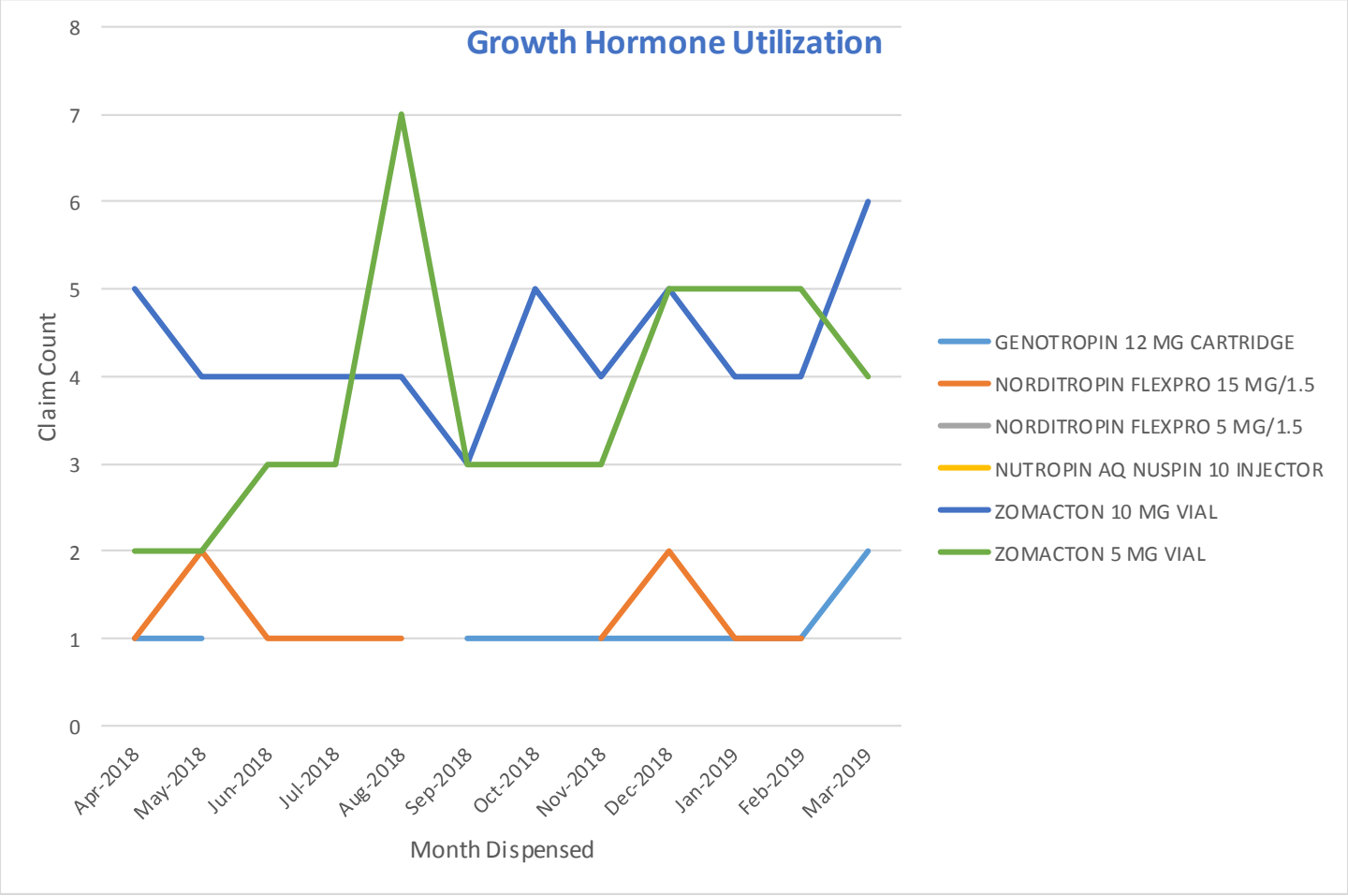
Anthem

Growth Hormone Products

Summary of Utilization

April 1, 2018 – March 31, 2019

Drug	Member Count	Claim Count	Days Supply	Total Quantity
GENOTROPIN 12 MG CARTRIDGE	2	11	309	60
NORDITROPIN FLEXPRO 15 MG/1.5	1	11	294	47
NORDITROPIN FLEXPRO 5 MG/1.5	1	1	25	3
NUTROPIN AQ NUSPIN 10 INJECTOR	1	1	25	8
ZOMACTON 10 MG VIAL	9	52	1399	165
ZOMACTON 5 MG VIAL	7	45	1199	190
Grand Total	**19**	**121**	**3251**	**473**

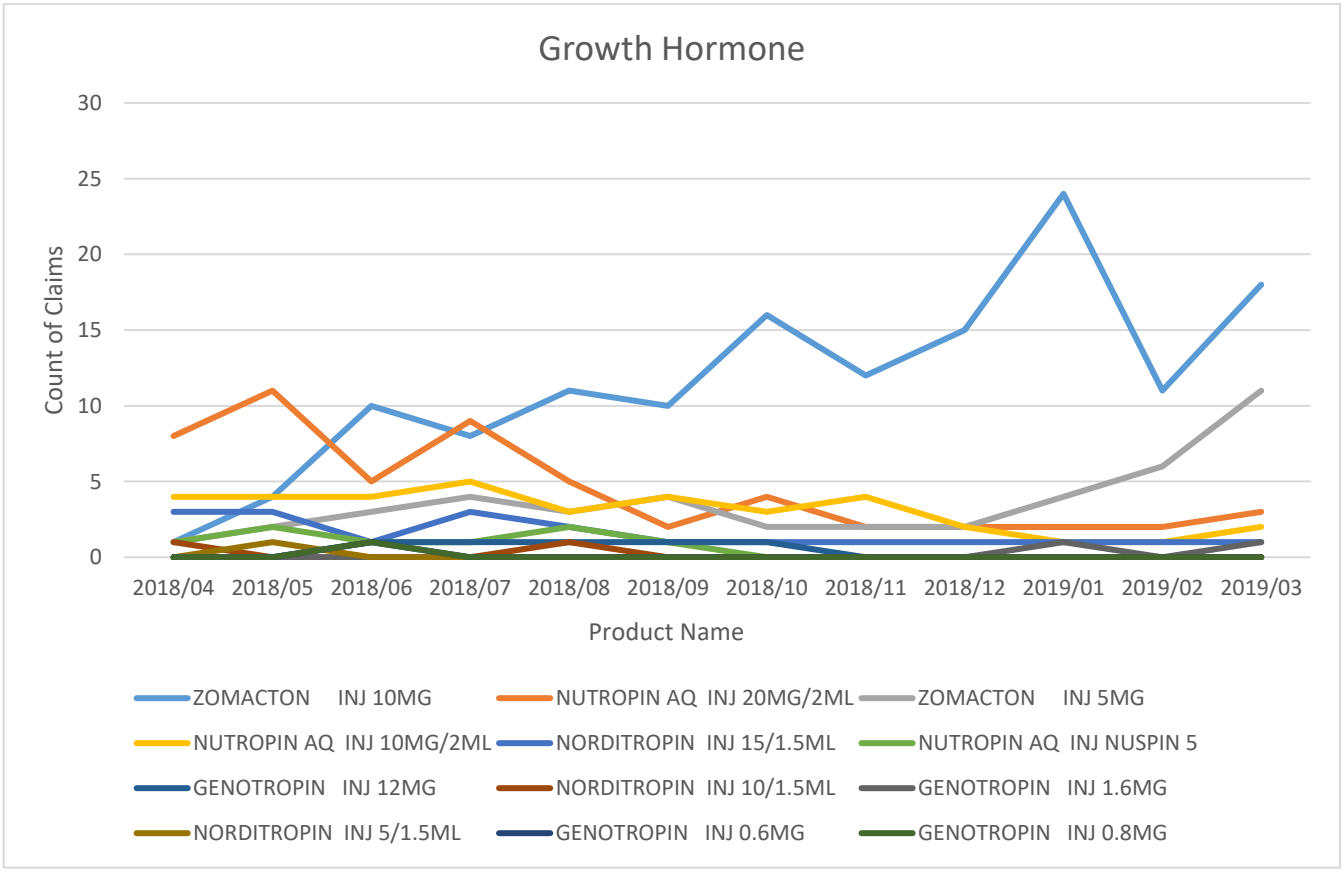


HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Growth Hormone

Summary of Utilization
April 1, 2018 - March 31, 2019
Health Plan of Nevada

Product Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
ZOMACTON INJ 10MG	65	140	3,742	743	NA
NUTROPIN AQ INJ 20MG/2ML	21	55	1,283	270	NA
ZOMACTON INJ 5MG	23	44	1,181	306	NA
NUTROPIN AQ INJ 10MG/2ML	19	37	1,004	300	NA
NORDITROPIN INJ 15/1.5ML	7	19	505	128	NA
NUTROPIN AQ INJ NUSPIN 5	2	8	176	32	NA
GENOTROPIN INJ 12MG	3	5	140	25	NA
NORDITROPIN INJ 10/1.5ML	2	2	58	27	NA
GENOTROPIN INJ 1.6MG	1	2	56	56	NA
NORDITROPIN INJ 5/1.5ML	1	1	25	5	NA
GENOTROPIN INJ 0.6MG	1	1	28	14	NA
GENOTROPIN INJ 0.8MG	1	1	28	14	NA
Grand Total	**146**	**315**	**8,226**	**1,919**	**NA**



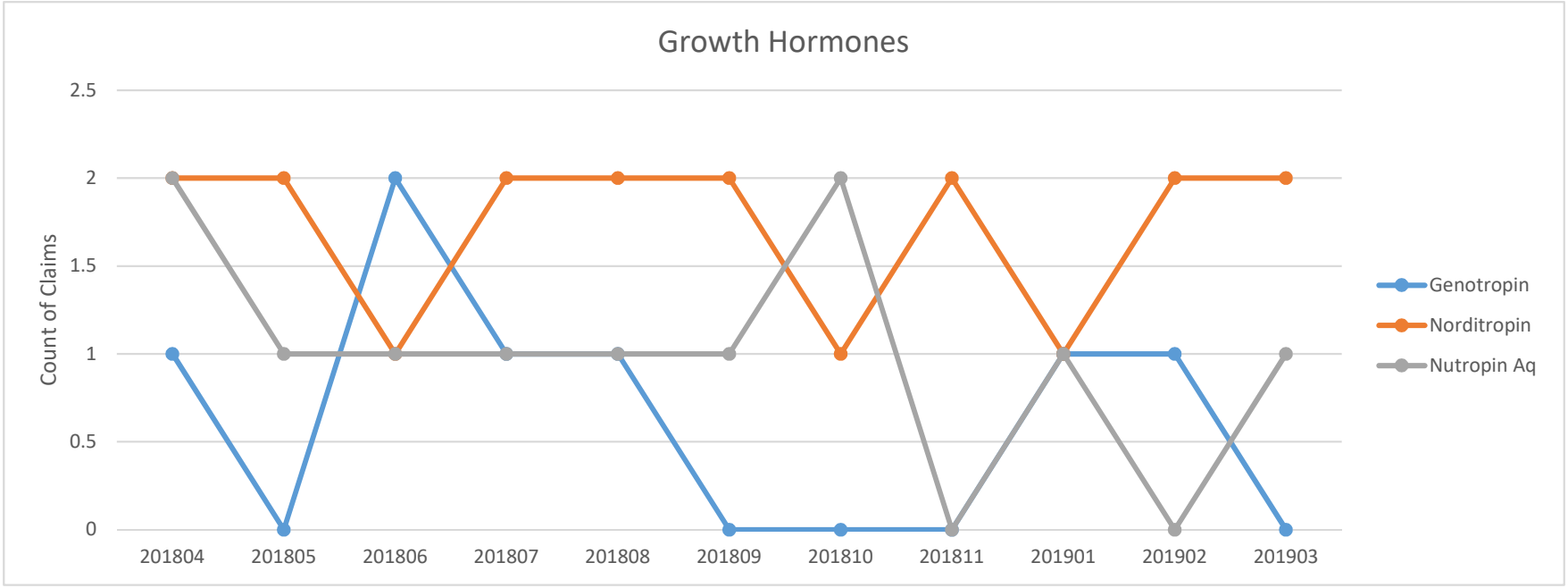
Growth Hormone Products

Summary of Utilization

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Qty	Sum of Days
GENOTROPIN INJ 12MG	3	7	25	200
NORDITROPIN INJ 5/1.5ML	3	19	136.5	546
NUTROPIN AQ INJ 20MG/2ML	1	11	110	298
Total	**7**	**37**	**271.5**	**1,044**



D. Growth Hormone

Therapeutic Class: Growth Hormone
Last Reviewed by the DUR Board: July 25, 2013

Growth Hormones are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the SSA Act 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. Genotropin® (somatropin); Humatrope® (somatropin); Norditropin® (somatropin); Nutropin® (somatropin); Omnitrope® (somatropin); Saizen® (somatropin); Tev-Tropin® (somatropin):

1. Children (up to age 21, with open epiphyses and with remaining growth potential) must meet all of the following:

a. The recipient has had an evaluation by a pediatric endocrinologist or pediatric nephrologist with a recommendation for growth hormone therapy; and

b. The recipient has had an evaluation ruling out all other causes for short stature; and

c. The recipient is receiving adequate replacement therapy for any other pituitary hormone deficiencies, such as thyroid, glucocorticoids or gonadotropic hormones.

The recipient must then meet one of the following:

1. The recipient has a diagnosis of Noonan Syndrome, Prader-Willi Syndrome or Turner Syndrome and their height is as least two standard deviations below the mean or below the third percentile for the patient's age and gender; or

2. The recipient has a diagnosis of chronic renal insufficiency (<75 mL/minute), and their height is at least two standard deviations below the mean or below the third percentile for the recipient's age and gender; or

3. The recipient has a diagnosis of being small for gestational age, the recipient is two years of age or older, and their height is at least two standard deviations below the mean or

below the third percentile for the recipient's age and gender; or

4. The recipient is a newborn infant with evidence of hypoglycemia, and has low growth hormone level (<20 ng/mL), low for age insulin like growth factor (IGF)-1 or IGF binding protein (BP) 3 (no stimulation test required for infants); or

5. The recipient has a diagnosis of growth hormone deficiency or hypothalamic pituitary disease (e.g., hypopituitarism due to structure lesions/trauma to the pituitary including pituitary tumor, pituitary surgical damage, trauma or cranial irradiation), and their height is at least two standard deviations below the mean or below the third percentile for the patient's age and gender.

   And recipient must meet one of the following:

   a. The recipient has failed two growth hormone stimulation tests (<10 ng/mL); or

   b. The recipient has failed one growth hormone stimulation test (<10 ng/mL) and one IGF-1 or IGFBP-3 test; or

   c. The recipient has failed one growth hormone stimulation test (<10 ng/mL) or IGF-1 or IGFBP-3 test and they have deficiencies in three or more pituitary axes (e.g., thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH), adrenocorticotropic hormone (ACTH) or antidiuretic hormone (ADH).

2. Adults (age 21 years and older, with closed epiphyses, and no remaining growth potential) must meet all of the following:

   a. The recipient is being evaluated by an endocrinologist; and

   b. The recipient is receiving adequate replacement therapy for any other pituitary hormone deficiencies, such as thyroid, glucocorticoids or gonadotropic hormones; and

   c. The recipient has a diagnosis of growth hormone deficiency or hypothalamic pituitary disease (e.g., hypopituitarism due to structure lesions/trauma to the pituitary including pituitary tumor, pituitary surgical damage, trauma or cranial irradiation); and

The recipient must then meet one of the following:

1. The recipient has failed two growth hormone stimulation tests (<5 ng/mL); or

2. The recipient has failed one growth hormone stimulation test (<5 ng/mL) and one IGF-1 or IGFBP-3 test; or

3. The recipient has failed one growth hormone stimulation test (<5 ng/mL) or IGFBP-3 test and has deficiencies in three or more pituitary axes (i.e., TSH, LH, FSH, ACTH, ADH), and has severe clinical manifestations of growth hormone deficiency as evident by alterations in body composition (e.g., decreased lean body mass, increased body fat), cardiovascular function (e.g., reduced cardiac output, lipid abnormalities) or bone mineral density.

3. Continued authorization will be given for recipients (up to age 21, with remaining growth potential) who meet all of the following:

   a. The recipient has a diagnosis of chronic renal insufficiency, growth hormone deficiency, hypothalamic pituitary disease, newborn infant with evidence of hypoglycemia, Noonan Syndrome, Prader-Willi Syndrome, small for gestational age or Turner Syndrome; and

   b. The recipient's epiphyses are open; and

   c. The recipient's growth rate on treatment is at least 2.5 cm/year; and

   d. The recipient does not have evidence of an expanding lesion or tumor formation; and

   e. The recipient has not undergone a renal transplant.

4. Continued authorization will be given for recipients (age 21 years and older, with closed epiphyses and no remaining growth potential) who meet all of the following:

   a. The recipient has a diagnosis of growth hormone deficiency or hypothalamic pituitary disease; and

   b. There is documentation of improvement in clinical manifestations associated with growth hormone deficiency.

b. Serostim® (somatropin)

Recipients must meet all of the following:

1. The recipient has a diagnosis of Human Immune Deficiency Virus (HIV) with wasting or cachexia; and

2. The medication is indicated to increase lean body mass, body weight and physical endurance; and

3. The recipient is receiving and is compliant with antiretroviral therapy; and

4. The recipient has experienced an involuntary weight loss of >10% pre-illness baseline or they have a body mass index of <20 kg/m^2; and

5. The recipient has experienced an adverse event, allergy or inadequate response to megestrol acetate, or the recipient has a contraindication to treatment with this agent; and

6. The recipient has experienced an adverse event, allergy or inadequate response to an anabolic steroid (e.g., testosterone, oxandrolone, nandrolone) or the recipient has a contraindication to treatment with these agents.

c. Zorbtive® (somatropin)

Recipients must meet all of the following:

1. The recipient has a diagnosis of short bowel syndrome; and

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

3. The medication is being prescribed by or following a consultation with a gastroenterologist; and

4. The recipient is receiving specialized nutritional support (e.g., high carbohydrate, low-fat diets via enteral or parenteral nutrition).

2. Prior Authorization Guidelines

a. Prior authorization approval will be 12 weeks for Serostim® (somatropin).

b. Prior authorization approval will be six months for initial authorization (for all somatropin products except for Serostim®).

c. Prior authorization approval will be one year for continuing treatment (for all somatropin products except Serostim®).

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

Therapeutic Class Overview
Growth Hormone

INTRODUCTION

- Growth hormone (GH) affects many of the metabolic processes carried out by somatic cells, most notably increasing body mass. Overall growth is stimulated by GH therapy; however, the effects are not evenly distributed among protein, lipid and carbohydrate compartments. Specifically, body protein content and bone mass increase, total body fat content decreases, and there is an increase in plasma and liver lipid content due to the mobilization of free fatty acids from peripheral fat stores. Another physiological effect of GH is stimulation of cartilage growth (*Molitch et al 2011*).
- Growth hormone deficiency (GHD) in pediatric patients is a clinical diagnosis that is confirmed by biochemical testing. A patient's growth patterns are compared to the established norms. The clinical manifestations of GHD vary depending on whether a patient has complete or partial deficiency. In complete deficiency, pediatric patients present with early severe growth failure, delayed bone age, central disposition of body fat and very low serum concentrations of GH, insulin-like growth factor-1 (IGF-1) and IGF binding protein-3. These patients are also more prone to hypoglycemia, prolonged jaundice, microphallus in males and giant cell hepatitis. GHD in pediatric patients with partial deficiency may be more difficult to diagnose, as these manifestations may not be as obvious (*Molitch et al 2011*).
- Once a diagnosis of GHD is confirmed in pediatric patients, GH therapy should be initiated and continued until cessation of linear growth. Therapy should be initiated as soon as possible, as evidence demonstrates that growth response is more robust when GH therapy is started at a younger age (*Molitch et al 2011*).
- Several preparations of GH are currently available for use in pediatric patients. Recombinant GH preparations, administered by subcutaneous (SC) injection, are currently the most widely utilized. Due to the variability in individual response to therapy, after initial dosing, the dose of GH is adjusted based on growth response and IGF-1 level. While not universally supported, the therapeutic goal of therapy is to achieve a level of IGF-1 that is slightly higher than average, because growth velocity is typically greatest at these levels. A patient's growth velocity, as compared to a similar population, should also be monitored to determine if the growth response is adequate (*Molitch et al 2011*).
- Possible explanations for an inadequate response to GH therapy include poor adherence, incorrect diagnosis of GHD, subtherapeutic dose of GH, or concurrent mild GH insensitivity. In pediatric patients, GH therapy is typically continued at least until linear growth is nearly complete (eg, decreased to less than 2.5 centimeters per year). At this point, retesting for GHD should occur to determine if GH therapy should be continued into adulthood (*Molitch et al 2011*).
- The majority of pediatric patients with idiopathic, isolated GHD in their childhood have normal GH secretion during late adolescence and young adulthood. In contrast, pediatric patients with genetic GHD, multiple pituitary hormone deficiencies, and/or those with structural defects in the hypothalamic-pituitary region rarely recover the ability to secrete GH as an adult. Therefore, retesting may not be required (*Molitch et al 2011*).
- GHD may also occur in adult patients. Approximately 15% to 20% of adult-onset GHD represents the continuation of childhood-onset GHD into maturity; the remainder is adult-onset acquired from damage to the pituitary gland or hypothalamus. GHD is associated with increased metabolic syndrome, increased cardiovascular morbidity and mortality rates, reduced lean body mass, increased abdominal adiposity, early atherosclerosis, dyslipidemia, coagulation abnormalities, insulin resistance, decreased bone mineral density, and a decreased quality of life (*Reed et al 2013*). The role of GH therapy in adults is not as clear as it is in pediatric patients in whom therapy is required for normal growth. There is evidence to demonstrate that when used in adult patients with GHD, GH therapy increases muscle mass and decreases body fat. Evidence of other potential beneficial effects of GH therapy in adults is not as well established and includes improvement in bone mineral density, sense of well-being, muscle strength, and lipid profile. GH therapy can be considered in adult patients with severe clinical manifestations and unequivocal evidence of GHD due to organic disease of childhood- or adult-onset (*Molitch et al 2011*).
- All of the GH preparations contain somatropin, otherwise known as recombinant human GH. The various preparations are Food and Drug Administration (FDA)-approved for use in a variety of pediatric conditions associated with a failure in growth, including chronic kidney disease (CKD), Turner syndrome, being born small for gestational age, Prader-Willi syndrome, mutations in the Short Stature Homeobox gene, Noonan syndrome, and idiopathic short stature.

- The majority of preparations are also indicated for the treatment of GHD in adults. Of note, Serostim is FDA-approved solely for the treatment of human immunodeficiency virus-associated wasting or cachexia in adults, while Zorbtive is approved for the treatment of short bowel syndrome in patients receiving specialized nutritional support. Specific FDA-approved indications for the various GH preparations are outlined in Table 2. All of the available GH preparations are available for SC injection, and there are currently no generics available within the class.
- GH preparations are available in various formulations, and several delivery devices are available. The dosing device may be a factor in patient adherence with the prescribed regimen.
- Medispan Class: Growth Hormones

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Genotropin (somatropin)	-
Humatrope (somatropin)	-
Norditropin Flexpro (somatropin)	-
Nutropin AQ (somatropin)	-
Omnitrope (somatropin)	-
Saizen (somatropin)	-
Sersotim (somatropin)	-
Zomacton (somatropin)	-
Zorbtive (somatropin)	-

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

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Genotropin	Humatrope	Norditropin Flexpro	Nutropin AQ	Omnitrope	Saizen	Serostim	Zomacton	Zorbtive
Growth failure associated with chronic renal insufficiency before renal transplant				✔					
Growth failure associated with Noonan syndrome			✔						
Growth failure associated with Prader-Willi syndrome	✔		✔		✔				
Growth failure associated with short-stature homeobox-containing gene deficiency		✔						✔	
Growth failure associated with Turner syndrome	✔	✔	✔	✔	✔			✔	
Growth failure in children born small for gestational age	✔	✔	✔		✔			✔	
Growth hormone deficiency	✔	✔	✔	✔	✔	✔		✔	
Idiopathic short stature	✔	✔	✔	✔	✔			✔	

Indication	Genotropin	Humatrope	Norditropin Flexpro	Nutropin AQ	Omnitrope	Saizen	Serostim	Zomacton	Zorbtive
Human immunodeficiency virus-associated wasting or cachexia							✔		
Treatment of short bowel syndrome in patients receiving nutritional support									✔

(Prescribing information: *Genotropin 2016, Humatrope 2016, Norditropin Flexpro 2018, Nutropin AQ 2016, Omnitrope 2016, Saizen 2018, Serostim 2018, Zomacton 2018, Zorbtive 2017*)

- 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

- There are limited head-to-head clinical trials comparing different GH preparations to one another.
- Clinical data support the use of GH for the treatment of growth failure associated with chronic renal insufficiency. A meta-analysis of 16 RCTs (N = 809) evaluating the effects of GH in children with CKD found that patients who were treated with GH had a greater increase in mean height velocity (3.88 cm) than those who received either no treatment or placebo after 1 year (*Hodson et al 2012*). A retrospective, matched control cohort study found that long-term therapy with GH (mean 4.2 years) reduced linear growth deceleration in children with CKD and improved final height (*Bizzarri et al 2018*).
- Clinical trials have demonstrated efficacy of GH for the treatment of growth failure in patients with Noonan syndrome. A randomized controlled trial evaluating GH in patients with Noonan syndrome found a positive effect of GH on linear growth. Specifically, there was a significantly greater change in height standard deviation score, and bone maturation was accelerated with GH compared to no treatment. In this trial, data also suggest that once treatment with GH is discontinued, “catch-down” (artificially stimulated growth declines once GH is discontinued) growth can occur (*Noordam et al 2001*). In a follow-up analysis of 29 patients treated with GH for a median of 6.4 years, a total of 22 children reached an adult height in the normal range (*Noordam et al 2008*). In a study of 65 patients enrolled in the National Cooperative Growth Study (NCGS) database, it was found that treatment with GH led to gains over predicted height of 9.2 cm in females and 10.9 cm in males (*Romano et al 2009*).
- Clinical trials have demonstrated the significant benefits of GH in pediatric patients with Prader-Willi syndrome in accelerating growth and in improving body composition. Benefits were also observed in improving bone mineral density, lipid profiles, energy expenditure, strength and agility, and pulmonary function (*Carrel et al 1999, Carrel et al 2004, Festen et al 2008, Lindgren et al 1997, Lindgren et al 1998, Lindgren et al 1999, Myers et al 1999, Myers et al, 2007*). Data from 1 trial suggested that growth velocity declines dramatically once treatment is discontinued (*Lindgren et al 1997*).
- Humatrope demonstrated efficacy in increasing first-year height velocity in patients with Short Stature Homeobox-containing gene deficiency when compared to no treatment ($p < 0.0001$) (*Blum et al 2007*).
- Several clinical trials have demonstrated that GH significantly increases the growth rate of pediatric patients with Turner syndrome. Overall, various dose ranging trials did not consistently demonstrate a superior weight-based GH dosing regimen over another; all doses of GH were beneficial. In addition, data suggested that increases in height are greatest during the first year of therapy (*Baxter et al 2007, Bertrand et al 1996, Massa et al 1995, Nienhuis et al 1993, Sas et al 1999a, Takano et al 1989a, Takano et al 1989b, Takano et al 1989c, Takano et al 1993, Takano 1995, van Pareren et al 2003, van Teunenbroek et al 1996*). A Cochrane Review of 4 randomized controlled trials demonstrated that GH (0.3 to 0.375 mg/kg/week) increased short-term growth in patients with Turner syndrome by approximately 3 cm during the first year of treatment. Despite the increase, the final height achieved was still below the normal range (*Baxter et al 2007*).
- For the treatment of growth failure in pediatric patients born small for gestational age, clinical trials have demonstrated the significant benefits of GH on increasing growth rates (*Arends et al 2003, Bannink et al 2010, Boguszewski et al 1998, Bozzola et al 2004, Chatelain et al 1994, De Schepper et al 2008, de Zegher et al 1996, de Zegher et al 2005, Jung et al 2009, Maiorana et al 2009, Sas et al 1999b*). Data from individual clinical trials and 3 meta-analyses found

that response to GH therapy is dose-dependent, and higher doses of GH resulted in additional gain (*de Zegher et al 1996, de Zegher et al 2005*).

- Treatment with GH has been shown to increase height velocity in both prepubertal and pubertal pediatric patients with GHD (*Coelho et al 2008, Cohen et al 2002, de Muinck Keizer-Schrama et al 1992, Kriström et al 2009, MacGillivray et al 1996, Mauras et al 2000, Romer et al 2009, Sas et al 2010, Shih et al 1994, Wilson et al 1985*). Two head-to-head trials demonstrated no differences in safety and efficacy with different GH preparations for the treatment of pediatric GHD. One of the trials compared 3 GH preparations (Genotropin, Humatrope, and Saizen), while the second evaluated 2 preparations (Genotropin and Omnitrope) (*Romer et al 2009, Shih et al 1994*).
- In pediatric patients with idiopathic short stature, somatropin has been shown to increase first-year growth velocity and final height (*Albertsson-Wikland et al 2008, Bryant et al 2007, Deodati et al 2011, Finkelstein et al 2002, Hopwood et al 1993, Kriström et al 2009, van Gool et al 2010, Wit et al 2005*). Additionally, once daily compared to 3 times weekly dosing and higher compared to lower dosing demonstrated a greater increase in growth velocity (*Bryant et al 2007, Finkelstein et al 2002*).
- A systematic review and meta-analysis of 54 placebo-controlled, randomized controlled trials enrolling over 3400 patients found that GH therapy was associated with reduced body fat and increased lean mass in adults with GHD (*Hazem et al 2012*). Eleven of 16 trials that assessed quality of life outcomes reported positive outcomes, but a meta-analysis was not possible. Furthermore, results from meta-analyses and randomized controlled trials have demonstrated that treatment with GH was associated with improved cardiac function and bone mineral density (*Barake et al 2014, Davidson et al 2004, Maison et al 2003*). However, there are currently conflicting data with regard to the effect of GH on cognitive function, quality of life, and exercise capacity (*Arwert et al 2005, Falleti et al 2006, Rubeck et al 2009, Widdowson, 2010*).
- In patients with human immunodeficiency virus-associated wasting, Serostim has been shown to increase body weight, lean body mass, and work output. However, effects on quality of life were variable (*Moyle et al 2004, Schambelan et al 1996*).
- A meta-analysis assessed the safety and efficacy of GH with or without glutamine supplementation for adult patients with short bowel syndrome; 5 studies were included in the review. Human GH with or without glutamine appeared to provide benefit in terms of increased weight (median [MD] 1.66 kg; 95% confidence interval [CI], 0.69 to 2.63; p = 0.0008), lean body mass (MD 1.93 kg; 95% CI, 0.97 to 2.9; p = 0.0001), energy absorption (MD 4.42 Kcal; 95% CI, 0.26 to 8.58; p = 0.04) and nitrogen absorption (MD 44.85 g; 95% CI, 0.2 to 9.49; p = 0.04) for patients with short bowel syndrome. One randomized controlled trial which focused on parenteral nutrition (PN) requirements demonstrated decreased PN volume, calories, and number of infusions in patients who received GH with or without glutamine supplementation. Only patients who received GH with glutamine maintained statistically significant PN reductions at 3-month follow-up. The results suggested a positive effect of GH on weight gain and energy absorption. However, after cessation of therapy, the effects returned to baseline in the majority of the trials (*Wales et al 2010*).

CLINICAL GUIDELINES

- For pediatric patients, treatment guidelines recommend the use of GH therapy with somatropin as a treatment option for children with growth failure associated with any of the following: GHD, GHD in childhood cancer survivors, Noonan syndrome, Turner syndrome, Prader-Willi syndrome, chronic renal insufficiency, born small for gestational age, and short stature homeobox-containing gene deficiency (*Cohen et al 2008, Deal et al 2013, Gravholt et al 2017, Grimberg et al 2016, Ketteler et al 2017, National Kidney Foundation 2009, Sklar et al 2018*). Routine use of GH in every child with idiopathic short stature is not recommended; decisions about GH therapy should take into account physical and psychological burdens as well as risks and benefits (*Grimberg et al 2016*). Guidelines do not prefer one GH agent over another. Choice of preparation should be individualized based on potential advantages and disadvantages of therapy, therapeutic need, and the likelihood of adherence.
- For adult patients, treatment guidelines recommend the use of GH therapy in patients with clinical features suggestive of adult GHD and biochemically proven evidence of adult GHD (*Cook et al 2009*). Therapy should be individualized independent of body weight. The dose of GH should be low initially and gradually increased to the minimally effective dose that normalizes IGF-1 levels without side effects (*Cook et al 2009, Molitch et al 2011).* The 2009 American Association of Clinical Endocrinologists guidelines state that no evidence exists to support any specific GH product over another (*Cook et al 2009*).
- Small studies evaluating the use of GH in short bowel syndrome have yielded conflicting results; methodological differences limit definitive conclusions on the efficacy of GH. In carefully selected patients who are candidates for growth factor treatment, the glucagon-like peptide-2 analog, teduglutide, is recommended as first-line therapy (*Pironi et al 2016*).

SAFETY SUMMARY

- Contraindications to GH products include active malignancy, diabetic retinopathy, hypersensitivity to the agent or any of its excipients, acute critical illness, and use for growth promotion in children with closed epiphyses. Somatropin is also contraindicated in children with Prader-Willi syndrome who are severely obese, have severe respiratory impairment, or have a history of upper airway obstruction or sleep apnea (Genotropin, Humatrope, Norditropin Flexpro, Nutropin AQ, Omnitrope, Saizen, Zomacton).
- Key Warnings/Precautions:
  - Somatropin may contribute to the increased mortality in patients with acute critical illness due to complications from open heart surgery, abdominal surgery, accidental trauma, or respiratory failure.
  - Somatropin may increase progression or recurrence of intracranial neoplasms, particularly meningiomas in patients treated with radiation to the head for their first neoplasm.
  - Undiagnosed or untreated hypothyroidism may impair optimal response to somatropin.
  - Somatropin may decrease insulin sensitivity, and previously undiagnosed diabetes mellitus may be unmasked during treatment.
  - Intracranial hypertension and pancreatitis have been reported with somatropin treatment.
  - Slipped capital femoral epiphyses and scoliosis can occur in pediatric patients.
  - Fluid retention has been associated with somatropin in adult patients.
  - Increases in serum levels of inorganic phosphorous, alkaline phosphatase, parathyroid hormone and IGF-1 may occur.
  - Tissue atrophy may occur when somatropin is SC administered at the same site over a long period of time.
  - Somatropin may reduce serum cortisol levels or unmask central hypoadrenalism in patients at risk for pituitary hormone deficiency.
- Adverse Drug Events: Arthralgia, myalgia, edema, carpal tunnel syndrome, paresthesia, hyperglycemia, headaches, lipoatrophy, and injection site reactions.
- Drug Interactions: Estrogens, glucocorticoids, and insulin or other hypoglycemic agents.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Genotropin (somatropin)	Injection	SC	Weekly dose divided into 6 or 7 injections to Daily	Injections should be rotated to help prevent lipoatrophy.
Humatrope (somatropin)	Injection	SC	Weekly dose divided into 6 or 7 injections to Daily	Injections should be rotated to help prevent lipoatrophy.
Norditropin Flexpro (somatropin)	Injection	SC	Weekly dose divided into 6 or 7 injections to Daily	Injections should be rotated to help prevent lipoatrophy.
Nutropin AQ (somatropin)	Injection	SC	Weekly dose divided into 3 to 7 injections to Daily	Injections should be rotated to help prevent lipoatrophy.
Omnitrope (somatropin)	Injection	SC	Weekly dose divided into 6 or 7 injections to Daily	Injections should be rotated to help prevent lipoatrophy.
Saizen (somatropin)	Injection	SC	Weekly dose divided into 3, 6, or 7 injections to Daily	Injections should be rotated to help prevent lipoatrophy.
Sersotim (somatropin)	Injection	SC	Daily	Injections should be rotated to avoid local irritation.
Zomacton (somatropin)	Injection	SC	Weekly dose divided into 3, 6, or 7 injections to Daily	Injections should be rotated to help prevent lipoatrophy.
Zorbtive (somatropin)	Injection	SC	Daily	Injections should be rotated to help prevent lipoatrophy. Dosage titration is recommended for fluid retention

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				and arthralgia/carpal tunnel syndrome.

See the current prescribing information for full details.

CONCLUSION

- The safety and efficacy of GH therapy in pediatric patients with growth failure are well established. Treatment guidelines recommend the use of somatropin as a treatment option for children with growth failure associated with any of the following: GHD, GHD in childhood cancer survivors, Turner syndrome, Prader-Willi syndrome, chronic renal insufficiency, born small for gestational age, and short stature homeobox-containing gene deficiency (*Clayton et al 2007*, *Cohen et al 2008, Deal et al 2013, Gravholt et al 2017, Grimberg et al 2016, Ketteler et al 2017, National Kidney Foundation 2009, Sklar et al 2018*). Routine use of GH in every child with idiopathic short stature is not recommended; decisions about GH therapy should take into account physical and psychological burdens as well as risks and benefits (*Grimberg et al 2016*). Guidelines do not prefer one GH agent over another. Choice of preparation should be individualized based on potential advantages and disadvantages of therapy, therapeutic need, and the likelihood of adherence.
- For adult patients, treatment guidelines recommend the use of GH therapy patients with clinical features suggestive of adult GHD and biochemically proven evidence of adult GHD. There should be a careful evaluation of the benefits and risks specific to the individual. The 2009 American Association of Clinical Endocrinologists Guidelines state that no evidence exists to support any specific GH product over another (*Cook et al 2009, Fleseriu et al 2016*).
- There are several GH preparations currently available, which all contain somatropin (recombinant human GH). The various preparations are equally biopotent and have the same natural sequence structure (*Rogol et al 2018*). Differences between products such as device features, dose increments, requirement for reconstitution, and requirement for refrigeration may influence individual patient preferences. All of the available GH preparations are available for SC injection, and there are currently no generics available within the class.
- Common adverse reactions that may be observed with GH therapy include arthralgia, myalgia, edema, carpal tunnel syndrome, paresthesia, hyperglycemia, headaches, lipoatrophy, and injection site reactions.

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Spravato® (esketamine)

Prior Authorization Guideline

Guideline Name Spravato (esketamine)

1 . Indications

Drug Name: Spravato (esketamine) **Indications** A non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults.

2 . Criteria

Product Name: Spravato (esketamine)

Diagnosis	Treatment-resistant Depression
Approval Length	4 Weeks
Therapy Stage	Initial Authorization (Induction)
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of treatment-resistant depression

AND

2. Administered under the direct supervision of a healthcare provider with post-administration observation.

AND

3. Treatment will be in conjunction with an oral antidepressant.

AND

4. Prescribed by a psychiatrist

Product Name: Spravato (esketamine)

Diagnosis	Treatment-resistant Depression
Approval Length	12 Months
Therapy Stage	Re-Authorization
Guideline Type	Prior Authorization

Approval Criteria

1. Diagnosis of treatment-resistant depression.

AND

2. Evidence of therapeutic benefit is documented in the chart.

AND

3. Administered under the direct supervision of a healthcare provider with post-administration observation

AND

4. Treatment will be in conjunction with an oral antidepressant.

AND

5. Prescribed by a psychiatrist

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: July 25, 2019

Prior Authorization Criteria being reviewed: Spravato

Managed Care Organization name: Choose an item.

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.

Consider adding the following:
Age restriction :

- 18 years of age or older

Diagnosis:

- (MDE) Moderate to severe major depressive disorder;(defined by less than 50% reduction in symptom severity using a standard rating scale that reliably measures depressive symptoms)

Exclusions: Not approved for:

- Individual has aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation; **OR**

- Individual has intracerebral hemorrhage.

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: _____L Todd_____

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: July 25, 2019

Prior Authorization Criteria being reviewed: Spravato

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.

Attached UHC Community Plan Spravato Drug Policy for details.

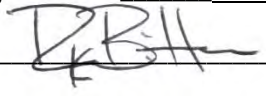
Summarized recommendations include:

- Allow if prescribed "in consultation with a psychiatrist"
- Attestation of baseline scoring with a clinical assessment (HAMD17, QIDS-C16, MADRS)
- Documentation of no improvement with three different antidepressants or treatment regimens of adequate dose, duration, and adherence
- Healthcare setting for administration is certified by Spravato REMS program
- Allow authorization for 12 weeks initially and only six months thereafter
- Reauthorization to include recent scoring of the clinical assessment used initially

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: 

KETALAR® (KETAMINE) AND SPRAVATO™ (ESKETAMINE)

Policy Number: CS2019D0069E **Effective Date**: June 1, 2019

Instructions for Use

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Commercial Policy

- Ketalar® (Ketamine) and Spravato™ (Esketamine)

APPLICATION

This Medical Benefit Drug Policy does not apply to the state of Kansas.

COVERAGE RATIONALE

This policy refers to the following ketamine products:

- Spravato (esketamine)
- Ketalar (ketamine)

Spravato (Esketamine) Nasal Spray

Spravato is proven and/or medically necessary for the treatment of treatment-resistant depression (TRD) when ALL of the following criteria are met:

Initial Therapy

- Diagnosis of major depressive disorder (treatment-resistant), according to the current DSM (i.e., DSM-5), by a mental health professional; **and**
- Prescribed by or in consultation with a psychiatrist; **and**
- Attestation of baseline scoring (prior to starting Spravato) on at least **one** of the following clinical assessments has been completed:
  - Baseline score on the 17-item *Hamilton Rating Scale for Depression (HAMD17)*
  - Baseline score on the 16-item *Quick Inventory of Depressive Symptomatology (QIDS-C16)*
  - Baseline score on the 10-item *Montgomery-Asberg Depression Rating Scale (MADRS)*

  and
- Patient has not experienced a clinically meaningful improvement after treatment with at least **three** different antidepressants or treatment regimens of adequate dose (maximally tolerated), duration (at least 8 weeks), and adherence in the current depressive episode
  - An antidepressant or treatment regimen would include any of the following classes or combinations **(document medication, dose, and duration)**:
    - Selective serotonin reuptake inhibitors (e.g., citalopram, fluoxetine, paroxetine, sertraline)
    - Serotonin norepinephrine reuptake inhibitors (e.g., duloxetine, venlafaxine, etc.)
    - Bupropion
    - Tricyclic antidepressants (e.g., amitriptyline, clomipramine, nortriptyline, etc.)
    - Mirtazapine
    - Monoamine oxidase inhibitors (e.g., selegiline, tranylcypromine, etc.)
    - Serotonin modulators (e.g., nefazodone, trazodone, etc.)
    - Augmentation with lithium, Cytomel (liothyronine), antipsychotics, or anticonvulsants

  and

- Spravato will be used in combination with a newly initiated daily oral depressant that has not previously been tried; **and**
- Provider and/or the provider's healthcare setting is certified in the Spravato REMS program; **and**
- Spravato dosing is in accordance with the United States Food and Drug Administration (FDA) approved labeling; **and**
- Initial authorization will be for no longer than 12 weeks

Continuation Therapy

- Patient has previously been treated with Spravato; **and**
- Documentation of remission or a positive clinical response to Spravato; **and**
- Submission of baseline and recent (within the last month) scoring on at least **one** of the following assessments demonstrating remission or clinical response (e.g., score reduction from baseline) as defined by the:
  - *Hamilton Rating Scale for Depression* (*HAMD17*; remission defined as a score of ≤7)
  - *Quick Inventory of Depressive Symptomatology* (*QIDS-C16*; remission defined as a score of ≤ 5)
  - *Montgomery-Asberg Depression Rating Scale* (*MADRS*; remission defined as a score of ≤ 12)

  and
- Patient is to receive Spravato therapy in conjunction with an oral antidepressant; **and**
- Provider and/or the provider's healthcare setting is certified in the Spravato REMS program; **and**
- Prescribed by or in consultation with a psychiatrist; **and**
- Spravato dosing is in accordance with the United States FDA approved labeling; **and**
- Authorization will be for no longer than 6 months

Spravato is unproven and not medically necessary for the following:

- Anesthetic agent
- Chronic pain (including but not limited to nonmalignant pain, fibromyalgia, neuropathic pain, complex regional pain syndrome, reflex sympathetic dystrophy)
- Migraine headaches

Ketalar (Ketamine) Injection

Ketamine injection is considered medically necessary and may be covered for the following:

- Anesthesia for diagnostic and surgical procedures that do not require skeletal muscle relaxation; **or**
- The induction of anesthesia prior to administration of other anesthesia agents; **or**
- As supplemental anesthesia for low-potency agents, such as nitrous oxide

Ketamine injection is investigational, and therefore not proven or medically necessary for the following:

- Psychiatric disorders (including, but not limited to depression, bipolar disorder, & posttraumatic stress disorder)
- Chronic pain (including but not limited to nonmalignant pain, fibromyalgia, neuropathic pain, complex regional pain syndrome, reflex sympathetic dystrophy)
- Migraine headaches

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J3490	Unclassified drugs

ICD-10 Diagnosis Code	Description
F33.0	Major depressive disorder, recurrent, mild
F33.1	Major depressive disorder, recurrent, moderate
F33.2	Major depressive disorder, recurrent severe without psychotic features
F33.3	Major depressive disorder, recurrent, severe with psychotic symptoms
F33.40	Major depressive disorder, recurrent, in remission, unspecified
F33.41	Major depressive disorder, recurrent, in partial remission
F33.42	Major depressive disorder, recurrent, in full remission

ICD-10 Diagnosis Code	Description
F33.8	Other recurrent depressive disorders
F33.9	Major depressive disorder, recurrent, unspecified

BACKGROUND

Major depressive disorder (MDD) is a serious and life-threatening condition with high rates of individual and society-level morbidity, and a chronic disease course. Over 16 million people in the United States and over 300 million people worldwide have depression. Patients with MDD may be unable to work, maintain relationships, attend to self-care, and in the most severe cases may become hospitalized or attempt or commit suicide.[16,17] MDD is considered the leading cause of disability worldwide and also is associated with increased mortality rates (at a median rate of 10 years of life lost).[18] About 30 to 40% of patients with MDD fail to respond to first-line treatments including oral antidepressant medications of all classes (selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), etc.) and/or psychotherapy.[19] In addition, the onset of treatment response for these modalities, even when effective, often takes at least four weeks, leading to greater suffering, expense, and risk.

Patients who have failed at least two trials of antidepressant treatment generally comprise the population with treatment-resistant depression (TRD). Relative to other patients with MDD, patients with TRD can incur even more severe morbidity, with higher rates of hospitalization, suicidal ideation and behavior, and medical complications. Standard of care measures for TRD include switching to a different antidepressant (of either the same or a different class), adding an adjunctive treatment to an ongoing antidepressant (typically a drug with a different mechanism of action), adding or switching psychotherapy, or referral for a procedure such as electroconvulsive therapy (ECT) or transcranial magnetic stimulation (TMS).[20]

Spravato (esketamine) is the S-enantiomer of racemic ketamine, and is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. The mechanism by which esketamine exerts its antidepressant effect is unknown.[14]

Ketamine is a rapid-acting general anesthetic producing an anesthetic state characterized by profound analgesia, normal pharyngeal-laryngeal reflexes, normal or slightly enhanced skeletal muscle tone, cardiovascular and respiratory stimulation, and occasionally a transient and minimal respiratory depression. The mechanism of action is primarily due to antagonism of NMDA receptors in the central nervous system.[1]

Ketamine for the treatment of psychiatric disorders and pain has been gaining popularity. Studies available currently are of poor design, lacking adequate sample size and duration. Because of this, additional studies are needed to determine the safety and efficacy for the use of ketamine for these indications.

CLINICAL EVIDENCE

Chronic Pain

Schwartzman et al conducted a randomized double-blind placebo controlled trial to evaluate the effectiveness of intravenous ketamine in the treatment of complex regional pain syndrome (CRPS).[2] Patients were evaluated for 2 weeks or longer before treatment and for 3 months after. All subjects received normal saline with or without ketamine intravenously for 4h (25ml/h) daily for 10 days. The results showed that intravenous ketamine administered in an outpatient setting resulted in statistically significant ($p<0.05$) reductions in many pain parameters. It also showed that subjects in the placebo group did not experience treatment effect in any parameter. The authors conclude that the results of this study warrant a larger randomized placebo controlled trial using higher doses of ketamine and a longer follow-up period.

Noppers et al performed a randomized double blind, active placebo-controlled trial to evaluate the analgesic efficacy of ketamine on fibromyalgia pain.[3] Twenty-four fibromyalgia patients were randomized to receive either ketamine or the active placebo, midazolam by intravenous infusion. Visual Analogue Pain Scores (VAS) and ketamine plasma samples were collected after the infusion. In addition, an 8 week follow up collected pain scores derived from the fibromyalgia impact questionnaire (FIQ) were collected weekly. Fifteen minutes after infusion completion, the number of patients showing a reduction in pain scores >50% was 8 vs. 3 ($P<0.05$), at t=180min 6 vs. 2 (ns), at the end of week-1 2 vs. 0 (ns), and at end of week-8, 2 vs. 2 in the ketamine and midazolam groups, respectively. For VAS and FIQ scores no significant differences in treatment effects were observed in the 2.5-h following infusion or during the 8-week follow-up. Adverse events were mild to moderate in both study groups. The authors conclude that a short-term infusion of ketamine is insufficient to induce long-term analgesic effects in fibromyalgia patients.

Psychiatric Disorders

Esketamine

Esketamine is indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults. Spravato is not approved as an anesthetic agent. The safety and effectiveness of Spravato as an anesthetic agent have not been established.[14]

The safety and efficacy of esketamine was examined in four phase 3 international randomized controlled trials comparing intranasal esketamine and intranasal placebo. Three studies were of similar short-term parallel group design, and one was a randomized withdrawal maintenance-of-effect design. The majority of subjects in all the studies were women in their 40s and 50s, white, with higher body mass index (BMI >24). Depending on the study, around 33 to 40% of enrolled subjects had failed three or more antidepressant (AD) treatments by the start of screening, and 12 to 17% had failed at least four. Each treatment was added to one of four newly initiated oral antidepressants (duloxetine, venlafaxine XR, escitalopram, or sertraline), each dosed daily beginning at the start of the treatment phase. For the first 4 weeks of treatment, the nasal spray was administered twice weekly. For the maintenance-of-effect study and for long-term open-label safety studies, the nasal spray was administered weekly for the next 4 weeks post-induction phase, then either weekly or every other week for ongoing maintenance.[20]

The primary outcome measure used for the studies was the Montgomery-Asberg Depression Rating Scale (MADRS). To decrease the introduction of bias, all MADRS score evaluations were performed by independent, remote (via telephone), blinded raters. Scales were administered on study visit days prior to intranasal esketamine (or placebo) dosing and with a few exceptions (shorter-term secondary endpoints) were meant to assess symptoms over the previous 7 days. Baseline mean MADRS total scores for 3 of the studies ranged from 37 to 38 and for the geriatric study, the mean was 35. These baseline mean scores indicate greater illness severity for the treatment population in the esketamine phase 3 studies than is typical for MDD development programs.[20]

The key inclusion criteria involved the definition of TRD for the patients included: Patients were required to meet DSM-5 diagnostic criteria for recurrent MDD or single-episode MDD (duration ≥ 2years) without psychotic features, which was verified by the structured Mini International Neuropsychiatric Interview (MINI).[21] Patients must have been experiencing moderate to severe depressive symptomatology based on specified scores of the Inventory of Depressive Symptomatology-Clinician rated, 30-item (ICD-C30), and MADRS at Weeks 1, 2, and 4 of the screening/observational phase. In all controlled phase 3 studies, treatment resistance was defined in accordance with the regulatory definition, i.e., a lack of clinically meaningful improvement (defined for phase 3 studies as ≤25%) in the current episode of depression after treatment with at least 2 different antidepressant (AD) agents prescribed in adequate dosages for an adequate duration (defined for phase 3 studies as at least 6 weeks).[20]

In two studies (one parallel-group study and the randomized withdrawal study), esketamine was statistically superior to placebo on the study's primary efficacy endpoint; in the other two short-term parallel group studies, esketamine was not. In the study, TRANSFORM-2, patients in the esketamine treatment group experienced statistically significantly greater improvement in depressive symptoms, as measured by the CFB to endpoint in the MADRS, than patients in the placebo group. On the MADRS, the mean difference between esketamine and placebo was statistically significant at most time points throughout the 28 days of double-blind treatment (except Day 15). In the SUSTAIN-1, trial, direct entry patients or from TRANSFORM-1 or TRANSFORM-2, were enrolled. All subjects who experienced ≥50% reduction from baseline in MADRS total score by the end of acute 4-week treatment were eligible to enter the optimization phase, where they received at least 12 weeks of open-label esketamine treatment with oral antidepressant ongoing. There was a statistically significant difference in time to relapse of depression favoring those patients randomized to continue esketamine versus those who were switched to placebo (with oral antidepressant ongoing in both arms) in the stable remitters group. The secondary endpoint of time to relapse in the stable responders group was also statistically significant.[20]

Ketamine

McCloud et al assessed the effects of ketamine and other glutamate receptor modulators in alleviating the acute symptoms of depression in people with bipolar disorder.[4] The authors included randomized controlled trials comparing ketamine with other active psychotropic drugs or saline placebo in adults with bipolar depression in their review. Regarding ketamine, the authors concluded that there is limited evidence in favor of a single intravenous dose of ketamine over placebo with regard to response rate in the first 24 hours after treatment. In addition, ketamine did not show any better efficacy regarding remission in bipolar depression. While ketamine may have the potential to have a rapid and transient antidepressant effect, the efficacy of a single intravenous dose is limited.

Coyle et al completed a systematic review of the literature, and analyzed data from 21 studies where ketamine was used as an antidepressant.[5] The authors concluded that effectiveness was significantly greater for repeat than single infusion at 4 h, 24 h and 7 days. For single infusion studies, effect sizes were large and significant at 4 h, 24 h and 7 days. Effectiveness for open-label and participant-blind infusions was not significantly different at any time point. The authors concluded that single ketamine infusions elicit a significant antidepressant effect from 4 h to 7 days. There

were a small number of studies at 12–14 days post infusion that failed to reach significance. Results suggest a discrepancy in peak response time depending upon primary diagnosis — 24 h for MDD and 7 days for BD. The authors concluded that further placebo-controlled studies are needed to evaluate the effect of ketamine over time.

Lee et al conducted a meta-analysis to assess the efficacy of ketamine compared to placebo for the reduction of depressive symptoms in patients who meet criteria for a major depressive episode.[6] The authors reviewed two electronic databases for randomized, placebo-controlled trials of ketamine treatment for patients with major depressive disorder or bipolar depression while using a standardized rating scale. The authors included 5 studies in the quantitative meta-analysis. The overall effect size at day 1 was large and statistically significant with an overall standardized mean difference of 1.01 (95% confidence interval 0.69–1.34) (Pb.001), with the effects sustained at 7 days after drug administration. The authors concluded that the effect of ketamine on depressive symptoms at days 1 and 7 post administration supports a potential, new and effective pharmacotherapy with rapid onset, efficacy and good tolerability.

Wan et al pooled data from 205 intravenous ketamine infusions in 97 participants with DSM-IV-defined major depressive disorder from 3 clinical trials.[7] They evaluated the safety and tolerability through attrition, adverse events (AEs), hemodynamic changes, and assessments of psychosis and dissociation. The overall antidepressant response rate, defined as a ≥ 50% improvement in Montgomery-Asberg Depression Rating Scale score, was 67%, or 65 of 97 patients. Four of 205 or 1.95% infusions were discontinued due to AEs. The overall attrition rate was 3.1% or 3 of 97 patients. The most frequent AEs within four hours of the infusion were drowsiness, dizziness, poor coordination, blurred vision, and feeling strange or unreal. Protocol-defined hemodynamic changes occurred in ~1/3 of patients. In addition, ketamine resulted in small but significant increases in psychotomimetic and dissociative symptoms (all $P < .05$). There were no cases of persistent psychotomimetic effects, adverse medical effects, or increased substance use in a subgroup of patients with available long-term follow-up information. The authors concluded that in this group of patients with TRD, ketamine was safe and well tolerated and further research investigating the safety of ketamine in severe and refractory depression is warranted.

Migraine Headache

Lauritsen et al (2016) evaluated the use of intravenous ketamine in patients with refractory migraine treated in the hospital setting. [8] The authors completed a retrospective chart review, which identified six patients with refractory migraine admitted from 2010 through 2014 for treatment with intravenous ketamine. A standard protocol was used to administer ketamine starting with a dose of 0.1 mg/kg/hr and increased by 0.1 mg/kg/hr every 3 to 4 h as tolerated until a target pain score of 3/10 was achieved and maintained for 8 hours or more. Visual Analogue Scale (VAS) scores at time of hospital admission were obtained as well as average baseline VAS scores prior to ketamine infusion. The age range of study patients was 29-54 years with a median age of 36.5. Additionally, 83% were women. Pre-treatment pain scores ranged from 9 to 10. All patients achieved a target pain level of 3 or less for 8 h; the average ketamine infusion rate at target was 0.34 mg/kg/hour (range 0.12-0.42 mg/kg/hr). One patient reported a transient out-of-body hallucination following an increase in infusion rate, which resolved after decreasing the rate. There were no other significant side effects. The authors concluded that IV ketamine was safely administered in the hospital setting to patients with refractory chronic migraine. Treatment was associated with short term improvement in pain severity in 6 of 6 patients with refractory chronic migraine. Prospective placebo-controlled trials are needed to assess short term and long-term efficacy of IV ketamine in refractory chronic migraine.

Pomeroy et al investigated the use of intravenous, subanesthetic ketamine for chronic migraine (CM) or new daily persistent headache (NDPH) in a retrospective review.[9] Upon admission, the mean headache pain rating, using a 0-10 pain scale was an average of 7.1 and decreased to 3.8 at discharge ($P < .0001$). Seventy-two percent (55/77) of patients experienced at least a 2-point improvement in headache pain at discharge. There were some acute responders that maintained this improvement in headache pain at their follow-up office visit but sustained response did not achieve statistical significance (15/77, 27.3%). The mean duration of infusion was 4.8 days. Overall, patients tolerated ketamine. The authors concluded that subanesthetic ketamine infusions may be beneficial in individuals with CM or NDPH who have failed other treatments. Controlled trials are needed to confirm this.

Etchison et al evaluated the efficacy and safety of low-dose intravenous (IV) ketamine for treatment of acute migraine in the emergency department (ED) in a randomized, double-blind, placebo-controlled trial.[10] 34 subjects were randomized to receive 0.2 mg/kg of IV ketamine or an equivalent volume of normal saline by IV push. Numeric Rating Scale (NRS-11) pain scores (0="no pain" and 10="worst pain imaginable"), categorical pain intensity scores from 0 to 3 (0="no headache" and 3="severe headache"), functional disability scores from 0 to 3 (0="no disruption of daily activities" and 3="performance of daily activities is severely impaired"), side effects using the Side Effects Rating Scale for Dissociative Anesthetics (SERSDA) model, and adverse events were assessed at baseline and 30 minutes post-treatment. The primary outcome was between-group difference in NRS-11 score reduction at 30 minutes, and required a 2 point difference in NRS-11 scale for statistical significance. The authors found no statistically significant difference or clinically significant difference in NRS-11 score reduction between the groups after 30 minutes (median NRS-11 score reduction = 1 (interquartile range [IQR] 0 to 2.25) for ketamine group and 2 (IQR 0 to 3.75) for

placebo group. SERDA scores in the ketamine group were significantly greater for generalized discomfort at 30 minutes (p=0.008) and fatigue at 60 minutes (p=0.0216). Authors concluded that ketamine was overall well tolerated; however, 0.2 mg/kg IV ketamine was not efficacious in treating migraine and future studies should be investigated for more effective dosing and routes of administration.

Technology Assessment

Psychiatric Disorders

Hayes compiled a Health Technology Brief on ketamine for treatment-resistant unipolar depression or posttraumatic stress disorder (PTSD) dated November 21, 2017. Regarding treatment-resistant depression (TRD) in adults, Hayes assigned a rating of C, potential but unproven benefit. This rating reflects preliminary positive evidence from a number of studies, and the potential for bias in these results due to shortcomings in study design. For PTSD, Hayes assigned a rating of D2, insufficient published evidence to assess the safety and/or impact on health outcomes or patient management. This rating reflects the small amount of evidence available for this use.[11]

For ketamine used as an adjunct to electroconvulsive therapy to increase antidepressant effects of this treatment in patients with TRD, Hayes assigned a rating of C. This rating reflects a large body of low quality, inconsistent evidence.[12]

Hayes compiled a Medical Technology Directory on ketamine for treatment-resistant bipolar depression (BPD), dated November 19. 2017. Hayes assigned a rating of D2. This rating reflects insufficient evidence regarding the efficacy and safety of ketamine as an add-on to medical treatment for treatment-resistant BPD. This rating also reflects a very-low quality body of evidence limited by a small number of studies, lack of long term follow up, and comparative studies.[13]

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Spravato (esketamine) is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults. Spravato is not approved as an anesthetic agent. The safety and effectiveness of Spravato as an anesthetic agent have not been established.[14]

Spravato is available only through a restricted program called the Spravato REMS program because of the risks of serious adverse outcomes from sedation, dissociation, and abuse and misuse.

Important requirements of the Spravato REMS program include the following:[14]

- Healthcare settings must be certified in the program and ensure that Spravato is:
  - Only dispensed in healthcare settings and administered to patients who are enrolled in the program.
  - Administered by patients under the direct observation of a healthcare provider and those patients are monitored by a healthcare provider for at least 2 hours after administration of Spravato.
- Pharmacies must be certified in the REMS program and must only dispense Spravato to healthcare settings that are certified in the program.

Further information, including a list of certified pharmacies is available at www.Spravatorems.com or 1-855-382-6022.

Ketamine is indicated as the sole anesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation. Ketamine is indicated for the induction of anesthesia prior to the administration of other general anesthetic agents. Ketamine is indicated to supplement low-potency agents, such as nitrous oxide.[1]

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) Ketamine injections used in treatment of depression or pain management. Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, Section 50 - Drugs and Biologicals. (Accessed January 11, 2019)

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Feedback

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
06/01/2019	**Title Change** • Previously titled *Ketamine* **Template Update** • Reorganized policy template: ○ Simplified and relocated *Application* section; previously titled *State Exceptions* ○ Relocated *Background* and *FDA* sections **Coverage Rationale** • Revised coverage criteria for Spravato (esketamine) nasal spray: ○ Replaced reference to "major depressive disorder (MDD)" with "major depressive disorder (*treatment-resistant*)" ***Initial Therapy*** ○ Replaced criterion requiring: ▪ "Patient has not experienced a clinically meaningful improvement after treatment with at least *two* different antidepressants of adequate dose, duration (at least *6* weeks), and adherence in the current depressive episode (must document medications, doses, and durations)" with "patient has not experienced a clinically meaningful improvement after treatment with at least *three* different antidepressants *or treatment regimens* of adequate dose *(maximally tolerated)*, duration (at least *8* weeks), and adherence in the current depressive episode" ▪ "*Patient is to receive* Spravato *therapy* in combination with *another* oral antidepressant" with "Spravato *will be used* in combination with *a newly initiated daily* oral depressant *that has not previously been tried*" ○ Added language to indicate an antidepressant or treatment regimen would include any of the following classes or combinations (document medication, dose, and duration): ▪ Selective serotonin reuptake inhibitors (e.g., citalopram, fluoxetine, paroxetine, sertraline) ▪ Serotonin norepinephrine reuptake inhibitors (e.g., duloxetine, venlafaxine, etc.) ▪ Bupropion ▪ Tricyclic antidepressants (e.g., amitriptyline, clomipramine, nortriptyline, etc.) ▪ Mirtazapine ▪ Monoamine oxidase inhibitors (e.g., selegiline, tranylcypromine, etc.) ▪ Serotonin modulators (e.g., nefazodone, trazodone, etc.) ▪ Augmentation with lithium, Cytomel (liothyronine), antipsychotics, or anticonvulsants ○ Added criterion requiring: ▪ Prescribed by or in consultation with a psychiatrist; and ▪ Attestation of baseline scoring (prior to starting Spravato) on at least one of the following clinical assessments has been completed: - Baseline score on the 17-item *Hamilton Rating Scale for Depression (HAMD17)* - Baseline score on the 16-item *Quick Inventory of Depressive Symptomatology (QIDS-C16)* - Baseline score on the 10-item *Montgomery-Asberg Depression Rating Scale (MADRS)* ***Continuation Therapy*** ○ Replaced criterion requiring "documentation *demonstrating* a positive clinical response *from baseline (e.g., improved Montgomery-Asberg Depression Rating Scale [MADRS], clinical remission, response, etc.), as defined by the*

Date	Action/Description
	provider" with "documentation *of remission or* a positive clinical response *to Spravato*" ○ Added criterion requiring: ▪ Submission of baseline and recent (within the last month) scoring on at least one of the following assessments demonstrating remission or clinical response (e.g., score reduction from baseline) as defined by the: - *Hamilton Rating Scale for Depression* (*HAMD17*; remission defined as a score of ≤7) - *Quick Inventory of Depressive Symptomatology* (*QIDS-C16*; remission defined as a score of ≤ 5) - *Montgomery-Asberg Depression Rating Scale* (*MADRS*; remission defined as a score of ≤ 12) ▪ Prescribed by or in consultation with a psychiatrist **Supporting Information** • Updated *References* section to reflect the most current information • Archived previous policy version CS2019D0069D

INSTRUCTIONS FOR USE

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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

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: July 25, 2019

Prior Authorization Criteria being reviewed: Spravato

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

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

Recommend approval criteria to also include:

2. Age ≥ 18 years;
3. Failure of two antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) from at least two different classes at up to maximally indicated doses but no less than the commonly recognized minimum therapeutic doses, each used for ≥ 8 weeks, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of two of the following antidepressant augmentation therapies, each used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced: second-generation antipsychotic, lithium, thyroid hormone, buspirone;
5. Currently on an oral antidepressant for at least two weeks (must not be one of the aforementioned agents previously failed);
6. Dose does not exceed 168 mg (6 nasal spray devices) per week.

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

Spravato (esketamine)

Summary of Utilization
April 1, 2018 - March 31, 2019
Fee for Service Medicaid

No Utilization for this time period

Anthem

Spravato (esketamine)

Summary of Utilization

April 1, 2018 – March 31, 2019

No Utilization

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Spravato (esketamine)

Summary of Utilization
April 1, 2018 - March 31, 2019
Health Plan of Nevada

No Utilization for this time period

Spravato (esketamine)

Summary of Utilization

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

No Utilization For This Time Period

New Drug Overview
Spravato (esketamine)

INTRODUCTION

- Major depressive disorder (MDD) is a serious and sometimes life-threatening condition with high rates of morbidity. Patients with MDD may be unable to work, maintain relationships, attend to self-care, and in the most severe cases may be hospitalized or attempt or commit suicide. MDD is considered the leading cause of disability worldwide and is associated with increased mortality rates; in the United States, over 16 million people are estimated to have depression *(Food and Drug Administration [FDA] Advisory Committee Spravato briefing document 2019)*.
- Approximately 30 to 40% of patients with MDD fail to respond to first-line treatments, including oral antidepressants (ADs) of all classes and/or psychotherapy. Patients who have failed at least 2 trials of AD treatment are generally considered to have treatment resistant depression (TRD). Relative to other patients with MDD, patients with TRD can experience more severe morbidity, with higher rates of hospitalization, suicidal ideation and behavior, and medical complications *(FDA Advisory Committee Spravato briefing document 2019)*.
- Standard of care measures for TRD include switching to a different AD (same or different class), adding an adjunctive treatment with a different mechanism of action, adding or switching psychotherapy, or procedures such as electroconvulsive therapy (ECT) or transcranial magnetic stimulation (TMS). For patients with TRD, there are no compelling data that indicate one class of ADs is superior to others *(FDA Advisory Committee Spravato briefing document 2019, Thase and Connolly 2019)*.
- Spravato (esketamine) nasal spray is the S-enantiomer of racemic ketamine and was FDA approved for the treatment of TRD in March 2019. Like ketamine, esketamine is an N-methyl-D-aspartic acid (NMDA) receptor antagonist. Although ketamine has been investigated as a treatment modality to rapidly relieve TRD, the mechanism by which ketamine and esketamine exert their antidepressant effect is unknown. Currently, ketamine is only indicated for anesthesia *(FDA Web site, Thase and Connolly 2019)*.
- Prior to the approval of esketamine nasal spray, the only medication FDA-approved for TRD was Symbyax (olanzapine and fluoxetine). The only other FDA-approved interventions for TRD are device-related (ECT, TMS, vagus nerve stimulator [VNS]). Additional off-label pharmacological interventions for TRD include ketamine infusion and augmentation with other ADs or antipsychotics, lithium, thyroid hormone, or buspirone *(FDA Advisory Committee Spravato briefing document 2019)*.
- Medispan Class: N-methyl-D-aspartic acid (NMDA) Receptor Antagonist

INDICATIONS

- Esketamine is indicated, in conjunction with an oral AD, for the treatment of TRD in adults *(Spravato prescribing information 2019)*.
  Limitations of Use: Esketamine is not approved as an anesthetic agent. The safety and effectiveness of esketamine as an anesthetic agent have not been established.
- Esketamine is a Schedule III (CIII) controlled substance under the Controlled Substances Act with a potential for abuse and misuse.

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

CLINICAL EFFICACY SUMMARY

- The clinical trial development program for esketamine in TRD consisted of 3 unpublished, Phase 3, short-term, double-blind (DB), randomized studies (fixed dose [TRANSFORM-1], flexible dose [TRANSFORM-2], and flexible dose in patients ≥ 65 years of age [TRANSFORM-3]); 1 unpublished, long-term, DB, withdrawal, maintenance of effect study (SUSTAIN-1); and 1 unpublished, open-label, long-term safety study (SUSTAIN-2) *(FDA Advisory Committee Spravato briefing document 2019)*.

- As criteria for inclusion for all of the clinical trials, patients had failed at least 2 prior AD trials for the current episode of depression, and baseline Montgomery-Asberg Depression Rating Scale (MADRS) scores, a 10-item instrument with total score ranging from 0 to 60 with a higher score indicating more severe depression, were required to be ≥ 28.
- Rather than randomizing severely ill patients to placebo alone, each study involved the addition of a new AD (duloxetine, escitalopram, sertraline, or venlafaxine extended release [XR]) at the same time that either esketamine or placebo was initiated. This ensured that all patients were receiving some form of active treatment.

- The evidence in support of esketamine's effectiveness primarily derives from the positive results of TRANSFORM-2 and SUSTAIN-1. The other studies failed to achieve statistical significance for their primary endpoints, although results were numerically better for the esketamine groups compared to placebo *(FDA Advisory Committee Spravato briefing document 2019)*.
- TRANSFORM-2 was a short-term, DB, placebo-controlled (PC), parallel-group (PG), multi-center (MC), flexible-dose, randomized controlled trial (RCT). Adults (ages 18 to 64) with TRD and experiencing moderate to severe symptomatology were randomized to intranasal esketamine 56 mg twice weekly for 4 weeks + a newly initiated oral AD daily (n = 114), or intranasal placebo + a newly initiated oral AD daily (n = 109). Patients could be titrated to esketamine 84 mg based on efficacy and tolerability. The primary endpoint was change from baseline (CFB) of the MADRS total score at Day 28 *(FDA Advisory Committee Spravato briefing document 2019).*
  - Patients treated with esketamine had statistically significantly greater improvement in depressive symptoms, as measured by the MADRS CFB at Day 28 vs placebo (see Table 1). The first key secondary endpoint, MADRS sustained response starting Day 2 through Day 28, was not statistically significantly different between the esketamine and placebo groups.
  - Although not statistically evaluated, the percentage of patients categorized as responders (≥ 50% MADRS reduction from baseline) and the percentage of patients achieving remission (MADRS score ≤ 12) were also reported (see Table 1).

Table 1. TRANSFORM-2 MADRS endpoints

Endpoint	Esketamine + oral AD n = 114	Placebo + oral AD n = 109
Baseline MADRS total score (SD)	37.0 (5.7)	37.3 (5.7)
LS mean CFB (SE) at Day 28	-19.8 (1.3)	-15.8 (1.2)
LS mean difference from placebo (SE) at Day 28 (1-sided p-value)	-4.0 (1.7) (p = 0.010)	N/A
MADRS sustained response starting Day 2	8% (p = 0.161)*	5%
	Esketamine + oral AD n = 101	**Placebo + oral AD n = 100**
MADRS responders at Day 28, n (%)	70 (69%)	52 (52%)
MADRS remitters at Day 28, n (%)	53 (53%)	31 (31%)

Abbreviations: LS = least squares, SD = standard deviation, SE = standard error
*Due to a fixed testing sequence, this was the only secondary endpoint that could be formally tested.

- SUSTAIN-1 was a DB, MC, randomized withdrawal trial in which patients were enrolled via transfer entry from the short-term trials (TRANSFORM-1 or TRANSFORM-2) (n = 268) or direct entry (n = 437). Patients received esketamine + an oral AD during an open-label optimization phase. At the end of the optimization phase, patients in stable remission and patients with stable response were randomized to continue esketamine + oral AD or to continue the oral AD but switch to placebo nasal spray for the variable duration maintenance phase. The primary endpoint was time to relapse, defined as MADRS total score ≥ 22 for 2 consecutive assessments, hospitalization for worsening depression, suicide attempt or completion, or any other clinically relevant event suggestive of relapse, among stable remitters during the maintenance phase *(FDA Advisory Committee Spravato briefing document 2019).*
  - For the primary endpoint, among stable remitters, 26.7% of patients in the esketamine + AD group and 45.3% of patients in the placebo + AD group experienced a relapse event during the maintenance phase. The median time to relapse was not estimable (NE) for the esketamine + AD groups, as the 50% relapse rate was not reached based on Kaplan-Meier estimates. The median time to relapse was 273.0 days (95% confidence interval [CI], 97.0 to NE) for the placebo + AD group. Esketamine + AD statistically significantly delayed relapse compared to placebo + AD (p = 0.003). The risk of relapse decreased by 51% in the esketamine + AD group compared to placebo + AD (estimated hazard ratio [HR], 0.49; 95% CI, 0.29 to 0.84).
  - Among stable responders, 25.8% of patients in the esketamine + AD group and 57.6% of patients in the placebo + AD group experienced relapse. The median time to relapse was 635 days (95% CI, 264 to 635) for the esketamine +

AD group and 88.0 days (95% CI, 46 to 196) for the placebo + AD group. Esketamine + AD significantly delayed relapse ($p < 0.001$) and decreased the risk of relapse by 70% (HR, 0.30; 95% CI, 0.16 to 0.55).

CLINICAL GUIDELINES

- For the treatment of MDD, guidelines from the American Psychiatric Association (APA) (2010) and the Veterans Affairs (VA)/Department of Defense (DoD) (2016) state that the effectiveness of AD medications is generally considered comparable between and within classes; therefore, the initial selection of an AD should be based on anticipated adverse effects (AEs), pharmacological properties of the medication, and additional individualized factors such as medication response in prior depressive episodes, cost, and patient preference *(APA 2010, VA/DoD 2016)*.
  - Selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), mirtazapine, and bupropion are considered optimal first-line choices for most patients.
  - For patients demonstrating partial or no response to initial maximized pharmacotherapy, a switch to another monotherapy (medication from the same or different class or psychotherapy) or augmentation with a second medication is recommended.
  - For patients who do not adequately respond to medication therapy, ECT should be considered.
  - The VA/DoD guidelines currently recommend against the use of ketamine infusion outside of a research setting due to the limited information on its safety and duration of effect.

SAFETY SUMMARY

- Esketamine is contraindicated in patients with aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation and intracerebral hemorrhage.
- Esketamine has a boxed warning for sedation; dissociation; abuse and misuse; and suicidal thoughts and behaviors. Because of the risks of serious adverse outcomes resulting from sedation, dissociation, and abuse and misuse, esketamine is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).
  - The goal of the esketamine REMS is to mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by esketamine administration, and abuse and misuse of esketamine by:
    - Ensuring that esketamine is only dispensed to and administered in medically supervised healthcare settings that provide patient monitoring; patients must be monitored for at least 2 hours after administration of esketamine.
    - Ensuring that pharmacies and healthcare settings that dispense esketamine are certified.
    - Ensuring that each patient is informed about serious adverse outcomes from dissociation and sedation and the need for monitoring.
    - Enrollment of all patients in the REMS (registry) to further characterize the risks and support safe use.
- Additional warnings for esketamine include cognitive impairment, impaired ability to drive and operate machinery, and embryo-fetal toxicity.
- The most commonly observed AEs (incidence ≥ 5% and at least twice that of placebo + oral AD) were dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, increased blood pressure, vomiting, and feeling drunk.

DOSING AND ADMINISTRATION

- Esketamine is intended for patient administration under the direct observation of a healthcare provider. Esketamine must never be dispensed directly to a patient for home use.

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Spravato (esketamine)	Nasal spray	Nasal	Induction Phase (Weeks 1 to 4): twice weekly Maintenance Phase: once weekly to every 2 weeks	• During and after esketamine administration at each treatment session, the patient must be observed for at least 2 hours until the patient is safe to leave.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				• If baseline blood pressure is elevated (eg, > 140 mmHg systolic, > 90 mmHg diastolic), the risks of short-term increases in blood pressure and benefit of esketamine treatment should be considered.

See the current prescribing information for full details

CONCLUSION

- MDD, estimated to affect more than 16 million adults in the US, is a serious condition resulting in high rates of disability and morbidity. Comparatively, patients considered to have TRD can experience more severe morbidity, with higher rates of hospitalization, suicidal behavior, and medical complications. Guideline-recommended treatment includes switching ADs, augmenting with other ADs or antipsychotic medications, psychotherapy, and/or procedures such as ECT.
- Esketamine, an NMDA receptor antagonist, is indicated for TRD in adult patients in conjunction with an oral AD. In the 3 short-term, Phase 3, TRANSFORM trials, esketamine + AD demonstrated efficacy in decreasing MADRS score vs placebo + AD, although only TRANSFORM-2 resulted in statistical significance. In SUSTAIN-1, a long-term maintenance withdrawal trial, esketamine + AD statistically significantly delayed relapse vs placebo + AD in patients who had achieved stable remission or response while receiving esketamine + an oral AD.
- Due to safety concerns regarding sedation, dissociation, and risk of abuse and misuse, esketamine has a REMS program that mandates certification of dispensing pharmacies and administration settings, patient registry enrollment, and patient monitoring. Esketamine may only be administered in a healthcare setting under direct supervision by a healthcare provider.
- Esketamine provides an important treatment option with a different mechanism of action for patients with TRD who have exhausted appropriate oral ADs. However, esketamine carries the risk of serious AEs, an intensive REMS program, and strict administration and monitoring requirements. Safety, efficacy, and discontinuation data for long-term maintenance use of esketamine are currently limited.

REFERENCES

- American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder, Third Edition. October 2010. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed May 20, 2019.
- Food and Drug Administration. Spravato FDA briefing document for the Psychopharmacologic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee meeting. February 12, 2019. https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/UCM630970.pdf. Accessed May 20, 2019.
- Food and Drug Administration/Center for Drug Evaluation and Research. FDA approved drug products. Food and Drug Administration Web site. https://www.accessdata.fda.gov/scripts/cder/drugsatfda/. Accessed May 20, 2019.
- Spravato [package insert], Titusville, NJ: Janssen Pharmaceuticals, Inc.; May 2019.
- Thase M, Connolly KR. Unipolar depression in adults: management of highly resistant (refractory) depression. UpToDate Web site. Updated May 9, 2019. www.uptodate.com. Accessed May 20, 2019.
- Veterans Affairs/Department of Defense (VA/DoD) clinical practice guideline for the management of major depressive disorder. Department of Veterans Affairs Web site. April 2016. https://www.healthquality.va.gov/guidelines/MH/mdd/. Accessed May 20, 2019.

Publication Date: June 3, 2019

Gastrointestinal Agents Used for the Treatment of Chronic Idiopathic Constipation (CIC)

OPTUMRx®

Prior Authorization Guideline

Guideline Name: Chronic Idiopathic Constipation (CIC) Agents

1 . Indications

Drug Name: Amitiza (lubiprostone) **Indications** **Chronic Idiopathic Constipation (CIC)** Indicated for the treatment of CIC in adults. **Opioid-Induced Constipation in Adult Patients with Chronic Non-Cancer Pain** Indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation. Limitations of Use: Effectiveness of Amitiza in the treatment of opioid-induced constipation in patients taking diphenylheptane opioids (e.g., methadone) has not been established. **Irritable Bowel Syndrome with Constipation** Indicated for the treatment of irritable bowel syndrome with constipation in women at least 18 years old.
Drug Name: Linzess (linaclotide) **Indications** **Irritable Bowel Syndrome with Constipation (IBS-C)** Indicated in adults for the treatment of irritable bowel syndrome with constipation (IBS-C). **CIC** Indicated in adults for the treatment of CIC.
Drug Name: Motegrity (prucalopride) **Indications** **CIC** Indicated for the treatment of CIC in adults.

Drug Name: Trulance (plecanatide)

Indications

CIC Indicated in adults for the treatment of CIC**.**

IBS-C Indicated in adults for the treatment of IBS-C.

2 . Criteria

Product Name: Amitiza, Linzess, Motegrity, Trulance

Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Chronic Idiopathic Constipation (CIC)

AND

2 Trial and failure, contraindication, or intolerance to one of the following:

- Lactulose
- Polyethylene glycol

AND

3 Requested drug is FDA approved for the patient's age.

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: July 25, 2019

Prior Authorization Criteria being reviewed: Chronic Idiopathic Constipation Agents

Managed Care Organization name: Choose an item.

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.

Suggested Addition:

Amitizia: OIC and IBS-C Dx

Linzess: OIC and IBS-C Dx

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: _____ L Todd _____

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: July 25, 2019

Prior Authorization Criteria being reviewed: Chronic Idiopathic Constipation 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

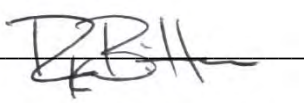
☐ I disapprove of the criteria as presented by OptumRx

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.

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: July 25, 2019

Prior Authorization Criteria being reviewed: Chronic Idiopathic Constipation Agents

Managed Care Organization name: Silver Summit Health Plan

Please place a check mark in the appropriate box:

☐ I approve the criteria as presented by OptumRx

☒ I disapprove of the criteria as presented by OptumRx

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

Recommend adding additional criteria for all:

1. Failure of one bulk forming laxative [e.g., psyllium (Metamucil®), methylcellulose (Citrucel®), calcium polycarbophil (FiberCon®)] unless all are contraindicated or clinically significant adverse effects are experienced;
2. Failure of one stimulant laxative (e.g., bisacodyl, senna) unless all are contraindicated or clinically significant adverse effects experienced;
3. Failure of polyethylene glycol (MiraLax®) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects experienced;
4. Dose does not exceed 48 mcg per day (2 capsules per day).

Trulance – Dose does not exceed 3 mg per day (1 tablet per day).
Amitiza - Dose does not exceed 48 mcg per day (2 capsules per day).
Linzess –Dose does not exceed 145 mcg per day (1 capsule per day).

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.

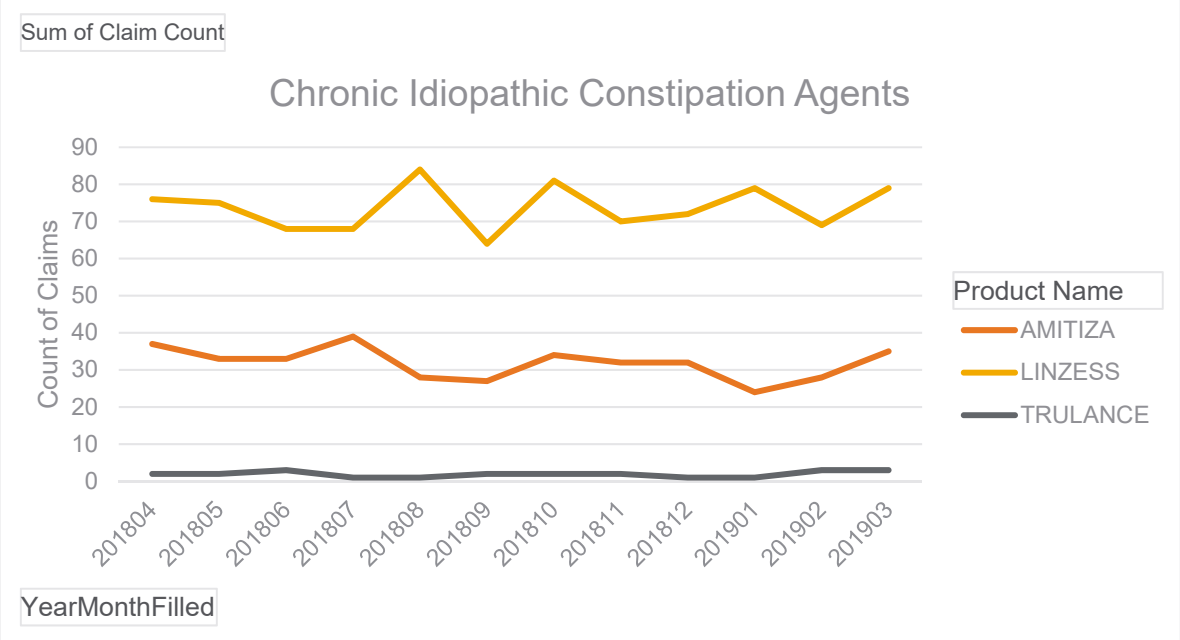
Please print the name of the individual completing this form: Tom Beranek

Signature of individual completing this form: *Tom Beranek*

Chronic Idiopathic Constipation Agents

Summary of Utilization
April 1, 2018 - March 31, 2019
Fee for Service Medicaid

Product Name	Member Count	Claim Count	Days Supply	Sum of Qty
AMITIZA	93	382	12,285	23,211
TRULANCE	6	23	720	720
LINZESS	215	885	33,851	33,971
Total	**314**	**1,290**	**46,856**	**57,902**



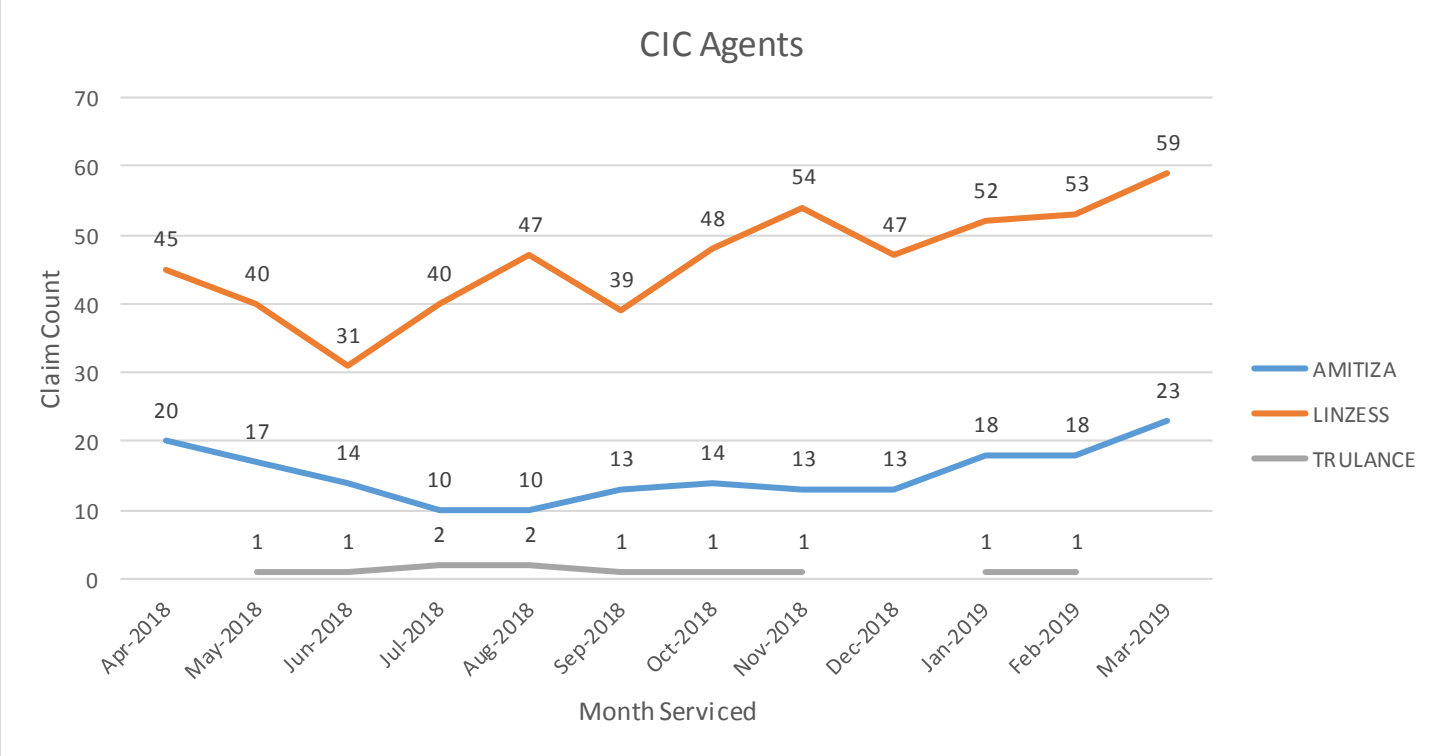
Anthem

Chronic Idiopathic Constipation Agents

Summary of Utilization

April 1, 2018 – March 31, 2019

Drug	Member Count	Claim Count	Days Supply	Quantity Dispensed
AMITIZA 24 MCG CAPSULES	42	147	4356	8352
AMITIZA 8 MCG CAPSULE	14	36	1080	2130
LINZESS 145 MCG CAPSULE	61	238	7170	7170
LINZESS 290 MCG CAPSULE	73	268	8040	8040
LINZESS 72 MCG CAPSULE	21	49	1470	1470
TRULANCE 3 MG TABLET	3	11	330	330
Grand Total	**197**	**749**	**22446**	**27492**

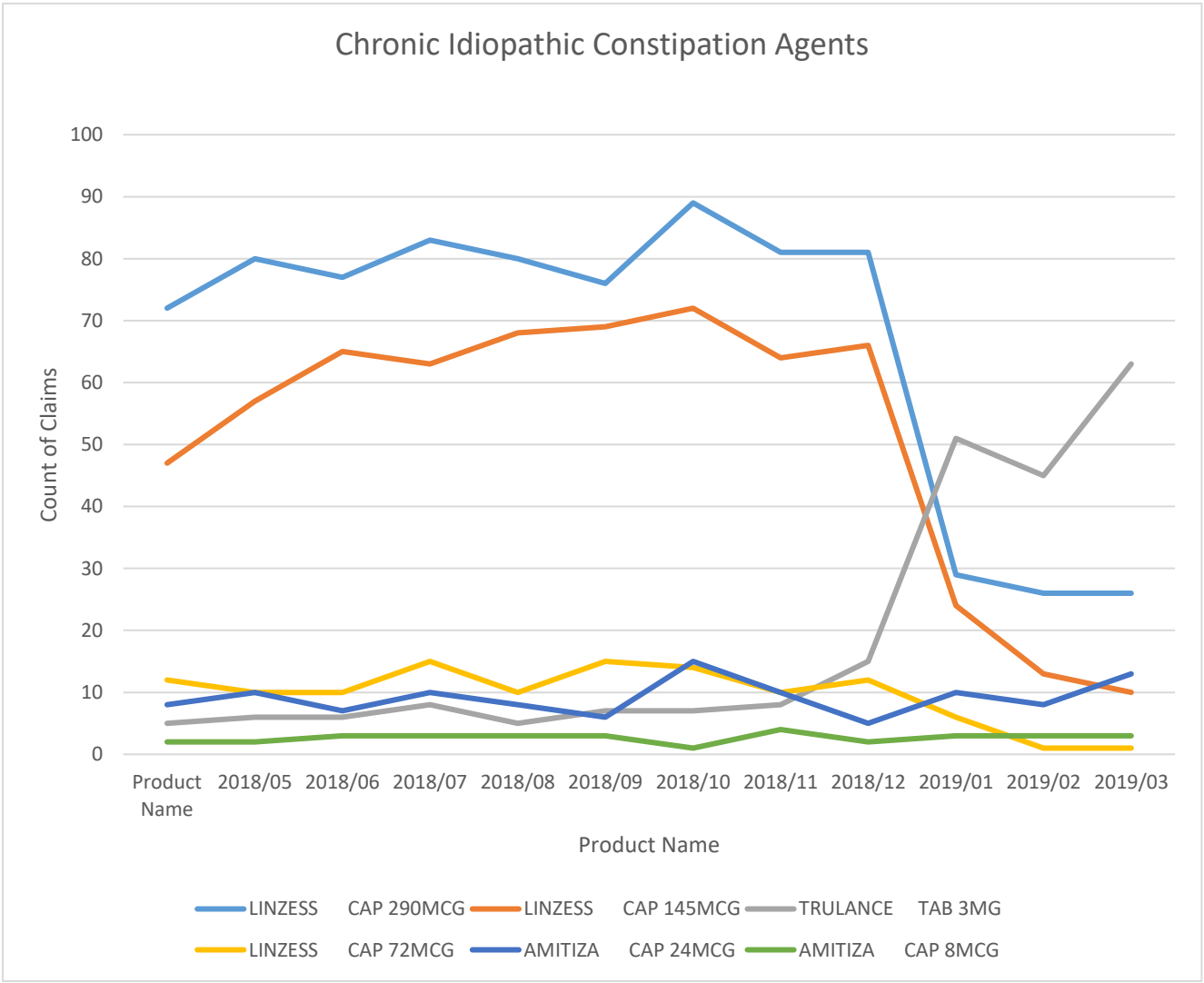


HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Chronic Idiopathic Constipation Agents

Summary of Utilization
April 1, 2018 - March 31, 2019
Health Plan of Nevada

Product Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
LINZESS CAP 290MCG	375	800	24,060	24,060	NA
LINZESS CAP 145MCG	331	618	18,510	18,630	NA
TRULANCE TAB 3MG	144	226	8,435	8,460	NA
LINZESS CAP 72MCG	68	116	3,480	3,480	NA
AMITIZA CAP 24MCG	58	110	3,250	5,865	NA
AMITIZA CAP 8MCG	16	32	910	1,520	NA
Grand Total	**992**	**1,902**	**58,645**	**62,015**	**NA**



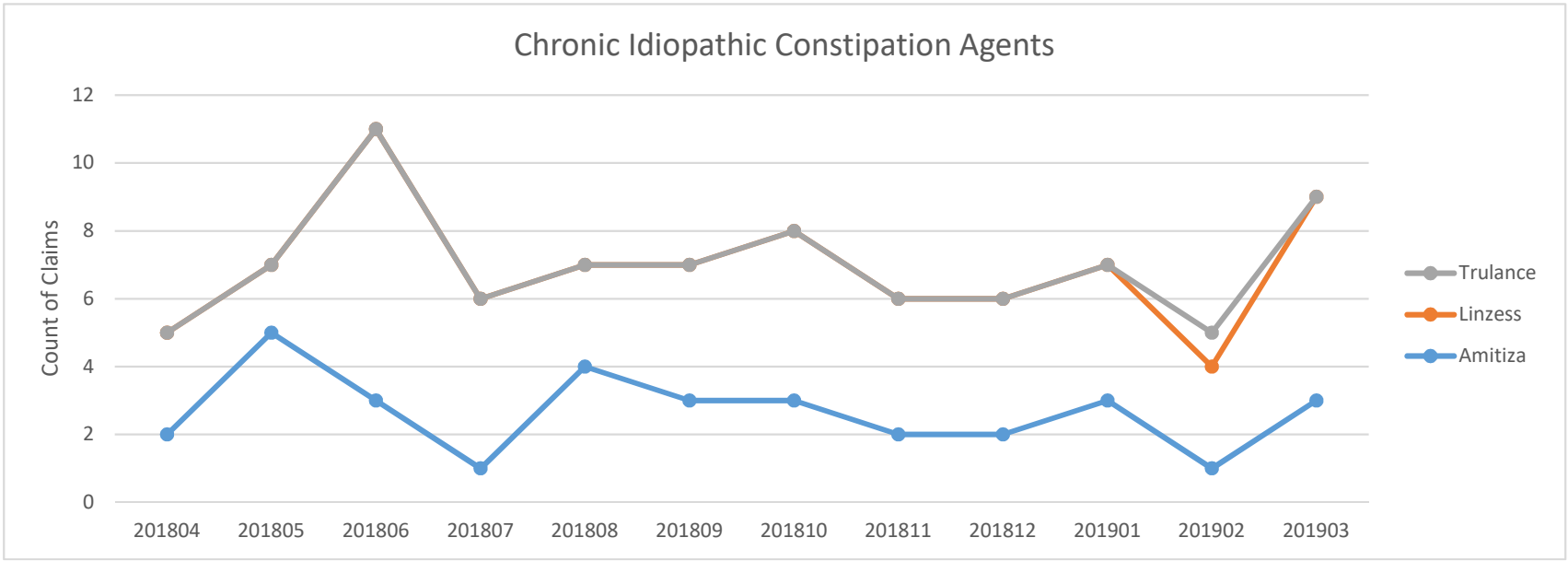
Chronic Idiopathic Constipation Agents

Summary of Utilization

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Qty	Sum of Days
AMITIZA CAP 8MCG	1	1	60	30
AMITIZA CAP 24MCG	10	31	1,530	930
LINZESS CAP 145MCG	11	19	570	570
LINZESS CAP 290MCG	7	18	540	540
LINZESS CAP 72MCG	4	14	420	420
TRULANCE TAB 3MG	1	1	30	30
Total	**34**	**84**	**3,150**	**2,520**



LLL. Opioid-Induced Constipation Agents

Therapeutic Class: Opioid-Induced Constipation Agents
Last Reviewed by the DUR Board: January 25, 2018

Opioid-induced constipation agents 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 will be given if all the following criteria are met and documented:

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

b. The requested medication is being used for an FDA approved indication; and

c. The recipient must meet the following criteria:

1. There is documentation in the recipient's medical record of an inadequate response, adverse reaction or contraindication to one agent from three of the four traditional laxative drug classes:

a. Bulk forming laxatives;

b. Osmotic laxatives;

c. Saline laxatives;

d. Stimulant laxatives

d. And, requests for methylnaltrexone bromide that exceed the quantity limit must meet all of the following criteria:

1. The recipient has opioid-induced constipation in advanced illness, is receiving palliative care, and is not enrolled in the DHCFP's hospice program; and

2. The requested dose is 0.15 mg/kg; and

3. The recipient's current weight is >114 kg.

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

WW. Irritable-Bowel Syndrome Agents

Therapeutic Class: Irritable-Bowel Syndrome Agents
Trulance® last reviewed by the DUR Board: July 26, 2018
Last Reviewed by the DUR Board: July 28, 2016
Viberzi® last reviewed by the DUR Board April 28, 2016

Irritable-Bowel Syndrome Agents 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

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

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

        2. The requested agent is being prescribed based on FDA approved guidelines; and

            a. For requests for a diagnosis of Irritable-Bowel Syndrome with Constipation (IBS-C):

                1. For requests for Amitiza® (lubiprostone), the recipient must be female.

                2. The requested dose is appropriate based on indication and age.

                    a. Linzess® (linaclotide): 290 µg daily.

                    b. Amitiza® (lubiprostone): 16 µg daily.

                    c. Trulance® (plecanatide): 3 µg daily.

            b. For requests for a diagnosis of Irritable-Bowel Syndrome with Diarrhea (IBS-D):

                1. The medication is being prescribed by or in consultation with a gastroenterologist; and

                2. The requested dose is appropriate based on indication and age.

                    a. Lotronex® (alosetron): 0.5 mg twice daily or 1 mg twice daily.

b. Viberzi® (eluxadoline): 75 mg twice daily or 100 mg twice daily.

c. Xifaxan® (rifaximin): 550 mg three times a day for 14 days.

2. Prior Authorization Guidelines

a. Prior authorization approval will be given for an appropriate length of therapy based on the requested agent and diagnosis, not to exceed one year.

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

INTRODUCTION

- Irritable bowel syndrome (IBS) is a gastrointestinal disorder that most commonly manifests as chronic abdominal pain and altered bowel habits in the absence of any organic disorder (*Wald 2017*).
- IBS may consist of diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), IBS with a mixed symptomatology (IBS-M), or unclassified IBS (IBS-U). Switching between the subtypes of IBS is also possible (*Ford et al 2018*).
- IBS is a functional disorder of the gastrointestinal tract characterized by symptoms of abdominal pain, discomfort and bloating, and abnormal bowel habits with bouts of diarrhea and/or constipation. The exact pathogenesis of the disorder is unknown; however, it is believed that altered gastrointestinal tract motility, visceral hypersensitivity, autonomic dysfunction, and psychological factors indicate disturbances within the enteric nervous system, which controls the gastrointestinal system (*Andresen et al 2008, Ford et al 2009, Quigley et al 2012, World Gastroenterology Organization [WGO] 2015*).
- Prevalence estimates of IBS range from 10 to 12%, and it typically occurs in young adulthood (*Ford et al 2018*). IBS-D is more common in men, and IBS-C is more common in women (*WGO 2015*).
- Symptoms of IBS often interfere with daily life and social functioning (*WGO 2015*).
- The general goals of therapy in IBS are to alleviate the patient's symptoms and to target any specific exacerbating factors (eg, medications, dietary changes), concerns about serious illness, stressors, or potential psychiatric comorbidities that may exist (*Wald 2017*).
- Non-pharmacological interventions to combat IBS symptoms include dietary modifications such as exclusion of gas-producing foods (eg, beans, prunes, Brussel sprouts, bagels, etc.), and consumption of probiotics, as well as psychosocial therapies (eg, hypnosis, biofeedback, etc.) (*Ford et al 2018*).
- Depending upon the clinical presentation of an individual's IBS condition, a number of therapies exist to help alleviate the constellation of disease symptoms. Commonly used agents that are often initiated for disease control include poorly absorbable antibiotics such as rifaximin; antispasmodics (eg, dicyclomine, hyoscine, etc.); selective chloride channel activators (eg, lubiprostone); serotonin-3 receptor antagonists (eg, alosetron); guanylate cyclase-C agonists (eg, linaclotide, plecanatide); opioid receptor agonist (eg, eluxadoline), antidepressants such as tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs); select probiotics; and peppermint oil (*Ford et al 2018*).
- Amitiza (lubiprostone), Linzess (linaclotide), Motegrity (prucalopride), and Trulance (plecanatide) are indicated for the treatment of chronic idiopathic constipation (CIC). Symptoms of constipation are common with a prevalence of approximately 16% in adults overall and 33% in adults >60 years of age. Constipation is defined as fewer than three bowel movements (BMs) per week with symptoms that may include hard stools, a feeling of incomplete evacuation, abdominal discomfort, bloating, and distention. Initial treatment typically includes osmotic laxatives, stimulant laxatives, and increased fiber intake (*American Gastroenterological Association [AGA] Medical Position Statement 2013, Bharucha et al 2013*).
  - Prucalopride, a selective serotonin type 4 (5-HT_4) receptor agonist, is a gastrointestinal prokinetic agent that stimulates colonic peristalsis (high-amplitude propagating contractions [HAPCs]), which increases bowel motility (*Shin et al 2014*).
  - The intestinal secretagogues, ie, lubiprostone, linaclotide, and plecanatide, exert their effects by increasing intestinal and colonic secretion of chloride-rich fluid into the intestinal lumen. There is no reported evidence indicating that these agents induce HAPCs.
- Opioid-induced constipation (OIC) is a frequent adverse event of opioid therapy. Opioids exert their action on the enteric nervous system causing dysmotility, decreased fluid secretion and sphincter dysfunction. Laxatives are typically prescribed but often are inadequate to completely relieve constipation (*Brock et al 2012*). There are 4 products are approved for use in OIC:
  - Amitiza (lubiprostone) is also Food and Drug Administration (FDA)-approved for the treatment of opioid-induced constipation (OIC) in adults with chronic, non-cancer related pain.

- Relistor (methylnaltrexone) injection is an opioid receptor antagonist indicated for treatment of OIC in adults with chronic non-cancer pain and in patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care. Relistor has also been FDA-approved in a tablet formulation, which is indicated for the treatment of OIC in adults with chronic non-cancer pain.
- Movantik (naloxegol) and Symproic (naldemedine) are once-daily oral peripherally acting mu-opioid receptor antagonists (PAMORA) indicated for the treatment of OIC in adult patients with chronic non-cancer pain.

- For management of OIC, the AGA recommends laxatives as a first-line treatment (*Crockett et al 2019*). For patients with laxative-refractory OIC, naldemedine or naloxegol are recommended over no treatment, methylnaltrexone is suggested over no treatment, and there are no recommendations for the use of lubiprostone or prucalopride.
- Zelnorm (tegaserod) was approved in July 2002 for short-term treatment of IBS-C in women and in August 2004 for treatment of CIC in men and women < 65 years of age. In March 2007, the FDA requested the manufacturer to discontinue the marketing of Zelnorm due to safety concerns related to increased rate of heart attack, stroke, and worsening heart-related chest pain. In July 2007, Zelnorm became available for use as a treatment investigational new drug (IND) protocol for IBS-C and CIC in women < 55 years of age meeting specific guidelines. However, in April 2008, the manufacturer discontinued its availability as a treatment IND. Zelnorm is currently available for use only in emergency situations that require patient hospitalization, and only with FDA authorization (*Clinical Pharmacology 2019*). Physicians with who are interested in using Zelnorm for an emergency situation may contact FDA's Division for Drug Information about the emergency IND process (*FDA Zelnorm information 2018*).
  - In 2018, the Gastrointestinal Drugs Advisory Committee of the FDA voted in favor of reintroducing Zelnorm (tegaserod) onto the market for the treatment of IBS-C in women without a history of cardiovascular ischemic disease and who have no more than 1 risk factor for cardiovascular disease (*Brown 2018*). At the date of this review, Zelnorm has yet to be formally re-approved by the FDA.
- IBS-D is an IBS subtype characterized mainly by loose or watery stools at least 25% of the time. Viberzi (eluxadoline) and Xifaxan (rifaximin) are both FDA-approved for the treatment of IBS-D. Viberzi is a mu-opioid receptor agonist and a schedule IV controlled substance; Xifaxan is a rifamycin antibacterial. Lotronex (alosetron) is FDA-approved with restrictions for the treatment of women who exhibit severe IBS-D and have failed conventional therapy.
- The scope of this review will focus upon Amitiza (lubiprostone), Linzess (linaclotide), Lotronex (alosetron), Motegrity (prucalopride), Movantik (naloxegol), Relistor (methylnaltrexone bromide), Symproic (naldemedine), Trulance (plecanatide), Viberzi (eluxadoline), and Xifaxan (rifaximin) for their respective FDA-approved indications, which are outlined in Table 2.
- Medispan Classes: Agents for CIC (Motegrity, Trulance); Gastrointestinal Chloride Channel Activators (Amitiza); IBS Agents (Lotronex, Linzess, Viberzi); Peripheral Opioid Receptor Antagonists (Movantik, Relistor, Symproic); Anti-infective Agents – Misc (Xifaxan)

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Amitiza (lubiprostone)	-
Linzess (linaclotide)	-
Lotronex (alosetron)	✔
Motegrity (prucalopride)	-
Movantik (naloxegol)	-
Relistor (methylnaltrexone bromide)	-
Symproic (naldemedine)	-
Trulance (plecanatide)	-
Viberzi (eluxadoline)	-
Xifaxan (rifaximin)	-

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

EFFICACY SUMMARY

- There are currently no head-to-head trials comparing the available agents used in the treatment of CIC, OIC, IBS-C, and IBS-D.

CIC

- A network meta-analysis demonstrated linaclotide and lubiprostone to be superior to placebo for the treatment of CIC. Treatment with linaclotide resulted in a significant increase in the proportion of patients with ≥ 3 complete spontaneous bowel movements (CSBMs)/week compared with placebo with a relative risk (RR) of 1.96 (95% confidence interval [CI], 1.12 to 3.44), and was superior vs placebo with an increase over baseline by ≥ 1 CSBM/week (RR, 1.72; 95% CI, 1.18 to 2.52). For change from baseline in the number of SBMs/week, the weighted mean difference (WMD) with lubiprostone was 1.91 (95% CI, 1.41 to 2.41) and WMD with linaclotide was 2.11 (95% CI, 1.68 to 2.54) (*Nelson et al 2017*).
- A meta-analysis demonstrated the total pooled treatment effect of spontaneous bowel movements (SBMs)/week in patients with CIC or IBS-C was greater in lubiprostone-treated patients compared with placebo (combined standardized difference in means, 0.419; 95% CI, 0.088 to 0.750; p < 0.001) (*Li et al 2016*).
- A meta-analysis of 16 RCTs evaluated the safety and efficacy of prucalopride in the management of CIC (*Sajid et al 2016*). The primary outcome measure was the incidence of spontaneous bowel movements (SBMs) per week, and the secondary outcome measure was adverse eventss.
  - Based on data from 9 trials, prucalopride 2 mg significantly reduced the incidence of SBMs per week compared with placebo (standardized mean difference [SMD] 0.34; 95% CI, 0.11 to 0.56; I^2 = 78%; p = 0.003).
  - The risk of developing adverse events (eg, headache, abdominal cramps, excessive flatulence, dizziness, diarrhea, rash) was higher in the prucalopride 2 mg group (odds ratio [OR], 1.76; 95% CI, 1.33 to 2.34; I^2 = 53%; p < 0.0001). The majority of adverse events were reported within the first 24 hours of initiation of therapy and were transient.
- A systematic review and meta-analysis evaluated the efficacy of serotonin type 4 (5-HT_4) agonists, including prucalopride, velusetrag, and naronapride (not approved in the U.S.) for the treatment of CIC. 5-HT_4 agonists were superior to control for all measured outcomes.
  - The proportion of patients randomized to a 5-HT_4 agonist who achieved a mean of ≥ 3 CSBMs per week was 27.5% vs 17.2% of patients randomized to control (RR, 1.85; 95% CI, 1.23 to 2.79; I^2 = 89%; p < 0.001).
  - Overall, 46.7% of patients randomized to a 5-HT_4 agonist achieved a mean increase of ≥ 1 CSBM per week over baseline vs 30.8% of control patients (RR, 1.57; 95% CI, 1.19 to 2.06; I^2 = 89%; p < 0.001).
  - 5-HT4 agonists also showed significant improvement over control for patient-reported QOL measures.
  - Adverse events were more common with 5-HT_4 agonists than with control (RR, 1.25; 95% CI, 1.14 to 1.38) and included headache, diarrhea, nausea, and abdominal pain.
- In another meta-analysis, treatment with linaclotide 145 mcg demonstrated significant improvements in the weekly frequency of CSBMs from baseline compared with placebo in patients with CIC (RR, 3.80; 95% CI, 2.20 to 6.55). Results were similar for abdominal discomfort or bloating responders for linaclotide 145 mg vs placebo, with pooled RRs of 1.57 (95% CI, 1.26 to 1.97) and 1.97 (95% CI, 1.44 to 2.69), respectively (*Videlock et al 2013*).
- A double-blind, placebo-controlled, multicenter, randomized controlled trial demonstrated that treatment with linaclotide 72 mcg improved the CSBM frequency over 12-weeks compared with placebo, with 13.4% of linaclotide-treated patients meeting responder requirements compared with 4.7% in the placebo group (95% CI, 1.8% to 5.2%) (*Schoenfeld et al 2018*).
- Results from a long-term safety study illustrated that overall lubiprostone was well tolerated. The most commonly reported events were diarrhea, nausea, urinary tract infection, sinusitis, abdominal distension, and headache. Significant changes from baseline in hematology, laboratory values, vital signs, weight, body mass index and physical examination were not seen over the study duration (*Chey et al 2012*).
- Two double-blind, placebo-controlled, multicenter, randomized controlled trials demonstrated that treatment with plecanatide 3 mg significantly increased weekly CSBM frequency as measured by the overall CSBM responder rate vs placebo (Study 1: 21.0% vs 10.2%; p < 0.001; Study 2: 20.1% vs 12.8%; p = 0.004) (*DeMicco et al 2017, Miner et al 2017*).
- Six double-blind, placebo-controlled, multicenter, randomized controlled trials of similar design in adults (N = 2484) evaluated the safety and efficacy of prucalopride for the treatment of CIC in an integrated analysis of the results (*Camilleri et al 2016, Prucalopride FDA briefing document 2018).*
  - The percentage of patients with a mean frequency of ≥ 3 CSBMs/week over a 12-week treatment period was significantly higher with prucalopride 2 mg/day (27.8%) vs placebo (13.2%) (OR, 2.68; 95% CI, 2.16 to 3.33; p < 0.001); the number needed to treat (NNT) with prucalopride was 8.8 (95% CI, 7.1 to 11.6). Efficacy and safety outcomes were not significantly different between men and women.
  - The proportion of patients with a mean increase of ≥ 1 CSBM/week was 47.0% with prucalopride vs 29.9% with placebo (p < 0.001).
  - Out of the 6 trials, the 24-week trial failed to demonstrate statistical significance for the primary endpoint after both 12 and 24 weeks, causing moderate heterogeneity. The reasons for the smaller treatment effect in this study remain unclear.

- Due to its differing mode of action, prucalopride may be beneficial for patients with CIC who have an insufficient quantity of high-amplitude propagating contractions (HAPCs) or in those who do not respond to other medications (*Camilleri et al 2016*).

IBS

- In 2 meta-analyses, linaclotide demonstrated significant improvements in the FDA-defined composite endpoint of improvement in both daily worst abdominal pain scores and CSBM frequency from baseline compared to placebo after 12 weeks and demonstrated a similar result when compared over 26 weeks (*Atluri et al 2014, Videlock et al 2013*). More patients in the placebo treatment arm failed to achieve the FDA endpoint compared with patients treated with linaclotide (82.6% vs 66%; RR of failure to respond, 0.80; 95% CI, 0.76 to 0.85).
- A 2018 network meta-analysis evaluated the same intestinal secretagogues in patients with IBS-C, and ranked linaclotide 290 mcg daily as highest for efficacy (among tenapanor [investigational agent], lubiprostone, and plecanatide 3 and 6 mg); plecanatide 6 mg once daily was ranked highest for safety (*Black et al 2018*).
- The American College of Gastroenterology commissioned a systematic review to assess the overall efficacy of available therapies for the treatment of IBS (*Ford et al 2018*). The secondary objectives included assessing efficacy according to predominant stool pattern reported (IBS-C, IBS-D, and IBS-M), as well as evaluating adverse events. Parallel-group, randomized controlled trials comparing active interventions with either placebo or no therapy were appraised. Crossover trials were eligible for inclusion if extractable data were provided at the end of the first treatment period before crossover. The following were identified as “strong” recommendations for IBS treatments:
  - Fiber for overall symptom improvement in IBS patients: Quality of evidence is moderate.
  - TCAs for overall symptom improvement in IBS patients: Quality of evidence is high.
  - Linaclotide for overall symptom improvement in IBS-C patients: Quality of evidence is high.
  - Plecanatide or lubiprostone for overall symptom improvement in IBS-C patients: Quality of evidence is moderate.
  - There is insufficient evidence to recommend loperamide for use in IBS. Quality of evidence is very low.
- For the treatment of IBS-C, placebo-controlled trials demonstrated that lubiprostone had a significantly higher percentage of overall responders. In multiple 12-week studies, lubiprostone-treated patients reported significant improvements in abdominal pain/discomfort, stool consistency, straining, constipation severity, and quality of life (*Drossman et al 2007, Drossman et al 2009, Johanson et al 2008b*).
- Treatment with alosetron is associated with a significantly greater proportion of patients reporting adequate relief of IBS pain and discomfort, and improvements in bowel function compared to placebo (*Camilleri et al 2000, Camilleri et al 2001, Chey et al 2004, Lembo et al 2001, Lembo et al 2004, Rahimi et al 2008, Watson et al 2001*).
- A meta-analysis concluded that the 5-hydroxytryptamine type 3 (5-HT3) antagonists as a class significantly improve symptoms of non-constipating or IBS-D in both men and women compared to placebo; however, these agents were also associated with a greater increase in the risk of causing constipation compared to placebo (*Andresen et al 2008*).
- Alosetron treatment has been shown to positively impact global symptoms, as well as pain and discomfort in non-constipated females with IBS. This analysis further supports the increased chance of developing constipation with alosetron compared to placebo (*Cremonini et al 2003*).
- The safety and efficacy of eluxadoline for treatment of IBS-D were established in 2 randomized, multicenter, multinational, double-blind, placebo-controlled, phase 3 clinical trials in which 2427 patients with IBS-D (meeting Rome III criteria), average abdominal pain scores greater than 3 on a 0 to 10 scale during the week prior to randomization, and a Bristol Stool Scale (BSS) of 5.5 or greater with at least 5 days of BSS of 5 or more during the week prior to randomization. Patients were randomly assigned to receive eluxadoline 75 mg, 100 mg, or placebo twice daily. The primary endpoint was defined by the simultaneous improvement in the daily worst abdominal pain score by 30% or more compared to the baseline weekly average and a reduction in the BSS to 5 or less on at least 50% of the days within a 12-week or 26-week time interval. From weeks 1 through 12, the primary endpoint was achieved by 23.9% of patients in the 75 mg group ($p = 0.01$) and 25.1% of patients in the 100 mg group ($p = 0.004$) versus 17.1% of patients in the placebo group. From weeks 1 through 26, 23.4% in the 75 mg group ($p = 0.11$) and 29.3% in the 100 mg group ($p < 0.001$) achieved the primary endpoint compared to 19% in the placebo group (*Lembo et al 2016a*).
- The safety and effectiveness of rifaximin for treatment of IBS-D were established in three double-blind, placebo-controlled trials.
  - In the first 2 trials, 1,258 patients with IBS-D (Rome II criteria) were randomly assigned to receive rifaximin 550 mg three times daily (n = 624) or placebo (n = 634) for 14 days, and then followed for a 10-week treatment-free period. The primary endpoint for both trials was the proportion of patients who achieved adequate relief of IBS signs and symptoms for at least 2 of 4 weeks during the month following 14 days of treatment. More rifaximin-treated patients reported improvements in abdominal pain and stool consistency than those on placebo (Trial 1: 47% vs 39%; $p < 0.05$; Trial 2: 47% vs 36%; $p < 0.01$ in rifaximin and placebo groups, respectively).

- TARGET3 was the third trial, which evaluated repeat courses of rifaximin in adult patients with IBS-D (Rome III criteria) for up to 46 weeks. During a 14-day open-label phase, 1,074 patients responded to rifaximin and were evaluated over 22 weeks for continued response or recurrence of IBS symptoms. A total of 636 patients who developed recurrent signs and symptoms after a single treatment course of rifaximin were randomized to receive either rifaximin 550 mg three times daily (n = 328) or placebo (n = 308) for 2 additional 14-day courses separated by 10 weeks. More patients treated with rifaximin than placebo were responders in abdominal pain and stool consistency in this phase of the study (38% vs 31% in rifaximin and placebo groups, respectively; p < 0.05) (*ClinicalTrials.gov 2019, Lembo et al 2016b*).

- In 2 randomized, double-blind, placebo-controlled, 12-week studies, there were significantly more overall responders (based on improved abdominal pain and weekly CSBM from baseline) with plecanatide 3 mg vs placebo in patients with IBS-C (Study 1: 30% vs 18%; Study 2: 21% vs 14%) (*Trulance prescribing information 2018*).

OIC

- Two randomized, double-blind, placebo-controlled trials, COMPOSE-1 and COMPOSE-2, were conducted in adult patients with chronic non-cancer pain and OIC to assess the efficacy and safety of naldemedine. The primary endpoint was the proportion of responders, where response was defined as at ≥ 3 SBMs per week. Patients in COMPOSE-1 and COMPOSE-2 were randomized to receive naldemedine 0.2 mg (n = 274; n = 277) or placebo (n = 273; n = 276) once daily for 12 weeks. Results from both COMPOSE-1 and COMPOSE-2 showed that participants receiving naldemedine 0.2 mg experienced a significantly higher response compared to patients receiving placebo in both studies (COMPOSE-1 responders: 47.6% vs 34.6%; p = 0.002 and COMPOSE-2 responders: 52.5% vs 33.6%; p<0.0001, respectively). Treatment-related adverse events due to gastrointestinal disorders were more common with naldemedine than with placebo in both studies (15% vs 7% and 16% and 7%, respectively) (*Hale et al 2017*).
- COMPOSE-4 was a 2-week randomized, double-blind, placebo-controlled trial of naldemedine 0.2 mg in patients with OIC and cancer, and COMPOSE-5 was a 12-week, open-label extension study. In COMPOSE-4, there were significantly more SBM responders in the naldemedine group compared to placebo (71.1% vs 34.4%; p < 0.0001). Treatment-emergent adverse events were also higher with naldemedine vs placebo (44.3% vs 26.0%; p = 0.01). In the extension study, 80.2% of patients experienced a treatment-emergent adverse event, most commonly gastrointestinal adverse events (*Katakami et al 2017*).
- A total of 1300 patients were enrolled in three, double-blind, randomized controlled trials evaluating lubiprostone compared to placebo in patients with chronic, non-cancer related pain on stable opioid therapy and constipation. In Study 1, overall responder rate, the primary outcome, was defined as ≥ 1 SBM improvement over baseline for all treatment weeks and ≥ 3 SBMs per week for at least 9 weeks of the 12-week study period. Lubiprostone (27.1%) had a significantly higher “overall responder rate” than placebo (18.9%; p = 0.03) (*Jamal et al 2015*). The primary outcome parameter for Study 2 and 3 was the mean change from baseline in SBM frequency at week 8. In Study 2, lubiprostone significantly increased the mean change from baseline in SBM frequency compared to placebo (p = 0.004). In Study 3, the difference was not statistically significant; however, Study 3 was the only study that enrolled patients who received diphenylheptane opioids such as methadone. Studies 2 and 3 have not been published in a peer-reviewed journal at this time.
- A prospective, randomized, double-blind, placebo-controlled trial was conducted to evaluate the efficacy and safety of lubiprostone for relieving symptoms of OIC in adult patients with chronic non-cancer pain. OIC was defined as less than three SBMs per week. Patients were randomized to receive lubiprostone 24 mcg (n = 210) or placebo (n = 218) twice daily for 12 weeks. The primary endpoint was change from baseline in SBM frequency at week 8. Changes from baseline in SBM frequency rates were significantly higher at week 8 (p = 0.005) and overall (p = 0.004) in patients treated with lubiprostone compared with placebo. The most common treatment-related adverse events with lubiprostone and placebo were nausea (16.8% vs 5.8%, respectively), diarrhea (9.6% vs 2.9%, respectively), and abdominal distention (8.2% vs 2.4%, respectively). No lubiprostone-related serious adverse events occurred (*Cryer et al 2014*).
- A 2013 systematic review evaluated pharmacological therapies for the treatment of OIC. A total of 14 randomized clinical trials of mu-opioid receptor antagonists were included. All treatments, including methylnaltrexone, naloxone, and alvimopan, were superior to placebo for the treatment of OIC. Lubiprostone was included in the review; however, the reporting of data precluded meta-analysis (*Ford et al 2013*).
- In 2014, another systematic review of 21 randomized clinical trials evaluated 7 pharmacological treatments for OIC. Efficacy assessment was based on objective outcome measures (OOMs): BM frequency, BM within 4 hours, and time to first BM. Methylnaltrexone showed improvements in all three OOMs. Randomized controlled trials with naloxone and alvimopan tended to be effective for BM frequency measures. Naloxegol (≥12.5 mg) improved all OOMs. Though effectiveness of lubiprostone was demonstrated for all OOMs, group differences were small to moderate. CB-5945 (not FDA-approved) and prucalopride (not FDA-approved for OIC) tended to increase BM frequency, especially with doses of

0.1 mg twice daily and 4 mg daily, respectively. Besides nausea and diarrhea, abdominal pain was the most frequent adverse event for all drugs except for alvimopan. Treatment-related serious adverse events were slightly higher for alvimopan (cardiac events) and prucalopride (severe abdominal pain, headache) (*Siemens et al 2015*).

- The efficacy of naloxegol has been established in K4 and K5, 2 replicate Phase 3 clinical trials with a total of 1,352 participants with OIC who had taken opioids for at least 4 weeks for non-cancer related pain. Participants were randomly assigned to receive oral naloxegol 12.5 mg or 25 mg or placebo once daily for 12 weeks. The trials were designed to measure a response rate, defined as ≥ 3 SBMs per week and an increase of ≥ 1 SBM from baseline.
  - Results from K4 showed that participants receiving naloxegol 25 mg or naloxegol 12.5 mg both experienced a significantly higher response rate compared to participants receiving placebo ($p = 0.001$ and $p = 0.02$, respectively). Results from K5 also showed significantly higher response rates in participants receiving naloxegol 25 mg vs placebo ($p = 0.02$) but did not show a significant difference in response rate in patients receiving naloxegol 12.5 mg vs placebo ($p = 0.2$) (*Chey et al 2014*).
  - In K4, patients with an inadequate response to laxatives achieved a significantly higher response with naloxegol 25 mg vs placebo ($p = 0.002$) and with naloxegol 12.5 mg vs placebo ($p = 0.03$). In K5, patients receiving naloxegol 25 mg achieved a significantly higher response rate vs placebo ($p = 0.01$); however, patients receiving naloxegol 12.5 mg did not have a significantly higher response rate.
  - Median time to first SBM was significantly shorter with both naloxegol 12.5 mg and 25 mg compared to placebo in K4 and was significantly shorter with naloxegol 25 mg in K5 ($p < 0.001$ for all comparisons).
  - Average pain scores and opioid use remained relatively stable in both studies for patients receiving naloxegol; thus, centrally mediated analgesia was preserved.
- Clinical trials of methylnaltrexone injection in patients with advanced illness have shown response over several months with most patients reporting laxative effects similar to SBMs and predictable timing (*Bull et al 2015, Thomas et al 2008*). Similar findings have been reported in patients with OIC with chronic non-cancer pain (*Michna et al 2011, Webster et al 2017*).
- The efficacy of methylnaltrexone tablets was demonstrated in a randomized, double-blind, placebo-controlled study in patients using opioids for chronic non-cancer pain. Patients were randomized to methylnaltrexone (150 mg, 300 mg, or 450 mg) or placebo once daily for a period of 4 weeks followed by as-needed dosing for 8 weeks. A responder to methylnaltrexone treatment was defined as a patient with three or more SBMs per week, with an increase of ≥ 1 SBMs per week over baseline, for at least three weeks in the 4-week treatment period. The percentage of patients classified as responders was 42.8%, 49.3% ($p = 0.03$ vs placebo), 51.5% ($p = 0.005$ vs placebo), and 38.3% in the methylnaltrexone 150 mg, 300 mg, 450 mg and placebo groups, respectively (*Rauck et al 2017*).
- A systematic review and network analysis compared the efficacy and safety of agents for the treatment of OIC, including lubiprostone, naldemedine, naloxegol, subcutaneous (SC) and oral methylnaltrexone, and prucalopride (not FDA-approved for OIC) and alvimopan (not FDA-approved for OIC) (*Sridharan and Sivaramakrishan 2018*). Observations from 16 randomized controlled trials with 4048 patients demonstrated that lubiprostone, naldemedine, naloxegol, and SC and oral methyl naltrexone performed better vs placebo in terms of rescue-free bowel movements (RFBM). Based on the odds ratios from direct and indirect pooled estimates, treatment with SC methylnaltrexone resulted in significantly improved RFBMs vs lubiprostone, naloxegol, and oral methylnaltrexone. Lubiprostone and naldemedine were associated with increased risks of adverse events, while SC methylnaltrexone did not significantly affect the analgesia due to background opioid use. Of note, the quality of evidence for the comparisons was either low or very low.
- Another systematic review and network analysis of 27 studies found methylnaltrexone, naloxone, naloxegol, naldemedine, alvimopan, and lubiprostone significantly more efficacious than placebo for OIC (*Nee et al 2018*).
- A systematic review and network meta-analysis of 27 studies compared the efficacy and safety of methylnaltrexone, naloxone, naldemedine, naloxegol, lubiprostone, linaclotide, plecanatide, and several agents that are not currently approved in the U.S. in OIC. The authors found that when non-response was defined as a failure to achieve an average of ≥ 3 BMs per week with an increase of ≥ 1 BM per week from baseline or an average of ≥ 3 BMs per week, naloxone was the most efficacious treatment for OIC (RR, 0.65; 95% CI, 0.52 to 0.80) and the safest when ranked against other agents. When non-response was defined as only failure to achieve an average of ≥ 3 BMs per week with an increase of ≥ 1 BM per week from baseline, naldemedine was found to be the most efficacious (RR, 0.66; 95% CI, 0.56 to 0.77), followed by alvimopan (RR, 0.74; 95% CI; 0.57 to 0.94) (*Luthra et al 2018*).

IBS and CIC

- A systematic review on IBS and CIC was commissioned by the American College of Gastroenterology to assess the efficacy of available therapies in treating IBS and CIC compared with placebo or no treatment (*Ford et al 2014*). The secondary objectives included assessing the efficacy of available therapies in treating IBS according to predominant stool pattern reported (IBS-C, IBS-D, and IBS-M), as well as assessing adverse events with therapies for both IBS and

CIC. Parallel-group, randomized controlled trials comparing active interventions with either placebo or no therapy were evaluated. Crossover trials were eligible for inclusion if extractable data were provided at the end of the first treatment period, before crossover. The following were identified as “strong” recommendations for IBS and CIC treatments:

- IBS
  - There is insufficient evidence to recommend loperamide for use in IBS. Quality of evidence is very low.
  - Mixed 5-HT 4 agonists/5-HT 3 antagonists are not more effective than placebo at improving symptoms of IBS-C. Quality of evidence is low.
  - Linaclotide is superior to placebo for the treatment of IBS-C. Quality of evidence is high.
  - Lubiprostone is superior to placebo for the treatment of IBS-C. Quality of evidence is moderate.
- CIC
  - Some medicinal and dietary fiber supplements increase stool frequency in patients with CIC. Quality of evidence is low.
  - PEG is effective in improving symptoms of CIC. Quality of evidence is high.
  - Lactulose is effective in improving symptoms of CIC. Quality of evidence is low.
  - Sodium picosulfate and bisacodyl are effective in CIC. Quality of evidence is moderate.
  - Prucalopride is more effective than placebo in improving symptoms of CIC. Quality of evidence is moderate.
  - Linaclotide is effective in CIC. It is generally safe, with the main adverse event being diarrhea. Quality of evidence is high.
  - Lubiprostone is effective in the treatment of CIC. Quality of evidence is high.

- A 2018 systematic review and meta-analysis compared the efficacy of intestinal secretagogues (ie, linaclotide, lubiprostone, plecanatide, and tenapanor [currently under investigation for IBS-C]) for the treatment of chronic constipation or IBS-C (*Lasa et al 2018*). For patients with chronic constipation, intestinal secretagogues were superior to placebo for increasing the number of CSBMs per week (RR, 1.87; 95% CI, 1.24 to 2.83 [analysis included linaclotide, lubiprostone, and plecanatide]) and for achieving ≥ 3 SBMs per week (RR, 1.56; 95% CI, 1.31 to 1.85 [analysis included linaclotide and lubiprostone]). For those with IBS-C, intestinal secretagogues were superior to placebo for increase in CSBMs per week (RR, 2.44; 95% CI, 1.51 to 3.93 [analysis included linaclotide and tenapanor]) and for achieving ≥ 3 SBMs per week (RR, 1.97; 95% CI, 1.74 to 2.24 [analysis included linaclotide only).
- In a systematic review and meta-analysis, both linaclotide and plecanatide were efficacious for IBS-C and CIC compared to placebo. Diarrhea was more frequent with both drugs compared to placebo. In an indirect comparison, there were no differences between the 2 agents for efficacy in CIC, efficacy in IBS-C, frequency of diarrhea, or study withdrawal due to diarrhea (*Shah et al 2018*).
- Another systematic review

INDICATIONS

Table 2. FDA Approved Indications

Indication	Amitiza (lubiprostone)	Linzess (linaclotide)	Lotronex (alosetron)	Motegrity (prucalopride)	Movantik (naloxegol)	Relistor (methylnaltrexone bromide)	Symproic (naldemedine)	Trulance (plecanatide)	Viberzi (eluxadoline)	Xifaxan (rifaximin)
Treatment of CIC in adults	✔	✔		✔				✔		
Treatment of OIC in adults with chronic, non-cancer pain	✔ *				✔	✔	✔			
Treatment of OIC in patients with chronic pain related to prior cancer or its treatment who do not require frequent (eg, weekly) opioid dosage escalation.	✔ *				✔	✔	✔			
Treatment of OIC in patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care						✔ †				

Indication	Amitiza (lubiprostone)	Linzess (linaclotide)	Lotronex (alosetron)	Motegrity (prucalopride)	Movantik (naloxegol)	Relistor (methylnaltrexone bromide)	Symproic (naldemedine)	Trulance (plecanatide)	Viberzi (eluxadoline)	Xifaxan (rifaximin)
Treatment of IBS-C in women ≥ 18 years of age	✔									
Treatment of IBS-C in adults		✔						✔		
Treatment of IBS-D in adults									✔	✔ ‡
Women with severe IBS-D who have: • chronic IBS symptoms (generally lasting 6 months or longer) • had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and not responded adequately to conventional therapy§			✔							

*Effectiveness of Amitiza in the treatment of opioid-induced constipation in patients taking diphenylheptane opioids such as methadone has not been established.
†Injection formulation only. Use of Relistor beyond 4 months in treatment of OIC in patients with advanced illness has not been studied.
‡Xifaxan has additional indications for treatment of traveler's diarrhea (TD) caused by noninvasive strains of *Escherichia coli* in adult and pediatric patients 12 years of age and older, and reduction in risk of overt hepatic encephalopathy recurrence in adults. Do not use Xifaxan in patients with TD complicated by fever or blood in the stool or diarrhea due to pathogens other than *E. coli*.
§IBS-D is severe if it includes diarrhea and ≥ 1 of the following: frequent and severe abdominal pain/discomfort, frequent bowel urgency or fecal incontinence, disability or restriction of daily activities due to IBS.

(*Prescribing information: Amitiza 2018, Linzess 2018, Lotronex 2016, Motegrity 2018, Movantik 2018, Relistor 2018, Symproic 2018, Trulance 2018, Viberzi 2018, Xifaxan 2018*)

- Lotronex was approved by the FDA in February of 2000 and was later withdrawn from the market due to numerous reports of serious and fatal gastrointestinal adverse events. Approval of a supplemental New Drug Application (sNDA) was accepted in July 2002 by the FDA to allow restricted marketing of Lotronex to treat only women with severe IBS-D. Physicians are required to complete training before prescribing Lotronex to ensure that the benefits and risks of the agent are considered before administering it to patients (*Lotronex FDA press release 2016*).

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

CLINICAL GUIDELINES

- Guidelines on management of constipation suggest increased fiber intake and osmotic laxatives. Stimulant laxatives are to be used as needed or as "rescue agents". Lubiprostone and linaclotide can be considered when symptoms of constipation do not respond to laxatives (*AGA 2013, Bharucha et al 2013, Lindberg et al 2010*).
- For management of OIC, the AGA recommends laxatives as a first-line treatment (*Crockett et al 2019*). For patients with laxative refractory OIC, naldemedine or naloxegol are recommended over no treatment. Methylnaltrexone is suggested over no treatment, but authors note that evidence supporting the use of this agent for OIC is low and costs may be prohibitive. The AGA does not make any recommendations for the use of lubiprostone or prucalopride for OIC due to lack of evidence.
- The 2014 American College of Gastroenterology monograph on the management of IBS and CIC makes the following statements (reported with the strength of recommendation and quality of evidence, respectively) (*Ford et al 2014*). Of note, only statements pertaining to CIC are included as the monograph on IBS management was updated in 2018:
  - Linaclotide is effective in CIC (strong; high)
  - Lubiprostone is effective in the treatment of CIC (strong; high)
  - Prucalopride is more effective than placebo in improving symptoms of CIC (strong; moderate)
- The 2018 American College of Gastroenterology monograph on the management of IBS makes the following statements (reported with the strength of recommendation and quality of evidence, respectively) (*Ford et al 2018*):

- Rifaximin is effective in reducing total IBS symptoms and bloating in IBS-D (weak; moderate)
- Linaclotide is superior to placebo for the treatment of IBS-C (strong; high)
- Plecanatide is effective in IBS-C (strong; moderate)
- Lubiprostone is superior to placebo for the treatment of IBS-C (strong; moderate)
- Eluxadoline is superior to placebo for the treatment of IBS-D (weak; moderate)
- Alosetron is effective in females with IBS-D (weak; low)

- The AGA guideline on management of IBS makes the following statements (reported with strength of recommendation and quality of evidence, respectively) (*Weinberg et al 2014*):
  - Recommends using linaclotide (over no drug treatment) in patients with IBS-C (strong; high)
  - Suggests using lubiprostone (over no drug treatment) in patients with IBS-C (conditional; moderate)
  - Suggests using rifaximin (over no drug treatment) in patients with IBS-D (conditional; moderate)
  - Suggests using alosetron (over no drug treatment) in patients with IBS-D to improve global symptoms (conditional; moderate)
- The 2015 WGO guideline on IBS lists rifaximin and alosetron as second-line therapies for IBS-D, although it notes a risk of ischemic colitis and constipation with alosetron. Lubiprostone and linaclotide are noted to be safe and effective for the treatment of IBS-C (*WGO, 2015*).
- In the 2014 Technical Review of the Pharmacological Management of Irritable Bowel Syndrome, the AGA Institute reviewed and graded the evidence for pharmacological interventions (linaclotide, lubiprostone, PEG laxative, rifaximin, alosetron, loperamide, TCAs, SSRIs, and antispasmodics) for treatment of IBS. Review of the evidence for these pharmacological treatments showed that across all outcomes, evidence was high for linaclotide; moderate for lubiprostone, rifaximin, and alosetron; low for TCAs, SSRIs, and PEG; and very low for loperamide and antispasmodics (*Chang et al 2014*).

SAFETY SUMMARY

- **Contraindications:**
  - Amitiza is contraindicated with known or suspected mechanical gastrointestinal obstruction.
  - Lotronex has several contraindications, including history of chronic or severe constipation or sequelae from constipation; intestinal obstruction, stricture, toxic megacolon, gastrointestinal perforation, and/or adhesions; ischemic colitis; impaired intestinal circulation, thrombophlebitis, or hypercoagulable state; Crohn's disease or ulcerative colitis; diverticulitis; severe hepatic impairment.
  - Linzess and Trulance are contraindicated in patients age 6 years or younger and in patients with known or suspected mechanical gastrointestinal obstruction.
  - Motegrity is contraindicated in patients with intestinal perforation or obstruction due to a structural or functional disorder of the gut wall, obstructive ileus, severe inflammatory conditions of the intestinal tract such as Crohn's disease, ulcerative colitis, and toxic megacolon/megarectum; and when there is a known serious or severe hypersensitivity reaction to the drug or any of its excipients.
  - Movantik is contraindicated in patients with known or suspected gastrointestinal obstruction and at increased risk of recurrent obstruction, in patients with concomitant use of strong cytochrome (CYP) 3A4 inhibitors (eg, clarithromycin, ketoconazole), and when there is a known serious or severe hypersensitivity reaction to the drug or any of its excipients.
  - Relistor is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction and at increased risk of recurrent obstruction.
  - Symproic is contraindicated in patients with known or suspected gastrointestinal obstruction or at increased risk of recurrent obstruction, and when there is a known serious or severe hypersensitivity reaction to the drug or any of its excipients.
  - Viberzi has several contraindications, including use in patients with the following conditions: known or suspected biliary duct obstruction or sphincter of Oddi disease or dysfunction; alcoholism, alcohol abuse, alcohol addiction, or more than three alcoholic beverages daily; history of pancreatitis or structural diseases of the pancreas including known or suspected pancreatic duct obstruction; severe hepatic impairment; history of severe constipation or sequelae from constipation; known or suspected mechanical gastrointestinal obstruction; use in patients without a gallbladder; or known hypersensitivity to the drug.
    - On March 15, 2017, the FDA warned that Viberzi should not be used in patients who do not have a gallbladder. The safety announcement was based on an FDA review that found these patients have an increased risk of developing serious pancreatitis that could result in hospitalization or death (*FDA Drug Safety Communication 2017*). A

contraindication was added to the prescribing label for patients without a gallbladder due to an increased risk of developing serious pancreatitis. Pancreatitis was reported in patients taking either the 75 mg or 100 mg dose with most of the cases of serious pancreatitis occurring within a week of starting treatment.
  - Xifaxan is contraindicated in patients with a hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents, or any of the components in Xifaxan.
- **Boxed Warnings:**
  - Linzess and Trulance are contraindicated in pediatric patients 6 years of age and younger due to the risk of serious dehydration; use should be avoided in children 6 to 17 years of age.
  - Lotronex has a Boxed Warning regarding serious gastrointestinal adverse reactions such as ischemic colitis and serious complications of constipation that may lead to hospitalization, blood transfusion, surgery, and/or death. If patients develop constipation or ischemic colitis, Lotronex should be discontinued. Lotronex should be used only in female patients with severe IBS-D who have not benefited from usual therapies.
- **Warnings/precautions:**
  - Amitiza: nausea (29% incidence in CIC), diarrhea (12% in CIC), syncope and hypotension, dyspnea, and bowel obstruction
  - Motegrity: Worsening of depression and emergence of suicidal thoughts and behavior may occur during therapy with Motegrity. Patients should stop Motegrity and contact their provider if these situations occur.
  - Viberzi: Constipation, sometimes requiring hospitalization, has been reported following administration of Viberzi. Patients who develop severe constipation should discontinue treatment and contact their health care provider immediately.
- **Risk Evaluation and Mitigation Strategy (REMS):**
  - Lotronex has REMS that distributes education to providers about the risks for ischemic colitis and serious complications of constipation (*FDA REMS program 2019*).
- Lubiprostone has warnings and precautions for nausea (with 29% incidence in CIC), diarrhea (12% in CIC), syncope and hypotension, dyspnea, and bowel obstruction
  - Amitiza: Diphenylheptane opioids such as methadone may interfere with the efficacy of Amitiza.
  - Lotronox: Clinically significant drug interactions associated with Lotronex include CYP1A2 moderate inhibitors, CYP3A4 inhibitors, drugs that decrease gastrointestinal motility, and fluvoxamine. Concomitant use of Lotronex and fluvoxamine is contraindicated.
  - Motegrity: Concomitant administration of Motegrity and erythromycin may increase erythromycin concentrations via an unknown mechanism. Concomitant administration of Motegrity and ketoconazole may increase the Motegrity concentrations.
  - Movantik: Concomitant use of Movantik should be avoided with the following drug classes: moderate CYP3A4 inhibitors (eg, diltiazem, erythromycin, verapamil) due to increased naloxegol concentrations, strong CYP3A4 inducers (eg, rifampin) due to decreased naloxegol concentrations, and other opioid antagonists due to potentially additive effects that may increase risk of opioid withdrawal. In the event concomitant use with moderate CYP3A4 inhibitors is unavoidable, a dose reduction of Movantik is warranted.
  - Relistor: Concomitant use of Relistor with other opioid antagonists should be avoided due to potentially additive effects that may increase risk of opioid withdrawal.
  - Symproic: Concomitant use of Symproic should be avoided with strong CYP3A inducers (eg, rifampin, carbamazepine, phenytoin, St. John's Wort) due to a significant decrease in naldemedine concentrations, and other opioid antagonists due to potentially additive effect of opioid receptor antagonism that may increase the risk of opioid withdrawal. Moderate CYP3A inhibitors (eg, fluconazole, atazanavir, aprepitant, diltiazem, erythromycin), strong CYP3A inhibitors (eg, itraconazole, ketoconazole, clarithromycin, ritonavir, saquinavir), and P-glycoprotein inhibitors (eg, amiodarone, captopril, cyclosporine, quinidine, verapamil) can increase Symproic concentrations.
  - Viberzi: Drug interactions with Viberzi which potentially may result in clinically relevant effects include the following drug classes: organic anion transporting polypeptide (OATP) 1B1 inhibitors (eg, cyclosporine, gemfibrozil, antiretrovirals, rifampin, eltrombopag, etc.), strong CYP inhibitors (eg, ciprofloxacin, fluconazole, clarithromycin, paroxetine, bupropion), constipation-inducing drugs (eg, alosetron, anticholinergics, opioids), OATP1B1 and breast cancer resistance protein (BCRP) substrates (eg, rosuvastatin), and CYP3A substrates (eg, alfentanil, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus).
  - Xifaxin: Concomitant administration of drugs that are P-glycoprotein inhibitors with Xifaxan can substantially increase systemic exposure to rifaximin. Caution should be exercised when concomitant use of Xifaxan and a P-glycoprotein inhibitor such as cyclosporine is needed.
- **Adverse events:**

○ The IBS and constipation agents are most commonly associated with gastrointestinal-related adverse events.

DOSING AND ADMINISTRATION

Table 4. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Amitiza (lubiprostone)	Capsules	Oral	Treatment of CIC in adults and OIC: twice daily Treatment of IBS-C in women ≥ 18 years of age: twice daily	• Safety and efficacy have not been established in pediatric patients. • Dose should be adjusted in moderate and severe hepatic impairment.
Linzess (linaclotide)	Capsules	Oral	IBS-C: once daily CIC: once daily	• Safety and efficacy have not been established in pediatric patients. • Capsule contents may be administered with applesauce or water if a patient is unable to swallow.
Lotronex (alosetron)	Tablets	Oral	Women with severe IBS-D: twice daily	• Pregnancy category B* • Safety and efficacy have not been established in pediatric patients. • Caution should be used in patients ≥ 65 years of age due to risk for constipation. • Caution should be used in patients with mild or moderate impairment; use should be avoided in severe hepatic impairment. • Treatment should be discontinued in patients who have not had adequate control of IBS symptoms after 4 weeks of treatment with 1 mg twice daily.
Motegrity (prucalopride)	Tablets	Oral	CIC in adults: once daily	• Safety and efficacy have not been established in pediatric patients. • Dose should be adjusted for severe renal impairment (creatine clearance [CrCl] < 30 mL/min).
Movantik (naloxegol)	Tablets	Oral	OIC in chronic non-cancer pain: once daily	• Safety and efficacy have not been established in pediatric patients. • Tablet may be crushed for patients who are unable to swallow the tablet whole; crushed tablets may also be administered via a nasogastric tube. • Use should be avoided in patients with severe hepatic impairment (Child-Pugh Class C). • Dose should be adjusted for renal impairment (CrCl < 60 mL/min). • Maintenance laxative therapy should be discontinued prior to initiating therapy. • Movantik should be discontinued when opioid pain medication is discontinued.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Relistor (methylnaltrex-one)	Single-use vials, single-use pre-filled syringes, tablets	Oral, SC injection	OIC in chronic non-cancer pain: SC injection once daily, or oral tablet(s) once daily in the morning OIC in advanced illness: Weight-based SC injection once every other day, as needed (maximum of once daily)	• Safety and efficacy have not been established in pediatric patients. • SC injection should be administered in the upper arm, abdomen, or thigh; injection sites should be rotated. • Oral dose should be adjusted in moderate and severe hepatic impairment; adjustment of SC injection dose should be considered in severe hepatic impairment. • Dose should be adjusted in moderate to severe renal impairment. • Maintenance laxative therapy should be discontinued prior to initiating therapy. • Relistor should be discontinued when opioid pain medication is discontinued.
Symproic (naldemedine)	Tablets	Oral	OIC in chronic non-cancer pain: once daily	• Safety and efficacy have not been established in pediatric patients. • Use should be avoided in patients with severe hepatic impairment (Child-Pugh Class C). • Symproic should be discontinued when opioid pain medication is discontinued.
Trulance (plecanatide)	Tablets	Oral	CIC and IBS-C: once daily	• Tablet may be crushed for patients who are unable to swallow the tablet whole; crushed tablets may also be administered via a nasogastric tube.
Viberzi (eluxadoline)	Tablets	Oral	Treatment of IBS-D in adults: twice daily	• Safety and efficacy have not been established in pediatric patients. • Dose should be adjusted in patients who are unable to tolerate the 100 mg dose, are receiving concomitant OATP1B1 inhibitors, or have mild or moderate hepatic impairment. • Use should be avoided in patients with severe hepatic impairment (Child-Pugh Class C).
Xifaxan (rifaximin)	Tablets	Oral	IBS-D: three times daily for 14 days TD: three times daily for three days Hepatic encephalopathy: twice daily	• Safety and efficacy have not been established in pediatric patients < 12 years of age with TD or patients < 18 years of age for hepatic encephalopathy and IBS-D. • Patients with IBS-D who experience recurrence may be retreated up to 2 times with the same regimen. • Should not be used in patients with TD complicated by fever or blood in the stool or diarrhea due to pathogens other than *E. coli*.

*Pregnancy Category B = No evidence of risk in humans, but there remains a remote possibility. Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women.

See the current prescribing information for full details.

CONCLUSION

- There are currently no head-to-head trials comparing the available agents used in the treatment of CIC, OIC, IBS-C, and IBS-D.
- IBS is a gastrointestinal disorder with symptoms of abdominal pain, discomfort and bloating, and abnormal bowel habits with bouts of diarrhea and/or constipation (*Andresen et al 2008, Ford et al 2018, Quigley et al 2012, WGO 2015*). IBS has 4 subtypes depending on the change in bowel habits: IBS-D, IBS-C, IBS-M, or IBS-U.
  - Most patients with mild disease are managed with disease state education and support, coupled with lifestyle modifications, including diet changes and stress reduction and, when possible, symptom control (*Andresen et al 2008, Ford et al 2009*).
  - The intestinal secretagogues Linzess (linaclotide), Amitiza (lubiprostone), and Trulance (plecanatide) are indicated for the treatment of IBS-C. Amitiza is a selective chloride channel activator and Linzess and Trulance are guanylate cyclase-C agonists.
  - Lotronex (alosetron), Viberzi (eluxadoline) and Xifaxan (rifaximin) are indicated for the treatment of IBS-D.
    - Viberzi is a mu-opioid receptor agonist and a schedule IV controlled substance.
    - Xifaxan is a rifamycin antibacterial. Patients with IBS-D who experience recurrence with Xifaxan treatment may be retreated up to 2 times with the same regimen.
    - Lotronex is limited to use in females with chronic, severe IBS-D who have not responded to conventional therapy. Due to serious safety concerns, Lotronex has a boxed warning regarding risk of gastrointestinal adverse events including ischemic colitis, and also has a REMS program.
  - The 2018 American College of Gastroenterology monograph on the management of IBS strongly recommends that Linzess and Amitiza are superior to placebo for the treatment of IBS-C, and Trulance is effective in IBS-C; they weakly recommend that Xifaxan is effective in reducing IBS symptoms and bloating in IBS-D, Lotronex is effective in females with IBS-D, and Viberzi is superior to placebo in IBS-D (*Ford et al 2018*).
- The 2014 American College of Gastroenterology monograph on the management of CIC and IBS notes that linaclotide and lubiprostone are each effective for the treatment of CIC, and prucalopride is more effective than placebo in improving symptoms of CIC (*Ford et al 2014*).
  - Additional guidelines on management of constipation suggest increased fiber intake and osmotic laxatives (*AGA 2013, Bharucha et al 2013, Lindberg et al 2010*). Stimulant laxatives are to be used as needed or as "rescue agents." Amitiza and Linzess can be considered when symptoms of constipation do not respond to laxatives.
  - Amitiza, Linzess, Motegrity (prucalopride), and Trulance are indicated for the treatment of CIC.
  - Motegrity is a selective 5-HT_4 receptor agonist that stimulates colonic peristalsis. Amitiza, Linzess, and Trulance are intestinal secretagogues and there is no reported evidence indicating that these agents induce peristalsis.
- For management of OIC, the AGA recommends laxatives as a first-line treatment (*Crockett et al 2019*). For patients with laxative refractory OIC, Symproic (naldemedine) or Movantik (naloxegol) are recommended over no treatment. Relistor (methylnaltrexone) is suggested over no treatment, but authors note that evidence supporting the use of this agent for OIC is low. The AGA does not make any recommendations for the use of Amitiza or Motegrity for OIC due to lack of evidence.
  - Amitiza, Movantik, Relistor, and Symproic are approved for treatment of OIC in patients with chronic non-cancer pain, and in those chronic pain related to prior cancer or its treatment in those who do not require frequent (eg, weekly) opioid dosage escalation. Relistor injection is also approved in patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.
  - Movantik, Relistor, and Symproic are PAMORAs.

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Publication Date: March 11, 2019

Anti-Migraine Medications – Serotonin Receptor Agonists (triptans)

Prior Authorization Guideline

Fee for Service – Nevada Medicaid

Guideline Name Migraine Quantity Limit – Triptans

1 . Indications

Drug Name: Amerge (naratriptan), Frova (frovatriptan), Imitrex (sumatriptan) tablets and nasal spray, Onzetra (sumatriptan), Relpax (eletriptan), Zembrace SymTouch (sumatriptan), Zomig (zolmitriptan) tablets, Zomig-ZMT (zolmitriptan) **Indications** **Migraine Headaches** Indicated for the acute treatment of migraine with or without aura in adults. Limitations of Use: Safety and effectiveness of respective triptan therapy have not been established for cluster headache (not applicable to Zembrace SymTouch). Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with therapy, reconsider the diagnosis of migraine before therapy is administered to treat any subsequent attacks. Therapy is not indicated for the prevention of migraine attacks.
Drug Name: Axert (almotriptan) **Indications** **Migraine Headaches** Indicated for the acute treatment of migraine attacks in adults with a history of migraine with or without aura. Indicated for the acute treatment of migraine headache pain in adolescents age 12 to 17 years with a history of migraine attacks with or without aura usually lasting 4 hours or more (when untreated). Important Limitations: Only use where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with Axert, the diagnosis of migraine should be reconsidered before Axert is administered to treat any subsequent attacks. In adolescents age 12 to 17 years, efficacy of Axert on migraine-associated symptoms (nausea, photophobia, and phonophobia) was not established. Axert is not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. Safety and effectiveness of Axert have not been established for cluster headache which is present in an older, predominantly male population.

Drug Name: Maxalt (rizatriptan), Maxalt-MLT (rizatriptan)

Indications

Migraine headaches Indicated for the acute treatment of migraine with or without aura in adults and in pediatric patients 6 to 17 years old. Limitations of Use: Maxalt should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with Maxalt, the diagnosis of migraine should be reconsidered before Maxalt is administered to treat any subsequent attacks. Maxalt is not indicated for use in the management of hemiplegic or basilar migraine. Maxalt is not indicated for the prevention of migraine attacks. Safety and effectiveness of Maxalt have not been established for cluster headache.

Drug Name: Migranal (dihydroergotamine mesylate)

Indications

Migraine Headaches Indicated for the acute treatment of migraine headaches with or without aura. Not intended for the prophylactic therapy of migraine or for the management of hemiplegic or basilar migraine.

Drug Name: Treximet (sumatriptan/naproxen)

Indications

Migraine Headaches Indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age or older. Limitations of Use: Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with Treximet, reconsider the diagnosis of migraine before Treximet is administered to treat any subsequent attacks. Treximet is not indicated for the prevention of migraine attacks. Safety and effectiveness of Treximet have not been established for cluster headache.

Drug Name: Zomig (zolmitriptan) nasal spray

Indications

Migraine Headaches Indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older. Limitations of Use: Only use Zomig if a clear diagnosis of migraine has been established. If a patient has no response to Zomig treatment for the first migraine attack, reconsider the diagnosis of migraine before Zomig is administered to treat any subsequent attacks. Zomig is not indicated for the prevention of migraine attacks. Safety and effectiveness of Zomig have not been established for cluster headache. Not recommended in patients with moderate or severe hepatic impairment.

Drug Name: Imitrex (sumatriptan) injection

Indications

Migraine Headache Indicated in adults for the acute treatment of migraine, with or without aura. Limitations of Use: Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine headache attack treated with Imitrex injection, reconsider the diagnosis before Imitrex injection is administered to treat any subsequent attacks. Imitrex injection is not indicated for the prevention of migraine headache attacks.

Cluster Headaches Indicated in adults for the acute treatment of cluster headache. Limitations of Use: Use only if a clear diagnosis of cluster headache has been established. If a patient has no response to the first cluster headache attack treated with Imitrex injection, reconsider the diagnosis before Imitrex injection is administered to treat any subsequent attacks. Imitrex injection is not indicated for the prevention of cluster headache attacks.

Drug Name: Sumavel DosePro (sumatriptan)

Indications

Migraine Headaches Indicated in adults for the acute treatment of migraine, with or without aura. Limitations of Use: Use only if a clear diagnosis of migraine headache has been established. If a patient has no response to the first migraine attack treated with Sumavel DosePro, reconsider the diagnosis of migraine before Sumavel DosePro is administered to treat any subsequent attacks. Sumavel DosePro is not indicated for the prevention of migraine attacks.

Cluster Headaches Indicated in adults for the acute treatment of cluster headache. Limitations of Use: Use only if a clear diagnosis of cluster headache has been established.

2 . Criteria

Approval Length	12 Month
Guideline Type	Quantity Limit

Approval Criteria

1 Diagnosis of one of the following:

- Acute migraines with or without aura
- Cluster headaches

AND

2 Prescribed by or in consultation with one of the following:

- Neurologist
- Pain management specialist

AND

3 Patient is experiencing 2 or more headaches per month

AND

4 Patient will not be treating 15 or more headaches per month

AND

5 Currently receiving prophylactic therapy with at least one of the following:

- Antidepressants
- Anticonvulsants
- Beta-blockers

AND

6 Not used in combination with another triptan or ergotamine-containing product

AND

7 One of the following:

a. Higher dose or quantity is supported in the Dosage and Administration section of the manufacturer's prescribing information

OR

b. Higher dose or quantity is supported by one of the following compendia:

- American Hospital Formulary Service Drug Information
- Micromedex DRUGDEX System

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: July 25, 2019

Prior Authorization Criteria being reviewed: Anti-Migraine Medications - Triptans

Managed Care Organization name: Choose an item.

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: _____LTodd_____

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: July 25, 2019

Prior Authorization Criteria being reviewed: Anti-Migraine Medications - Triptans

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.

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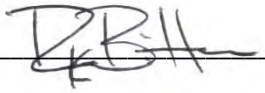
If this form is not completed and returned to the policy specialist with DHCFP by the designated deadline, the assumption will be made that you approve all prior authorization criteria as presented.

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

Signature of individual completing this form: 

DRUG USE REVIEW BOARD
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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: July 25, 2019

Prior Authorization Criteria being reviewed: Anti-Migraine Medications - Triptans

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.

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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.

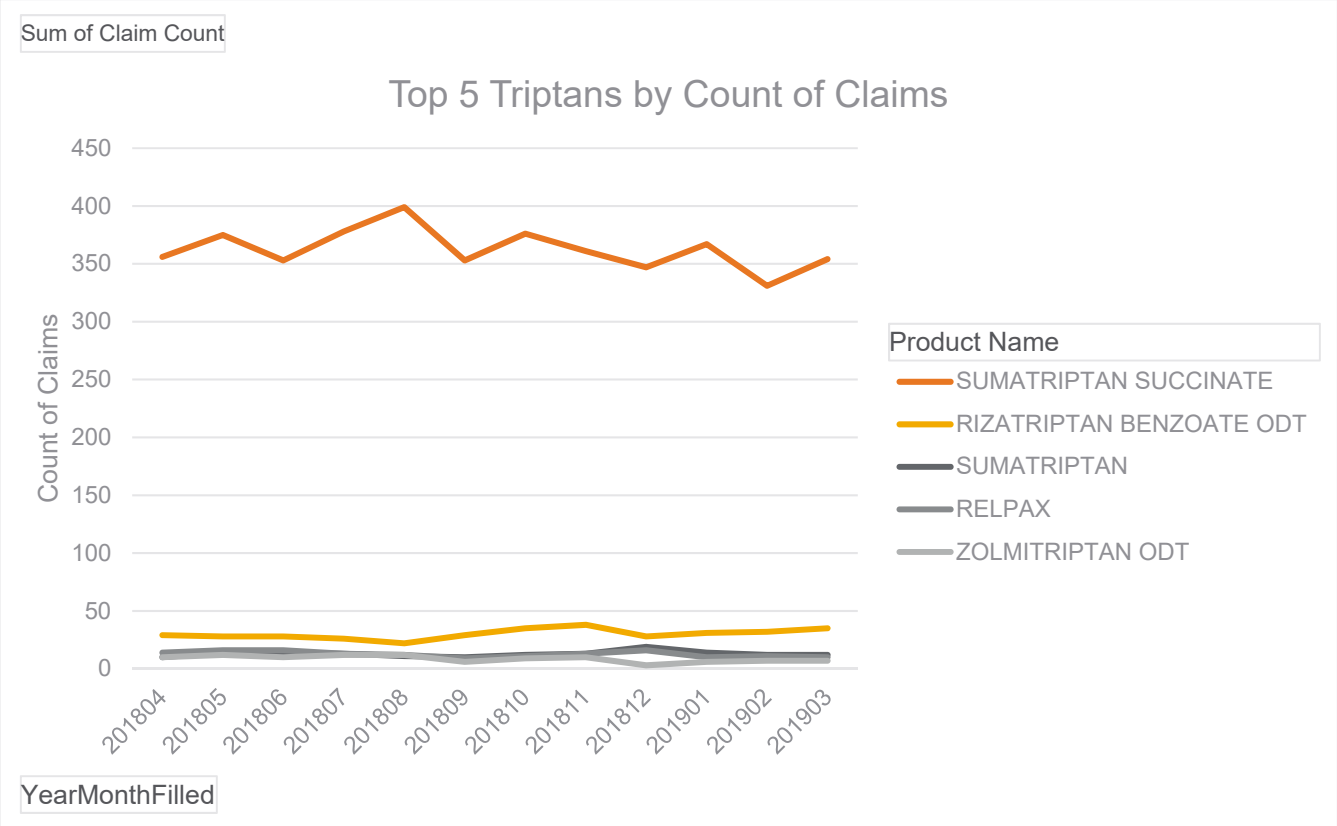
Please print the name of the individual completing this form: Tom Beranek

Signature of individual completing this form: Tom Beranek

Antimigraine Agents - Triptans

Summary of Utilization
April 1, 2018 - March 31, 2019
Fee for Service Medicaid

Product Name	Member Count	Claim Count	Days Supply	Sum of Qty
ELETRIPTAN HYDROBROMIDE	2	5	150	54
FROVATRIPTAN SUCCINATE	1	11	246	99
IMITREX	4	4	41	21
IMITREX STATDOSE SYSTEM	1	1	1	1
NARATRIPTAN HCL	5	38	710	360
ONZETRA XSAIL	1	10	300	160
RELPAX	37	151	2,822	1,225
RIZATRIPTAN BENZOATE	25	82	1,824	1,108
RIZATRIPTAN BENZOATE ODT	147	361	6,845	3,625
SUMATRIPTAN	59	154	3,273	919
SUMATRIPTAN SUCCINATE	1,484	4,350	88,672	37,038
SUMATRIPTAN SUCCINATE REF	5	15	196	30
ZEMBRACE SYMTOUCH	2	4	114	8
ZOLMITRIPTAN	6	13	279	114
ZOLMITRIPTAN ODT	21	104	2,395	942
ZOMIG	2	12	342	72
Total	**1,802**	**5,315**	**108,210**	**45,776**



Anthem

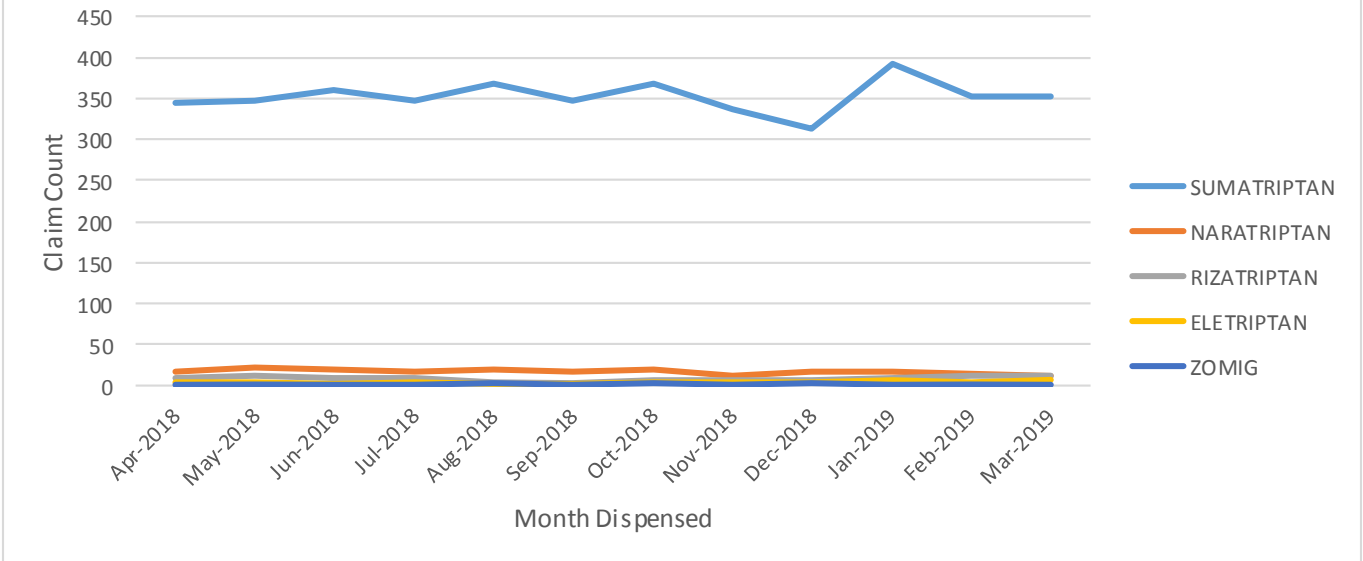
Anti-Migraine Agents--Triptans

Summary of Utilization

April 1, 2018 – March 31, 2019

Drug	Member Count	Claim Count	Days Supply	Total Quantity
ELETRIPTAN HBR 20 MG TABLET	1	1	30	9
ELETRIPTAN HBR 40 MG TABLET	8	43	735	330
FROVATRIPTAN SUCC 2.5 MG TAB	2	9	270	81
NARATRIPTAN HCL 1 MG TABLET	8	18	309	162
NARATRIPTAN HCL 2.5 MG TABLET	54	185	4510	1665
ONZETRA XSAIL 11 MG	2	3	88	48
RIZATRIPTAN 10 MG ODT	11	40	921	340
RIZATRIPTAN 10 MG TABLET	25	45	1011	376
RIZATRIPTAN 5 MG ODT	3	4	96	33
RIZATRIPTAN 5 MG TABLET	5	8	187	73
SUMATRIPTAN 20 MG NASAL SPRAY	14	50	1286	396
SUMATRIPTAN 5 MG NASAL SPRAY	5	5	67	30
SUMATRIPTAN 6 MG/0.5 ML INJECT	19	70	1264	197
SUMATRIPTAN 6 MG/0.5 ML VIAL	5	9	228	22
SUMATRIPTAN SUCC 100 MG TABLET	751	2268	46148	19962
SUMATRIPTAN SUCC 25 MG TABLET	291	534	11224	4660
SUMATRIPTAN SUCC 50 MG TABLET	613	1292	25480	11323
ZOLMITRIPTAN 2.5 MG ODT	1	1	30	6
ZOLMITRIPTAN 2.5 MG TABLET	1	1	3	6
ZOLMITRIPTAN 5 MG ODT	2	2	35	18
ZOLMITRIPTAN 5 MG TABLET	2	4	93	33
ZOMIG 2.5 MG NASAL SPRAY	1	1	30	6
ZOMIG 5 MG NASAL SPRAY	8	19	474	126
Grand Total	**1680**	**4612**	**94519**	**39902**

Top 5 Triptans By Count of Claims



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Anti-Migraine Medications - Triptans

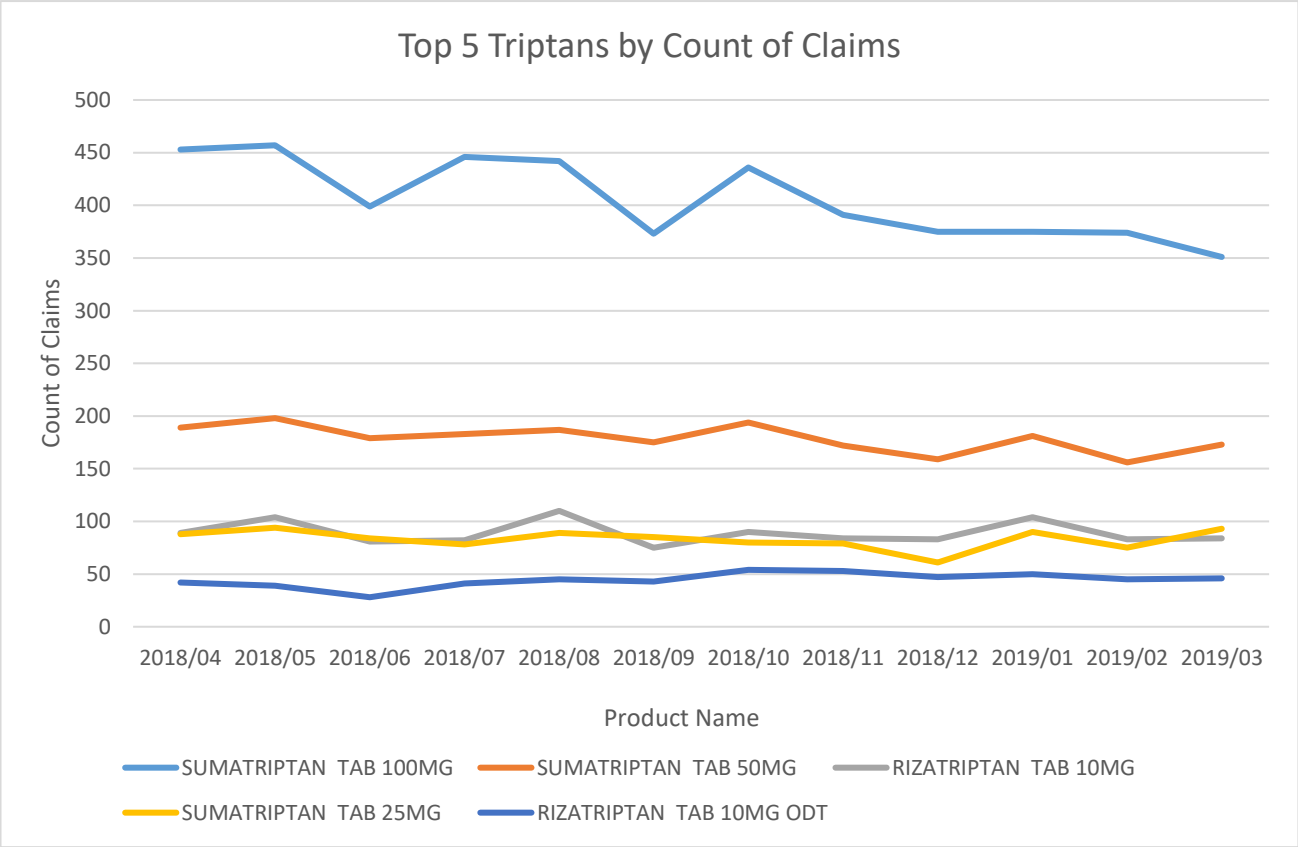
Summary of Utilization
April 1, 2018 - March 31, 2019
Health Plan of Nevada

Product Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
SUMATRIPTAN TAB 100MG	2,696	4,872	92,025	46,170	NA
SUMATRIPTAN TAB 50MG	1,474	2,146	43,651	19,219	NA
RIZATRIPTAN TAB 10MG	605	1,069	20,341	9,172	NA
SUMATRIPTAN TAB 25MG	745	996	20,638	9,141	NA
RIZATRIPTAN TAB 10MG ODT	308	533	9,961	4,836	NA
SUMATRIPTAN INJ 6MG/0.5	269	531	9,759	1,142	NA
SUMATRIPTAN SPR 20MG/ACT	183	326	7,464	1,988	NA
NARATRIPTAN TAB 2.5MG	126	207	4,192	1,722	NA
ELETRIPTAN TAB 40MG	67	139	2,538	1,308	NA
RIZATRIPTAN TAB 5MG	82	137	2,654	1,119	NA
SUMATRIPTAN SPR 5MG/ACT	49	69	1,545	464	NA
ZOLMITRIPTAN TAB 5MG	26	46	742	556	NA
RIZATRIPTAN TAB 5MG ODT	37	45	871	390	NA
ZOMIG SPR 5MG	22	38	662	258	NA
SUMATRIPTAN INJ 4MG/0.5	21	37	521	57	NA
ELETRIPTAN TAB 20MG	11	17	212	119	NA
ZEMBRACE SYM INJ 3/0.5ML	7	14	420	36	NA
ZOLMITRIPTAN TAB 2.5 MG	6	9	270	159	NA
ZOLMITRIPTAN TAB 5MG ODT	5	6	86	49	NA
ZOLMITRIPTAN TAB 2.5MG	4	4	82	19	NA
ALMOTRIPTAN TAB 12.5MG	3	4	41	23	NA
ONZETRA XSAI MIS 11MG	2	3	86	48	NA
RELPAX TAB 40MG	2	2	11	15	NA
NARATRIPTAN TAB 1MG	2	2	46	18	NA
FROVATRIPTAN TAB 2.5MG	1	1	6	6	NA
IMITREX INJ 6MG/0.5	1	1	30	2	NA
ALMOTRIPTAN TAB 6.25MG	1	1	23	6	NA
Grand Total	**6,755**	**11,255**	**218,877**	**98,042**	**NA**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Anti-Migraine Medications - Triptans

Summary of Utilization
April 1, 2018 - March 31, 2019
Health Plan of Nevada



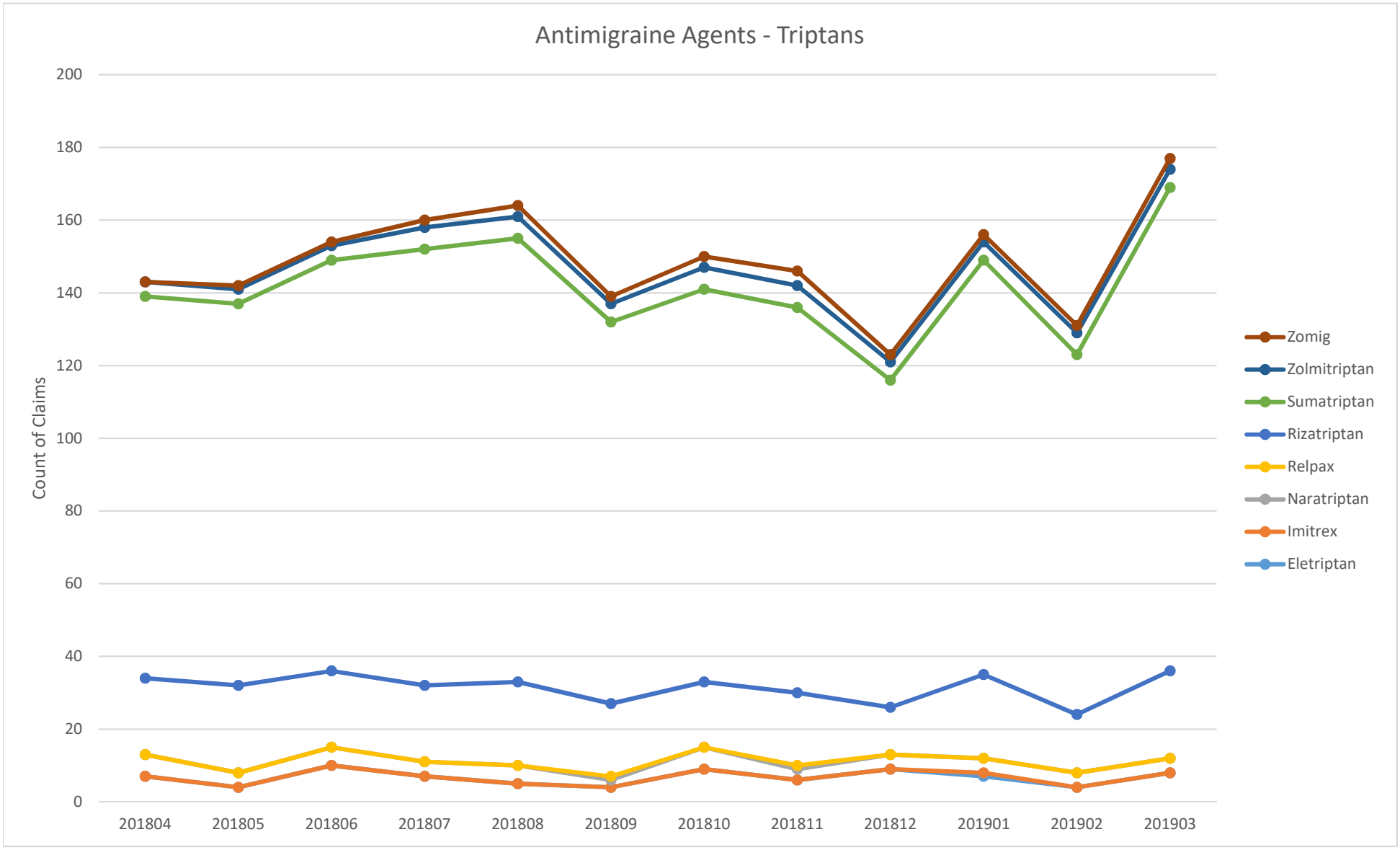
Antimigraine Agents - Triptans

Summary of Utilization

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Product Name	Count of Members	Count of Claims	Sum of Qty	Sum of Days
ELETRIPTAN TAB 20MG	5	14	83	400
ELETRIPTAN TAB 40MG	18	66	415	1,842
IMITREX TAB 25MG	1	1	27	30
NARATRIPTAN TAB 2.5MG	16	51	515	1,486
RELPAX TAB 40MG	1	2	17	17
RIZATRIPTAN TAB 5MG	6	20	183	554
RIZATRIPTAN TAB 5MG ODT	2	2	18	60
RIZATRIPTAN TAB 10MG	52	168	1,622	4,381
RIZATRIPTAN TAB 10MG ODT	25	54	516	1,228
SUMATRIPTAN INJ 4MG/0.5	2	2	6	60
SUMATRIPTAN INJ 6MG/0.5	26	90	161	2,570
SUMATRIPTAN SPR 5MG/ACT	5	9	54	270
SUMATRIPTAN SPR 20MG/ACT	20	68	414	1,931
SUMATRIPTAN TAB 25MG	86	160	1,650	4,446
SUMATRIPTAN TAB 50MG	154	299	2,811	8,542
SUMATRIPTAN TAB 100MG	217	692	6,213	19,767
ZOLMITRIPTAN TAB 2.5MG ODT	1	10	60	300
ZOLMITRIPTAN TAB 2.5MG	2	2	7	35
ZOLMITRIPTAN TAB 5MG	6	46	249	1,211
ZOLMITRIPTAN TAB 5MG ODT	2	4	24	120
ZOMIG SPR 2.5MG	1	1	6	6
ZOMIG SPR 5 MG	7	24	144	702
Total	**655**	**1,785**	**15,195**	**49,958**


Antimigraine Agents - Triptans
Count of Claims
200
180
160
140
120
100
80
60
40
20
0
201804
201805
201806
201807
201808
201809
201810
201811
201812
201901
201902
201903
Zomig
Zolmitriptan
Sumatriptan
Rizatriptan
Relpax
Naratriptan
Imitrex
Eletriptan

S. Anti-Migraine Medications

Therapeutic Class: Serotonin 5-HT1 receptor agonists (triptans)
Last Reviewed by the DUR Board: September 21, 2006

Therapeutic Class: Calcitonin Gene-Related Peptide (CGRP) Receptor Inhibitor Medications
Last Reviewed by the DUR Board: October 18, 2018

Serotonin 5-HT1 receptor agonists commonly referred to as "triptans" and CGRP Receptor Inhibitor medications or anti-migraine medications 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.

Serotonin 5-HT1 Receptor Agonists (triptans)

1. Coverage and Limitations

An approved prior authorization is required for any prescription exceeding the quantity limits. Approval for additional medication beyond these limits will be considered only under the following circumstances:

a. The recipient's current medication history documents the use of prophylactic medications for migraine headache or the medical provider agrees to initiate such therapy which includes beta-blockers, tricyclic antidepressants, anticonvulsants, Selective Serotonin Reuptake Inhibitors (SSRIs) and/or calcium channel blockers; or

b. The medical provider is aware of and understands the implications of daily use and/or overuse of triptans and agrees to counsel the patient on this issue in an effort to taper the quantity of triptan medication required monthly.

1. Recipient's current medication history must NOT have Monoamine Oxidase (MAO) Inhibitors present for approval of Imitrex® (sumitriptan), Maxalt® (rizatriptan) or Zomig® (zolmitriptan).

2. Recipients whose current medication history indicates the use of propranolol will NOT be granted prior authorization of Maxalt® (rizatriptan) 10mg tablet or 10mg orally disintegrating tablet.

3. Prior authorization will NOT be given to patients with ischemic heart disease.

Approval for exceeding the quantity limits on tripitans will be given for a two month time period.

2. Prior Authorization Guidelines

The prior authorization must be initiated by the prescriber. The approved prior authorization must be available if requested.

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

Calcitonin Gene-Related Peptide (CGRP) Receptor Inhibitor Medications

1. Coverage and Limitations

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

Episodic Migraines

1. Initial request:

a. The recipient must have a documented diagnosis of episodic migraines; and

b. The recipient must be 18 years of age or older; and

c. The recipient must have four to 14 migraine days per month, but no more than 14 headache days per month; and

d. One of the following:

1. The recipient has a documented history of failure (after at least a two-month trial) or intolerance to Elavil® (amitriptyline) or Effexor® (venlafaxine); or

2. The recipient has a contraindication to both Elavil® (amitriptyline) and Effexor® (venlafaxine); and

e. One of the following:

1. The recipient has documented history of failure (after at least a two-month trial) or intolerance to Depakote®/Depakote ER (divalproex) or Topamax® (topiramate); or

2. The recipient has a contraindication to both Depakote®/Depakote ER (divalproex) and Topamax® (topiramate); and

f. One of the following:

1. The recipient has a history of failure (after at least a two-month trial) or intolerance to one of the following beta blockers: atenolol, propranolol, nadolol, timolol or metoprolol; or

2. The recipient has a contraindication to all of the following beta blockers: atenolol, propranolol, nadolol, timolol and metoprolol; and

g. The medication must not be used in combination with another CGRP Inhibitor.

Chronic Migraines

2. Initial request:

a. The recipient has a documented diagnosis of chronic migraines; and

b. The recipient must be 18 years of age or older; and

c. The recipient has been evaluated for medication overuse headache (MOH) and if the recipient is diagnosed with MOH, then treatment plan will include a taper off the offending medication; and

d. The recipient has ≥ 15 headache days per month, of which at least eight must be migraine days for at least three months; and

e. One of the following:

1. The recipient has a documented history of failure (after at least a two-month trial) or intolerance to Elavil® (amitriptyline) or Effexor® (venlafaxine); or

2. The recipient has a contraindication to both Elavil® (amitriptyline) and Effexor® (venlafaxine); and

f. One of the following:

1. The recipient has documented history of failure (after at least a two-month trial) or intolerance to Depakote®/Depakote ER (divalproex) or Topamax® (topiramate); or

2. The recipient has a contraindication to both Depakote®/Depakote ER (divalproex) and Topamax® (topiramate); and

g. One of the following:

1. The recipient has a history of failure (after at least a two-month trial) or intolerance to one of the following beta blockers: atenolol, propranolol, nadolol, timolol or metoprolol; or

2. The recipient has a contraindication to all of the following beta blockers: atenolol, propranolol, nadolol, timolol and metoprolol; and

h. The medication will not be used in combination with another CGRP Inhibitor; and

i. The medication will not be used in combination with Botox (onabotulinumtoxinA).

2. Recertification Request:

a. The recipient must have documented positive clinical response to CGRP therapy; and

b. The use of acute migraine medications (e.g., NSAIDs, triptans) has decreased since the start of CGRP therapy.

3. Prior Authorization Guidelines

a. Prior authorization approvals will be for:

1. Initial prior authorization approval: three months.

2. Recertification approval: 12 months.

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

Therapeutic Class Overview
Anti-migraine Agents (triptans)

INTRODUCTION

- Migraine is a common disabling primary headache disorder that can be divided into 2 major subtypes: without aura (the most common subtype and is associated with a higher average attack frequency) and with aura. According to the International Classification of Headache Disorder (IHS), migraine is a common primary headache disorder manifesting in attacks lasting 4 to 72 hours in adults and 1 to 72 hours in children. Migraines range from moderate to very severe and are sometimes debilitating. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity, and association with nausea and/or photophobia and phonophobia. When attacks occur ≥15 days/month for >3 months, patients are considered to have chronic migraines (Cutrer et al, 2017; Snow et al, 2002; IHS, 2018[a], IHS, 2018[b]).
- The migraine 1-year prevalence rate in Americans is approximately 12% (17% of women and 6% of men) (Cutrer et al, 2017; Lipton et al, 2001).
- The Food and Drug Administration (FDA) Industry Guidance recommendations and the IHS recommend 2 co-primary endpoints for trials measuring efficacy of acute treatment of migraines. One is the proportion of patients who are pain-free at 2 hours and the other is the reduction of the most bothersome migraine-associated symptom at 2 hours (FDA Industry Guidance [migraine], 2018; Tfelt-Hansen et al, 2012).
- The serotonin (5-HT1) receptor agonists, also referred to as triptans, work in the management of migraine via the promotion of vasoconstriction, inhibition of dural vasodilation and inflammation, and blockade of pain pathways in the brainstem (Clinical Pharmacology, 2018). In contrast to analgesics, the triptans are considered to be “specific” migraine therapies because they act at the pathophysiologic mechanisms of headaches (Bajwa et al, 2018).
- In adults, all triptans are FDA-approved for the acute treatment of migraines with or without aura. In addition to the acute treatment of migraines, subcutaneous sumatriptan is also approved for cluster headaches. The agents FDA-approved in pediatric patients include almotriptan, sumatriptan/naproxen, zolmitriptan nasal spray (for ≥12 years of age), and rizatriptan (for ≥6 years of age).
- There is well-established evidence demonstrating the triptans to be an effective option for acute treatment of migraine; however, there is inconsistent head-to-head data demonstrating the superiority of any triptan, making it difficult to recommend the use of 1 over another (Bajwa et al, 2018). Some treatment guidelines do not differentiate among various formulations (Evers et al, 2009; Francis et al, 2010; Matchar et al, 2000; Silberstein, 2000; Silberstein et al, 2012 [guideline reaffirmed in 2015]; Erratum in Subcommittee of the American Academy of Neurology [AAN] and the American Headache Society [AHS], 2013; Snow et al, 2002). Additional key therapies for the treatment of migraines include nonsteroidal anti-inflammatory drugs (NSAIDs), dihydroergotamine (DHE nasal spray or inhaler), and opioid medications; however, some medications are not recommended for regular use (Marmura et al, 2015; Silberstein et al, 2012 [guideline reaffirmed in 2015]; Erratum in Subcommittee of the AAN and the AHS, 2013). For the treatment of cluster headaches, the 2016 AHS guidelines recommend subcutaneous sumatriptan and zolmitriptan nasal spray (Robbins et al, 2016). In pediatric patients, the Child Neurological Society recommends ibuprofen, followed by acetaminophen, and sumatriptan nasal spray when all other analgesics fail (Lewis et al, 2004). An update of the 2004 Child Neurological Society guideline is currently in progress.
- FDA-approved triptans are available as an oral tablet (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, sumatriptan/naproxen combination, zolmitriptan), orally disintegrating tablet (rizatriptan, zolmitriptan), nasal spray (sumatriptan, zolmitriptan), nasal powder (sumatriptan), and subcutaneous injection (sumatriptan) (DRUGS@FDA, 2018). Branded products are outlined in Table 1.
- According to DRUGS@FDA, the marketing status of ALSUMA and SUMAVEL DOSEPRO is discontinued; therefore, these products have been removed from the therapeutic class overview (DRUGS@FDA, 2018).
- In October 2017, the FDA announced Teva’s voluntary discontinuation of ZECUITY (sumatriptan iontophoretic transdermal system) due to post-marketing reports of application site reactions, including severe redness, cracked skin, blistering/welts, and burns/scars associated with the product (FDA Drug Shortages and Discontinuations, 2017). Therefore, this product has been removed from the therapeutic class overview.

- Medispan class: Migraine Products – Selective Serotonin Agonists 5-HT(1); Selective Serotonin Agonist-NSAID Combinations

Table 1. Medications Included Within Class Review

Drug	Manufacturer	FDA Approval Date	Generic Availability
AMERGE (naratriptan hydrochloride tablet)	various	02/10/1998	✔
AXERT (almotriptan malate tablet)	various	05/07/2001	✔
FROVA (frovatriptan succinate tablet)	various	11/08/2001	✔
IMITREX (sumatriptan tablet, nasal spray, injection)	various	12/28/1992	✔
IMITREX STATDOSE (sumatriptan cartridges for injection)	various	12/23/1996	✔
MAXALT (rizatriptan benzoate tablet)	various	06/29/1998	✔
MAXALT MLT (rizatriptan benzoate orally disintegrating tablet)	various	06/29/1998	✔
ONZETRA XSAIL (sumatriptan nasal powder)	Merck & Co., Inc.	01/27/2016	-
RELPAX (eletriptan hydrobromide tablet)	Pfizer	12/26/2002	✔
TREXIMET (sumatriptan/naproxen sodium tablet)	GlaxoSmithKline	04/15/2008	✔
ZEMBRACE SYMTOUCH (sumatriptan injection)	Nupathe Inc.	01/28/2016	-
ZOMIG (zolmitriptan nasal spray, tablet)	various	09/30/2003	✔ (tablets only)
ZOMIG-ZMT (zolmitriptan orally disintegrating tablet)	various	02/13/2001	✔

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

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

	AMERGE (naratriptan tablet)	AXERT (almotriptan tablet)	FROVA (frovatriptan tablet)	IMITREX (sumatriptan tablets, nasal spray, injection)	IMITREX STATDOSE (sumatriptan cartridges for injection)	MAXALT (rizatriptan tablet)	MAXALT MLT (rizatriptan ODT)	ONZETRA XSAIL (sumatriptan nasal powder)	RELPAX (eletriptan tablet)	ZEMBRACE SYMTOUCH (sumatriptan injection)	ZOMIG (zolmitriptan nasal spray, tablet)	ZOMIG ZMT (zolmitriptan ODT)	TREXIMET (sumatriptan/naproxen tablet)
Acute treatment of migraine with or without aura	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔ ‡	✔	✔
Acute treatment of cluster headache				✔ *	✔								
Acute treatment of migraine with or without aura (aged ≥ 6 years)						✔	✔						
Acute treatment of migraine headache pain in adolescents with a history of migraine with or without aura, and who have migraine attacks usually lasting ≥ 4 hours when untreated (aged ≥ 12 years)		✔ §											
Acute treatment of migraine with or without aura (aged ≥ 12 years)											✔ †‡		✔

Abbrv: ODT = orally disintegrating tablet
*Indication applies only to the injection formulation
†Indication applies only to the nasal spray formulation
Class Limitations of Use: All agents in class are not intended to be used as prophylactic migraine therapy. Use is recommended only after a clear diagnosis of migraine (or cluster headache, if FDA-approved for use) has been established. Agents are not indicated for the treatment of cluster headache unless FDA-approved.
Additional Limitations of Use:
‡Nasal spray is not recommended in patients with moderate to severe hepatic impairment
§For adolescents aged 12 to 17 years, efficacy on migraine-associated symptoms was not established.

(Prescribing information: AMERGE, 2016; AXERT, 2017; FROVA, 2018; IMITREX injection, 2018; IMITREX nasal spray, 2017; IMITREX tablets, 2017; MAXALT, 2015; MAXALT MLT, 2015; ONZETRA XSAIL, 2016; RELPAX, 2013; TREXIMET, 2016; ZEMBRACE SYMTOUCH, 2017; ZOMIG nasal spray, 2016; ZOMIG tablets, 2018; ZOMIG ZMT, 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

- In general, clinical trial data consistently demonstrate the superiority of the triptans over placebo in achieving headache pain relief and freedom from pain at 2 hours and sustained pain-free response, reducing rescue medication use and improving migraine-associated symptoms such as nausea, photophobia and phonophobia (Bird et al, 2014; Brandes et al, 2007; Cady et al, 2015; Derry et al, 2012 [a]; Derry et al, 2012[b]; Derry et al, 2012[c]; Derry et al, 2014; Ferrari et al, 2002; Law et al, 2016; Oldman et al, 2002; Pascual et al, 2007; Poolsup et al, 2005; Prescribing information: IMITREX, 2018; ZEMBRACE SYMTOUCH, 2017; Richer et al, 2016).
- While there appear to be differences in the relative efficacies among the triptans, direct head-to-head trials do not consistently support the use of 1 over another, suggesting that individual variations in response to different triptans exist. 5-HT_1 receptor agonists have been evaluated in numerous meta-analyses and comparative trials with sumatriptan often used as the benchmark standard as it has the most clinical experience available. All 5-HT_1 receptor agonists are effective at treating migraines and are well-tolerated; however, there are some notable differences between the different agents and formulations. Based on older evidence and reviews, the following conclusions were drawn (Derry et al, 2012[a]; Derry et al, 2012[b]; Derry et al, 2012[c]; Derry et al, 2014; Ferrari et al, 2002; Oldman et al, 2002; Pascual et al, 2007):
  - o Rizatriptan 10 mg has the fastest onset of action and the highest efficacy rates of pain-free and headache relief at 2 hours post-dose for oral agents (Oldman et al, 2002); however, the rate of recurrence at 24 hours appears to be higher with rizatriptan (Ferrari et al, 2002; Pascual et al, 2007). Naratriptan 2.5 mg has lower efficacy rates of pain-free and headache relief at 2 hours (Pascual et al, 2007) while eletriptan has a lower rate of recurrence (Ferrari et al, 2002).
  - o Subcutaneous sumatriptan is the most effective for migraine treatment but is associated with more adverse events (AEs) relative to the other 5-HT_1 receptor agonist formulations (Oldman et al, 2002; Derry et al, 2012[c]).
  - o Frovatriptan has the least number of head-to-head trials with active comparators. A recent pooled analysis of 3 studies showed similar efficacy at 2 hours post-dose with pain-free and pain relief responses between frovatriptan and the comparator group (consisting of almotriptan, rizatriptan, and zolmitriptan); however, frovatriptan had less recurrent episodes at 48 hours post-dose than the comparator group (P<0.001) (Cortelli et al, 2011).
  - o Sumatriptan/naproxen fixed-dose combination is more effective for migraine treatment than monotherapy or placebo when measuring headache relief at 2 hours and associated symptoms of migraine, with a similar AE profile to sumatriptan monotherapy (Brandes et al, 2007).
  - o Most 5-HT_1 receptor agonists are well-tolerated; however, naratriptan 2.5 mg and almotriptan 12.5 mg appear to have the lowest risk of causing an AE (Ferrari et al, 2002).
- Recent evidence is summarized below:
  - o The newest intranasal sumatriptan formulation, ONZETRA XSAIL, was evaluated in 2 double-blind (DB), randomized trials in 498 patients with moderate to severe migraines through the TARGET and COMPASS studies. The TARGET study (n=230) resulted in significantly more patients who experienced headache relief at 2 hours post-dose among those who received nasal powder sumatriptan 22 mg compared to placebo (68% vs. 45%, respectively; P=0.002). At 30 minutes post-dose, a significant difference in relief was maintained between treatment groups (42% vs. 27%; P=0.03) (Cady et al, 2015). The COMPASS study was a cross-over study with a high drop-out rate, which compared nasal powder sumatriptan 22 mg to oral sumatriptan 100 mg (n=275; 1,531 migraines assessed) in patients with 2 to 8 migraines/month at baseline. Primary endpoint results demonstrated a significant reduction in the adjusted mean difference in pain intensity scores (P<0.001). At 2 hours, the rates of pain relief (freedom) were comparable (Tepper et al, 2015).
  - o Data to support the approval of ZEMBRACE SYMTOUCH were based on subcutaneous sumatriptan succinate bioequivalence studies. The safety and efficacy of subcutaneous sumatriptan succinate were evaluated in 3 controlled, unpublished studies in over 1,000 patients with moderate to severe migraines. Studies demonstrated that the onset of relief began as early as 10 minutes following a 6 mg sumatriptan injection. Within 2 hours, headache relief was achieved in 82% of patients treated with a sumatriptan 6 mg injection, and 65% were pain free (Prescribing Information: ZEMBRACE SYMTOUCH, 2017; IMITREX, 2018).
  - o In a randomized, double-blind, crossover study, the efficacy and tolerability of 3 mg subcutaneous sumatriptan (ZEMBRACE SYMTOUCH) and 6 mg subcutaneous sumatriptan (SUMAVEL DOSEPRO – now discontinued) were compared in 20 patients with rapidly-escalating migraine attacks. The proportion of patients who were pain-free at 1-hour post-dose was similar following treatment with 3 mg and 6 mg subcutaneous sumatriptan (50% vs

52.6%, respectively; P=0.87). Tolerability was also similar for both doses; although, sumatriptan 3 mg was associated with fewer triptan sensations (ie, paresthesia, neck pain, flushing, and involuntary muscle contractions of the neck) when compared to the the 6-mg dose (1 patient vs 4 patients) (Cady et al, 2017).
  - A summary of Cochrane Reviews evaluating the various routes of administration for sumatriptan demonstrated that the injectable (particularly the 6 mg subcutaneous dose) routes of administration were most effective in reducing pain within the first 2 hours of treatment compared to placebo (number needed to treat [NNT], 2.3) and sustained pain-free after 24 hours (NNT, 6.1). Efficacy was dose-related with the oral sumatriptan 50 mg dose demonstrating the highest NNT for most endpoints. Compared to other triptans, only rizatriptan 5 mg (vs. sumatriptan 25 mg), rizatriptan 10 mg (vs. sumatriptan 25 to 100 mg), and eletriptan 40 to 80 mg (vs. sumatriptan 50 to 100 mg) were superior to sumatriptan for various endpoints. No differences in the incidence AEs were found (Derry et al, 2014).
  - A Cochrane Review of zolmitriptan trials concluded that zolmitriptan 2.5 to 5 mg benefited the same proportion of patients as sumatriptan 50 mg for headache relief at 2 hours (range 66 to 68%) with no significant difference in safety (Bird et al, 2014).
  - The TEENZ study assessed the efficacy and safety of zolmitriptan nasal spray for the acute treatment of a single migraine headache in 798 adolescents aged 12 to 17 years. The DB, 4-arm parallel study randomized patients in a ratio of 5:3:3:5 to placebo or zolmitriptan nasal spray in doses of 0.5 mg, 2.5 mg, or 5 mg, respectively. Zolmitriptan 5 mg nasal spray was statistically superior to placebo for the primary endpoint of pain-free status after 2 hours of administration (29.7% vs. 16.6%, respectively; P<0.001). Dysgeusia was the most frequently reported AE with zolmitriptan 5 mg nasal spray (occurring in 11.4% more of patients) (Winner et al, 2016).
  - In pediatric patients, 1 Cochrane review concluded that triptans (moderate quality of evidence) and ibuprofen (low quality evidence) are effective at providing pain freedom in children and adolescents. There are limited safety data available for AEs associated with ibuprofen use, and there may be with higher rates of minor AEs associated with triptan use. Further studies are needed in this population to validate conclusions (Richer et al, 2016).

SAFETY SUMMARY

- All triptans are contraindicated in patients with significant underlying cardiovascular (CV) disease (eg, angina pectoris, history of myocardial infarction, documented silent ischemia, or coronary artery vasospasm); peripheral vascular disease; ischemic bowel disease; uncontrolled hypertension; a history of stroke, transient ischemic attack or history of hemiplegic or basilar migraine because these patients are at a higher risk of stroke; and recent use (ie, within 24 hours) of ergotamine-containing medication, ergot-type medication (such as DHE or methysergide) or another 5-HT_1 receptor agonist. Additional contraindications include:
  - Naratriptan, sumatriptan and sumatriptan/naproxen are contraindicated in severe hepatic impairment. Naratriptan is also contraindicated in severe renal impairment (creatinine clearance [CrCL] < 15 mL/min).
  - Frovatriptan, naratriptan, eletriptan, sumatriptan, sumatriptan/naproxen, or zolmitriptan are contraindicated in patients with Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders.
  - Concurrent administration of rizatriptan, sumatriptan, sumatriptan/naproxen, or zolmitriptan with a monoamine oxidase (MAO)-A inhibitor or recent (within 2 weeks) use of an MAO-A inhibitor.
  - Eletriptan is contraindicated in patients with recent use (within at least 72 hours) of potent cytochrome P450 (CYP) 3A4 inhibitors including ketoconazole, itraconazole, nefazodone, clarithromycin, ritonavir, or nelfinavir.
  - Sumatriptan/naproxen is contraindicated in the setting of coronary artery bypass graft (CABG) surgery; use during the third trimester of pregnancy; and in asthma, rhinitis, and in those patients with a history of asthma, urticaria, or allergic-type reactions after taking aspirin (ASA) or NSAIDs.
- Sumatriptan/naproxen has a boxed warning of potentially fatal CV and gastrointestinal (GI) risks associated with NSAID-use. NSAIDs can increase CV thrombotic events (eg, myocardial infarction and stroke); use is contraindicated in the setting of CABG; and increased reports of GI events such as bleeding, ulceration, and perforation of the stomach or intestines have been reported, including fatal events.
- The following warnings and precautions are associated with medications in class:
  - Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, sumatriptan/naproxen, and zolmitriptan have a higher risk of myocardial ischemia, infarction, Prinzmetal angina, arrhythmias, and other adverse cardiac events in certain patients; cerebrovascular events and associated fatalities in certain patients; other vaso-spasm-

related events (ie, GI ischemic and peripheral vasospastic); chest, throat, neck, and jaw pain, tightness and pressure; exacerbation of headache with medication overuse; and serotonin syndrome.
  - o Almotriptan has additional warnings of corneal opacities and possible accumulation and subsequent toxicity due to the binding of melanin-containing tissues in certain patients. Almotriptan should be used with caution in patients with hypersensitivity to sulfonamides. Almotriptan, rizatriptan, and zolmitriptan, have had reports of significant elevations of blood pressure.
  - o All sumatriptan-containing products have reports of seizures reported following administration. Sumatriptan/naproxen also has warnings associated with NSAID use, which include: increased exacerbations of asthma, nasal polyps, or fatal bronchospasm due to ASA-sensitivity or cross-reactivity; increases in fluid retention and edema may worsen heart failure or cause hyperkalemia and renal toxicity; serious skin reactions (eg, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis); the potential to mask inflammation and fever; and elevated liver enzymes have been reported with use.
  - o Injectable sumatriptan (IMITREX and IMITREX STATDOSE) has a warning for hypersensitivity reactions, including anaphylaxis and angioedema. In addition, the needle shield of the prefilled syringe contains a latex derivative that has the potential to cause allergic reactions in patients sensitive to latex.
  - o Zolmitriptan ODTs contain phenylalanine, in which the labeling warns of use in patients with phenylketonuria.
- Triptan-containing medications have a large number of potential AEs, but the incidence of most individual reactions is relatively low and often dose-related. Among the oral preparations, no triptan is clearly safer than the others. In general, the injectable triptans are associated with more AEs compared with the oral/topical dosage forms. Triptans are often associated with atypical sensations, including numbness tingling, flushing, heaviness/tightness of the chest and throat, heat, burning, cold, or pressure.
  - o Generally, the most common AEs associated with 5-HT_1 receptor agonists are dizziness, numbness, tingling, flushing, sleepiness, and fatigue.
  - o Serious cardiac events, including myocardial infarction and coronary artery vasospasm, have occurred following use of 5-HT_1 receptor agonists. These events are extremely rare and have been reported in patients with risk factors predictive of coronary artery disease. Other events reported in association with drugs in this class have included ventricular tachycardia and fibrillation.
- A 2017 meta-analysis including 141 trials compared the tolerability of 14 oral treatments for acute migraine. In indirect comparisons of PC trials utilizing triptans, naratriptan had the lowest odds of any AE (odds ratio [OR]=1.11; 95% confidence interval [CI], 0.84 to 1.43) and treatment-related AE (OR=0.86, 95% CI, 0.51 to 1.55); zolmitriptan had the highest odds of any AE (OR, 2.22; 95% CI, 1.83 to 2.70) and sumatriptan had the highest odds of treatment-related AE (OR=2.23, 95% CI, 1.83 to 2.73). Results from the meta-regression reported that the dose of triptans had a significant effect on the occurrence of any AE and treatment-related AE, with higher doses yielding a higher probability of AE occurrence and lower doses lessening the risk (Thorlund, 2017).

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
Oral agents			
AMERGE (naratriptan)	Tablet: 1 mg 2.5 mg	Adult: 1 mg or 2.5 mg orally as a single dose; may repeat administration in 4 hours. Max daily dose: 5 mg.	Safety of treating > 4 migraines in 1 month has not been established.
AXERT (almotriptan)	Tablet: 6.25 mg 12.5 mg	Adult and adolescent (≥12 years): 6.25 mg or 12.5 mg orally as a single dose; may repeat administration in 2 hours. Max daily dose for adults: 25 mg.	Safety of treating >4 migraines in 1 month has not been established. In adults, 12.5 mg dose is more effective.
FROVA (frovatriptan)	Tablet: 2.5 mg	Adult: 2.5 mg orally as a single dose; may repeat administration in 2 hours. Max daily dose: 7.5 mg.	Safety of treating >4 migraines in 1 month has not been established.

Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
IMITREX (sumatriptan)	Tablet: 25 mg 50 mg 100 mg	Adult: 25, 50, or 100 mg orally as a single dose; may repeat administration in 2 hours. Max daily dose: 200 mg.	Safety of treating >4 migraines in 1 month has not been established. Doses of 100 mg may not provide a greater effect than the 50 mg dose.
MAXALT, MAXALT MLT (rizatriptan)	Tablet; Orally disintegrating tablet: 5 mg 10 mg	Adult: 5 mg or 10 mg orally as a single dose. Max daily dose: 30 mg. Pediatric (≥6 years): Weight based dosing of 5 mg for <40 kg and 10 mg for ≥40 kg. May repeat administration in 2 hours in adults and 24 hours in pediatric patients. Dose adjustments are needed for patients taking propranolol concomitantly.	Safety of treating >4 migraines/month in adults or children, and >1 dose within 24 hours in patients 6 to 12 years of age have not been established.
RELPAX (eletriptan)	Tablet: 20 mg 40 mg	Adult: 20 or 40 mg orally as a single dose; may repeat administration in 2 hours. Max daily dose: 80 mg. Max single dose: 40 mg.	Safety of treating >3 migraines in 1 month has not been established.
TREXIMET (sumatriptan/ naproxen)	Tablet: 10/60 mg 85/500 mg	Adult and adolescent (≥12 years): 1 tablet (85/500 mg for adults and 10/60 mg for adolescents) orally as a single dose. Max daily dose: 2 tablets in 24 hours, taken at least 2 hours apart for adults and 1 tablet in a 24 hour period for adolescents.	Safety of treating >5 migraines in adults and >2 migraines in pediatric patients over the span of 1 month has not been established.
ZOMIG, ZOMIG-ZMT (zolmitriptan)	Orally disintegrating tablet; Tablet: 2.5 mg 5 mg	Adult: starting dose is 1.25 or 2.5 mg dose; may repeat administration in 2 hours. Max daily dose: 10 mg. Max single dose: 5 mg.	Safety of treating >3 migraines in 1 month has not been established.
Intranasal agents			
IMITREX nasal spray (sumatriptan)	Nasal spray: 5 or 20 mg/actuator unit-of-use inhaler	Adult: 5, 10, or 20 mg administered as a single dose intranasally; may repeat administration in 2 hours. Max daily dose: 40 mg. Max single dose: 20 mg.	Safety of treating >4 migraines in 1 month has not been established.
ONZETRA XSAIL (sumatriptan)	Nasal powder: 2 breath-powered delivery systems containing 11 mg sumatriptan per each nosepiece	Adult: 22 mg (2 nosepieces) administered using the breath-powered delivery device; may repeat administration in 2 hours. Max daily dose: 2 doses (44 mg/4 nosepieces).	Safety of treating >4 migraines in 1 month has not been established. Breath-powered powder delivery requiring a forceful blow into each nostril.
ZOMIG (zolmitriptan)	Nasal spray: 2.5 or 5 mg/spray single-use nasal spray units	Adult and adolescent (≥12 years): 2.5 mg administered as a single dose intranasally; may repeat administration in 2 hours. Max daily dose: 10 mg. Max single dose: 5 mg.	Safety of treating >4 migraines in 1 month has not been established.
Subcutaneous agents			
IMITREX (sumatriptan)	Subcutaneous injection: 6 mg single dose vial	Adult: 6 mg administered subcutaneously; may repeat administration in 1 hour. Max daily dose: 12 mg. Max single dose: 6 mg,	Administer the needle only to the skin; intramuscular (IM) or intravascular (IV)

Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
		particularly for cluster headaches; however, lower doses (1 to 5 mg) may be administered for the treatment of migraine.	delivery should be avoided.
IMITREX STATDOSE (sumatriptan)	Subcutaneous injection: 4 and 6 mg single dose, prefilled cartridges for pen use	Adult: 6 mg administered subcutaneously; may repeat administration in 1 hour. Max daily dose: 12 mg. Max single dose: 6 mg, particularly for cluster headaches; however, lower doses (1 to 5 mg) may be administered for the treatment of migraine.	Administer where the needle penetrates ¼ inch of skin; IM or IV delivery should be avoided.
ZEMBRACE SYMTOUCH (sumatriptan)	Subcutaneous injection: 3 mg single dose, prefilled autoinjector	Adult: 3 mg injected subcutaneously; each dose should be separated by at least 1 hour. May administer up to 4 times per day. Max daily dose: 12 mg. Max single dose: 3 mg.	Administer where the needle penetrates ¼ inch of skin; IM or IV delivery should be avoided. Administer dose to the upper arm or thigh. May be administered at least 1 hour following a dose of another sumatriptan agent.

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
AXERT (almotriptan)	Safety and efficacy have not been established. In general, start at the low end of the dosing range. A CV evaluation is recommended for geriatric patients who have other CV risk factors.	Safety and efficacy have not been established in children <12 years of age.	For CrCL ≤30 mL/minute, an initial dose of 6.25 mg and a max dose of 12.5 mg/day are recommended.	Dosage adjustment required for moderate to severe impairment, reduce dose to 6.25 mg and a max dose of 12.5 mg/day.	Pregnancy Category C* Unknown whether excreted in breast milk; use with caution.
RELPAX (eletriptan)	No overall difference in safety or efficacy between elderly and younger patients. BP was increased to a greater extent in elderly patients. Additionally, a statistically	Safety and efficacy have not been established.	No significant change in clearance for patients with mild, moderate, or severe impairment; although, BP elevations were observed in this population. No	Use in severe impairment is not recommended.	Pregnancy Category C* Excreted in breast milk. AAP classifies drug as compatible with breastfeeding. Drug would not be expected to cause any adverse effects in breastfed infants,

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
	significant increased half-life (from 4.4 hours to 5.7 hours) was observed between elderly and younger patients. No dose adjustments are recommended.		dosage adjustment required.		especially if the infant is >2 months; use with caution.
FROVA (frovatriptan)	Mean blood concentrations were 1.5 to 2 times higher in elderly patients versus younger patients. No dose adjustments are recommended.	Safety and efficacy have not been established.	No dosage adjustment is required.	An estimated 2-fold increase in AUC is predicted with severe impairment; use with caution. No dosage adjustment is required for mild to moderate impairment.	†Unclassified There are no adequate data on the developmental risk associated with the use of frovatriptan in pregnant women. Several studies have suggested women with migraine may be at increased risk of preeclampsia. Use with caution. Unknown whether excreted in breast milk; use with caution.
AMERGE (naratriptan)	Safety and efficacy have not been established. In general, start at the low end of the dosing range. A CV evaluation is recommended for geriatric patients who have other CV risk factors.	Safety and efficacy have not been established.	For mild to moderate impairment, reduce initial dose to 1 mg and a max dose of 2.5 mg/day. Use in severe impairment (CrCL ≤15 mL/min) is contraindicated.	For mild to moderate impairment, reduce initial dose to 1 mg and a max dose of 2.5 mg/day. Use in severe impairment (Child-Pugh C) is contraindicated.	†Unclassified Several studies have suggested women with migraine may be at increased risk of preeclampsia. Post-marketing reports of naratriptan included mainly first trimester exposures. The incidence of major birth defects with naratriptan was similar to the incidence of the general US population (2.2% vs. 2.2 to 2.9%, respectively). Use with caution.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
					Unknown whether excreted in breast milk; use with caution.
MAXALT, MAXALT MLT (rizatriptan)	Safety and efficacy have not been established. In general, start at the low end of the dosing range. A CV evaluation is recommended for geriatric patients who have other CV risk factors.	Safety and efficacy have not been established in children <6 years of age.	No dosage adjustment is required.	Drug plasma concentrations are 30% greater with moderate impairment. No dosage adjustment is required for mild to moderate impairment.	Pregnancy Category C* Unknown whether excreted in breast milk; use with caution.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
IMITREX, IMITREX STATDOSE, ONZETRA XSAIL, ZEMBRACE SYMTOUCH (sumatriptan)	Safety and efficacy have not been established. In general, start at the low end of the dosing range. A CV evaluation is recommended for geriatric patients who have other CV risk factors.	Safety and efficacy have not been established.	Not studied.	The maximum single oral dose should not exceed 50 mg. Use of IMITREX, IMITREX STATDOSE, ONZETRA XSAIL, and ZEMBRACE SYMTOUCH in severe impairment is contraindicated.	Pregnancy Category C* (ONZENTRA XSAIL, ZEMBRACE SYMTOUCH) †Unclassified (IMITREX, IMITREX STATDOSE) Overall, data from a pregnancy exposure registry have not detected an increased frequency of birth defects or a consistent pattern of birth defects associated with sumatriptan exposure during pregnancy. Several studies have suggested women with migraine may be at increased risk of preeclampsia. A registry study reported a 4.2% occurrence of major birth defects during first-trimester exposure and during any trimester of exposure which is numerically higher than the 2.2% to 2.9% rate of major birth defects among deliveries to women with migraine. ALL FORMULATIONS: Excreted in breast milk after subcutaneous administration. Unknown excretion after oral administration. Withhold breastfeeding for 12 hours after oral, nasal, or subcutaneous administration to minimize infant exposure.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
TREXIMET (sumatriptan/ naproxen)	Safety and efficacy have not been established. In general, start at the low end of the dosing range. A CV evaluation is recommended for geriatric patients who have other CV risk factors.	Safety and efficacy have not been established in children <12 years of age.	No renal dosage adjustment required for mild to moderate impairment. Not recommended for severe impairment (CrCL ≤30 mL/min). Renal effects of the drug may hasten progression of renal dysfunction in pre-existing renal disease.	Administer 1 10/60 mg tablet in a 24 hour period for mild to moderate impairment. Use in severe impairment is contraindicated.	Pregnancy Category C during the first 2 trimesters; Pregnancy Category X during the third trimester* Both agents are excreted in breast milk. Limited information indicates that levels are low and adverse effects in breastfed infants are apparently uncommon. However, because of naproxen's long half-life and reported serious adverse reaction in a breastfed neonate, other agents may be preferred while nursing a newborn or preterm infant; use with caution.
ZOMIG, ZOMIG-ZMT (zolmitriptan)	Safety and efficacy have not been established. In general, start at the low end of the dosing range. A CV evaluation is recommended for geriatric patients who have other CV risk factors.	Safety and efficacy have not been established for the nasal spray in children <12 years of age and <18 years of age for oral formulations.	Clearance was reduced by 25% in patients with severe impairment (CrCL ≤25 mL/min); no significant change in clearance was observed in moderate impairment (CrCL 26 to 50 mL/min). No dosage adjustment required.	Dosage adjustment required for moderate to severe impairment, reduce dose to 1.25 mg and a max dose of 5 mg/day.	Pregnancy Category C* Unknown whether excreted in breast milk; use with caution.

Abbrv: AAP = American Academy of Pediatrics; AUC = area under the curve; BP = blood pressure; CrCL = creatinine clearance; CV = cardiovascular; ODT = orally disintegrating tablet

*Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus, and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. Pregnancy Category X = Contraindicated in pregnant women due to evidence of fetal abnormalities from adverse effects data from investigational or marketing experience. Risks of use of the drug in pregnant women clearly outweigh potential benefits.

†In accordance with the FDA's Pregnancy and Lactation Labeling Rule (PLLR), this product is not currently assigned a Pregnancy Category. Consult product prescribing information for details.

(American Academy of Pediatrics, 2001; LactMed, 2018)

CONCLUSION

- The 5-HT_1 receptor agonists, commonly referred to as triptans, are a well-established therapy for the acute treatment of migraine attacks with or without aura. These agents work via the promotion of vasoconstriction, inhibition of dural vasodilation and inflammation and blockade of pain pathways in the brainstem. In contrast to analgesics, the triptans are considered to be specific migraine therapies because they act at the pathophysiologic mechanisms of headaches (Bajwa et al, 2018; Clinical Pharmacology, 2018).
- Currently, there are 7 single-entity triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan) and 1 fixed-dose triptan/nonsteroidal anti-inflammatory combination product (sumatriptan/naproxen) available. All triptans are available as a tablet; however, some are available in a variety of other dosage formulations. Specifically, sumatriptan (nasal spray, nasal powder, subcutaneous injection, and tablet) and zolmitriptan (nasal spray, orally disintegrating tablet, and tablet) are available in the greatest number of dosage formulations. While it is noted that the subcutaneous sumatriptan injection has the fastest onset of action, there is no evidence to suggest that different oral triptan formulations have a faster onset of action than others (Francis et al, 2010). Almotriptan, eletriptan, naratriptan, rizatriptan, sumatriptan, sumatriptan/naproxen and zolmitriptan are available generically in at least 1 dosage form or strength (DRUGS@FDA, 2018).
- Triptan selection is based on the characteristics of the headache, dosing convenience, and patient preference. All available triptans are FDA-approved for the acute treatment of migraine with or without aura. The subcutaneous sumatriptan injections (with the exception of ZEMBRACE SYMTOUCH) are also FDA-approved for the acute treatment of cluster headache episodes. In pediatric patients, almotriptan, zolmitriptan nasal spray (fastest onset), and sumatriptan/naproxen are approved for use in children 12 years of age and older, while rizatriptan is approved for use in children as young as 6 years of age.
- While there are data to suggest that the available triptans differ in comparative efficacy, because of the lack of consistent superiority of 1 triptan over another in direct head-to-head comparisons, it appears that individual variations in response to the different triptans exist. There are no pediatric comparative effectiveness data and studies are sparse. Based on pharmacokinetic and –dynamic data, subcutaneous and intranasal formulations generally have a quicker onset of action and subcutaneous formulations generally have a lower NNT but more AEs. Frovatriptan and naratriptan have the longest onset of action, which may be responsible for lower incidences of AE. Meta-analyses and systematic reviews point to a potential for lower efficacy with naratriptan and frovatriptan; however, more studies are needed to validate findings.
- Triptan-containing medications have a large number of potential AEs, but the incidence of most individual reactions is relatively low and often dose-related. Among the oral preparations, no triptan is clearly safer than the others. A 2017 meta-analysis including 141 trials compared the tolerability of 14 oral treatments for acute migraine. In indirect comparisons of placebo-controlled trials utilizing triptans, naratriptan had the lowest odds of any AE (odds ratio [OR]=1.11; 95% confidence interval [CI], 0.84 to 1.43) and treatment-related AE (OR=0.86, 95% CI, 0.51 to 1.55); zolmitriptan had the highest odds of any AE (OR, 2.22; 95% CI, 1.83 to 2.70) and sumatriptan had the highest odds of treatment-related AE (OR=2.23, 95% CI, 1.83 to 2.73). Results from the meta-regression reported that the dose of triptans had a significant effect on the occurrence of any AE and treatment-related AE, with higher doses yielding a higher probability of AE occurrence and lower doses lessening the risk (Thorlund, 2017).
- In general, the injectable triptans are associated with more AEs compared with the oral dosage forms. Triptans are often associated with atypical sensations, including numbness, tingling, flushing, heaviness/tightness in the chest and throat, heat, burning, cold, or pressure.
- According to the AAN, American College of Physicians-American Society of Internal Medicine, and U.S. Headache Consortium, 5-HT_1 receptor agonists are clinically interchangeable for the treatment of migraines. These guidelines do not provide a recommendation for the use of 1 agent over another. In addition, non-oral formulations provide relief for patients unable to swallow due to symptoms of nausea and vomiting (Evers et al, 2009; Francis et al, 2010; Matchar et al, 2000; Silberstein, 2000; Silberstein et al, 2012 (guideline reaffirmed in 2015); Erratum in Subcommittee of the AAN and the AHS, 2013; Snow et al, 2002). According to the 2015 AHS evidence assessment, triptans (regardless of formulation) and DHE (nasal spray or inhaler) have been established to be effective treatments for acute migraines in adults. Reaffirming the AAN migraine guidelines, the recommendation remains that clinicians should consider medication efficacy and potential AEs when prescribing acute medications

for migraine. Opioid medications are probably effective; however, they are not recommended for regular use (Marmura et al, 2015). For the treatment of cluster headaches, the 2016 AHS guideline provides an update to the 2010 AAN guidelines (Francis et al, 2010; Robbins et al, 2016). For acute treatment, subcutaneous sumatriptan and zolmitriptan nasal spray are recommended with a higher level of evidence; although zolmitriptan nasal spray is not FDA-approved for use (Robbins et al, 2016). In pediatric patients, older guidelines published by the Child Neurological Society recommend ibuprofen as first-line therapy for the treatment of migraines, followed by acetaminophen, and sumatriptan nasal spray when all other analgesics fail (Lewis et al, 2004). An update of the 2004 Child Neurological Society guideline is currently in progress.

- All 5-HT_1 receptor agonists are generally effective for the acute treatment of migraine attacks and are well-tolerated with a similar safety profile. Although some 5-HT_1 receptor agonists have been shown to be significantly superior to other 5-HT_1 receptor agonists in direct comparator studies, these results may not translate to significant differences within meta-analyses and systematic reviews. Additionally, the clinical superiority cannot be determined as an individual patient's response to a particular drug may vary. In general, injection treatments have been associated with the fastest onset of action; therefore, are amenable to quick relief. However, injectable triptans are associated with more AE compared to oral or topical dosage forms. Treatment guidelines do not recommend 1 agent over another; rather, choice of treatment should be individualized based on patient needs, response, and preference, migraine severity, and tolerability.

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Publication date: January 4, 2019

Board Requested Reports

Opioid Utilization – top prescribers and members

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): Q1 2019
Report Period Start Date: 1/1/2019
Report Period End Date: 3/31/2019
Submission Date of Report:

Opioid Utilization

Year/Month Filled	Member Count	Claim Count	Sum of Days Supply	Sum of Quantity	Sum of Paid Amount
April 2018	8,680	12,225	232,182	791,869	$ 542,286.02
May 2018	8,695	12,630	233,170	797,291	$ 516,954.80
June 2018	8,521	12,010	223,813	762,628	$ 503,097.21
July 2018	8,452	12,101	221,966	756,852	$ 452,162.77
August 2018	8,423	12,133	223,855	755,231	$ 524,070.43
September 2018	8,015	11,144	206,015	702,642	$ 447,337.28
October 2018	8,352	12,010	217,036	743,580	$ 468,150.51
November 2018	8,200	11,697	216,308	740,634	$ 480,141.49
December 2018	7,663	10,857	197,435	668,966	$ 438,135.91
January 2019	8,533	12,218	221,444	746,864	$ 502,531.32
February 2019	7,818	10,777	197,324	658,050	$ 456,527.24
March 2019	8,081	11,460	209,599	695,148	$ 516,941.75

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	NV	135	538	15,378	65,175	$ 60,092.07
B	Pain Management	Carson City	NV	90	341	7,419	18,327	$ 152,945.68
C	Maxillofacial Surgery	Henderson	NV	192	307	9,061	28,297	$ 18,238.66
D	Pain Management	Las Vegas	NV	190	298	8,085	24,292	$ 18,957.56
E	Unknown	Las Vegas	NV	109	296	8,789	29,190	$ 18,009.83
F	Pain Management	Las Vegas	NV	184	290	8,450	26,034	$ 19,105.85
G	General Surgery	Las Vegas	NV	69	290	8,257	31,155	$ 14,949.13
H	Internal Medicine	Las Vegas	NV	39	241	3,765	5,599	$ 79,118.76
I	Pain Management	Las Vegas	NV	85	237	6,803	23,006	$ 6,806.70
J	Family Practice	Las Vegas	NV	160	237	6,716	21,834	$ 6,184.40

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	NV	140	520	14,692	58,008	$ 54,346.41
C	Maxillofacial Surgery	Henderson	NV	171	381	10,970	34,372	$ 20,775.98
B	Pain Management	Carson City	NV	108	371	8,397	21,562	$ 138,907.21
F	Pain Management	Las Vegas	NV	165	327	9,626	29,632	$ 26,060.60
L	Family Practice	Fallon	NV	95	289	6,030	26,279	$ 9,559.94
E	Unknown	Las Vegas	NV	95	276	7,793	25,812	$ 15,406.98
K	Pain/Anethesiology	Las Vegas	NV	107	268	7,020	23,322	$ 16,036.79
H	Internal Medicine	Las Vegas	NV	42	233	3,303	6,784	$ 43,126.11
H	Orthopedic Surg	Las Vegas	NV	80	221	6,197	21,879	$ 33,195.88
D	Pain Management	Las Vegas	NV	135	218	5,821	17,407	$ 12,320.96

Opioid Utilization by Member

Top 10 Members by Claim Count

April 1, 2018 - March 31, 2019

Fee for Service Medicaid

MemberIDEncrypted	Prescriber NPI	Claim Count	Days Supply	Qty Disp
88884905646		**175**	**787**	**4,356**
	II	158	701	3,952
	AD	16	79	390
	AU	1	7	14
66668619978		**127**	**497**	**2,725**
	GG	9	45	200
	NN	19	87	487
	OO	1	30	90
	RR	82	294	1,670
	SS	2	2	2
	UU	1	1	1
	XX	1	1	1
	AI	10	32	254
	AX	2	5	20
33333376249		**126**	**708**	**2,786**
	EE	4	32	69
	II	4	20	120
	LL	3	23	46
	ZZ	4	20	120
	AE	20	90	392
	AF	70	411	1,534
	AI	1	10	20
	AS	17	88	405
	AW	3	14	80
33330492333		**105**	**695**	**1,974**
	II	44	334	1,000
	AJ	61	361	974
29457655656		**100**	**738**	**2,781**
	BB	9	70	330
	MM	23	23	72
	WW	10	90	371
	AK	18	147	755
	AM	39	405	1,235
	AN	1	3	18
11116193955		**88**	**784**	**2,529**
	CC	8	8	8
	HH	10	300	1,025
	KK	6	180	630
	SS	10	10	36
	XX	31	31	51
	AC	4	4	8
	AL	10	10	29
	AP	8	240	740
	AQ	1	1	2

MemberIDEncrypted	Prescriber NPI	Claim Count	Days Supply	Qty Disp
76028922323		**83**	**154**	**392**
	AA	2	2	3
	CC	6	6	7
	DD	1	6	24
	FF	1	2	12
	JJ	1	7	24
	PP	2	20	50
	QQ	1	7	15
	SS	29	29	50
	TT	1	3	12
	XX	13	13	17
	AB	1	7	30
	AC	13	13	23
	AG	1	5	10
	AH	5	5	9
	AL	2	2	2
	AT	1	10	15
	AV	1	5	30
	AY	1	5	20
	AZ	1	7	40
88883847895		**76**	**498**	**1,782**
	GG	10	85	270
	AF	63	398	1,478
	AO	3	15	34
00001004825		**76**	**424**	**1,414**
	VV	9	270	990
	YY	64	64	64
	AR	3	90	360
99997035188		**75**	**355**	**1,823**
	GG	1	7	20
	II	63	271	1,617
	AF	8	56	144
	AU	3	21	42
Grand Total		**1,031**	**5,640**	**22,562**

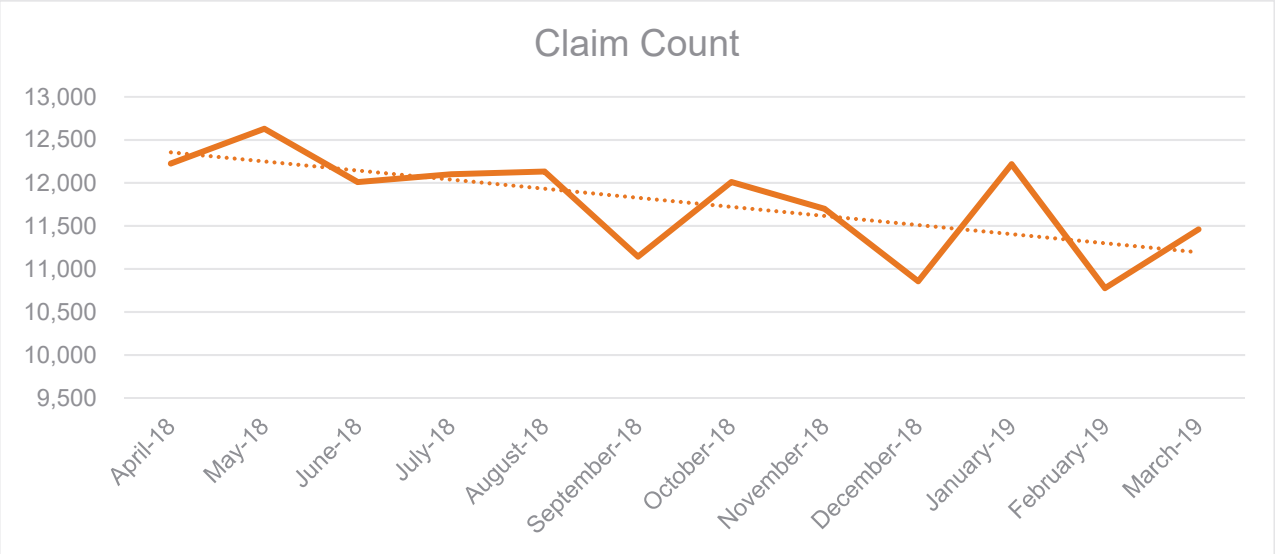
Opioid Utilization

Overall Summary

April 1, 2018 - March 31, 2019

Fee for Service Medicaid

Year Month Filled	Member Count	Claim Count	Claims per Member	Sum of Days Supply	Sum of Qty	Qty per Member
April-18	8,680	12,225	1.4	232,182	791,869	91.2
May-18	8,695	12,630	1.5	233,170	797,291	91.7
June-18	8,521	12,010	1.4	223,813	762,628	89.5
July-18	8,452	12,101	1.4	221,966	756,852	89.5
August-18	8,423	12,133	1.4	223,855	755,231	89.7
September-18	8,015	11,144	1.4	206,015	702,642	87.7
October-18	8,352	12,010	1.4	217,036	743,580	89.0
November-18	8,200	11,697	1.4	216,308	740,634	90.3
December-18	7,663	10,857	1.4	197,435	668,966	87.3
January-19	8,534	12,219	1.4	221,445	746,865	87.5
February-19	7,818	10,777	1.4	197,324	658,050	84.2
March-19	8,081	11,460	1.4	209,599	695,148	86.0



Top 10 Opioid Utilizers

Overall Summary

April 1, 2018 - March 31, 2019

Fee for Service Medicaid

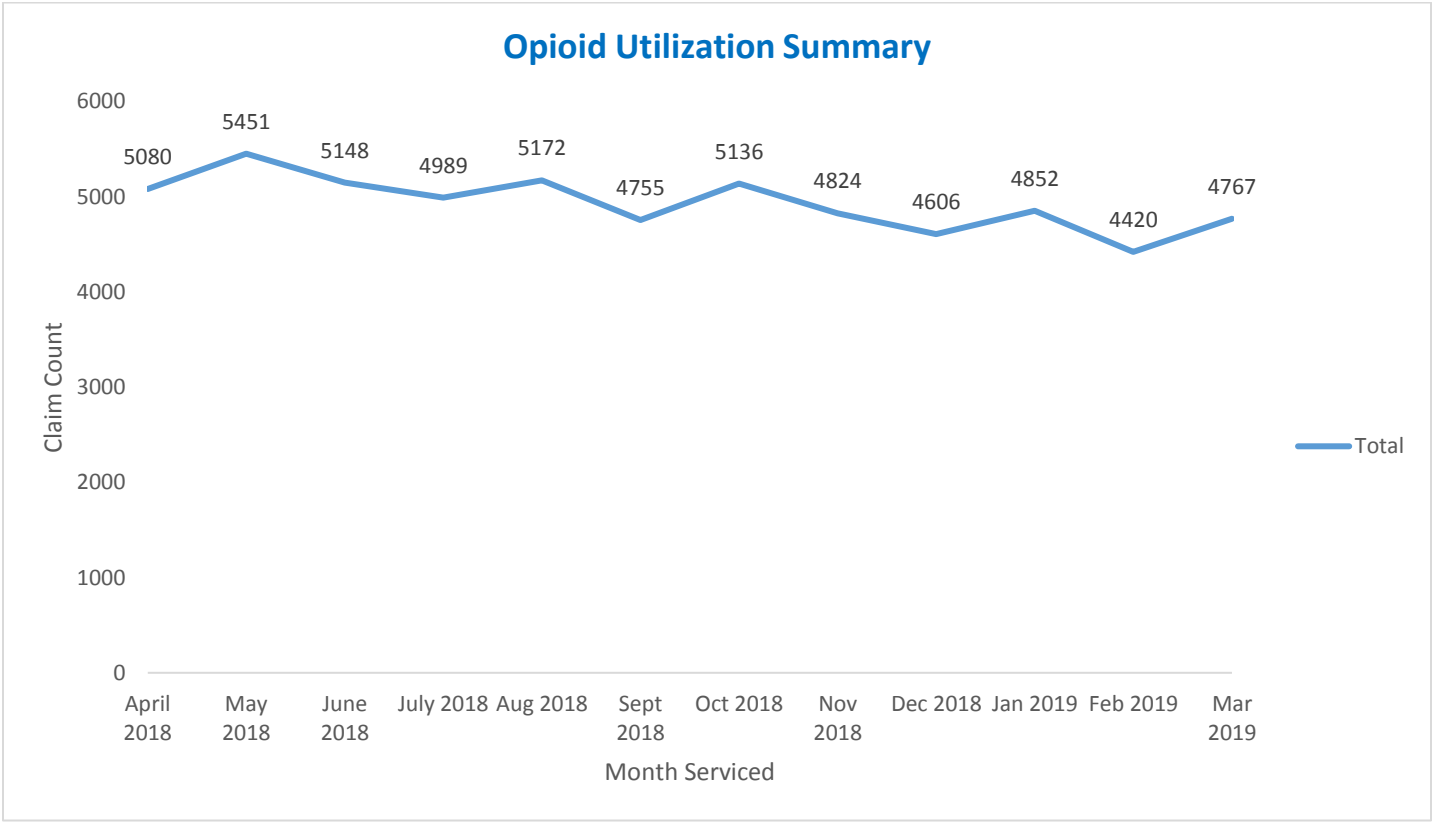
MemberIDEncrypted	DrugLabelName	Count of Claims	Sum of Qty	Sum of Days Sup
77779814158	SUBOXONE MIS 8-2MG	60	718	359
77779814158 Total		**60**	**718**	**359**
69350344545	SUBLOCADE INJ 300/1.5	1	1.5	28
69350344545	SUBOXONE MIS 4-1MG	16	224	203
69350344545	SUBOXONE MIS 8-2MG	38	472	237
69350344545 Total		**55**	**697.5**	**468**
33333487769	METHADONE TAB 10MG	1	60	30
33333487769	SUBOXONE MIS 4-1MG	2	60	60
33333487769	SUBOXONE MIS 8-2MG	50	575	286
33333487769 Total		**53**	**695**	**376**
33336598709	MORPHINE SUL TAB 30MG ER	25	700	350
33336598709	OXYCOD/APAP TAB 10-325MG	23	1486	321
33336598709	OXYCOD/APAP TAB 7.5-325	2	112	28
33336598709 Total		**50**	**2298**	**699**
22222264138	HYDROMORPHON TAB 8MG	1	70	14
22222264138	SUBLOCADE INJ 100/0.5	1	0.5	28
22222264138	SUBLOCADE INJ 300/1.5	2	3	56
22222264138	SUBOXONE MIS 12-3MG	2	34	34
22222264138	SUBOXONE MIS 4-1MG	7	210	210
22222264138	SUBOXONE MIS 8-2MG	35	764	397
22222264138 Total		**48**	**1081.5**	**739**
33336596143	SUBLOCADE INJ 300/1.5	1	1.5	28
33336596143	SUBOXONE MIS 12-3MG	21	372	370
33336596143	SUBOXONE MIS 2-0.5MG	10	244	244
33336596143	SUBOXONE MIS 8-2MG	14	367	367
33336596143 Total		**46**	**984.5**	**1009**
55552607564	MORPHINE SUL TAB 15MG ER	18	555	217
55552607564	NUCYNTA ER TAB 50MG	5	300	150
55552607564	OXYCOD/APAP TAB 10-325MG	23	1876	365
55552607564 Total		**46**	**2731**	**732**
55555689066	HYDROCO/APAP TAB 10-325MG	46	2716	323
55555689066 Total		**46**	**2716**	**323**
11110100737	FENTANYL DIS 100MCG/H	11	165	330
11110100737	HYDROCO/APAP TAB 10-325MG	10	600	300
11110100737	METHADONE TAB 10MG	12	3500	360
11110100737	MORPHINE SUL TAB 100MG ER	12	1080	360
11110100737 Total		**45**	**5345**	**1350**
44445409888	OXYCOD/APAP TAB 10-325MG	45	1352	338
44445409888 Total		**45**	**1352**	**338**

Anthem

Opioid Utilization

April 1, 2018 – March 31, 2019

Opioid Utilization Summary					
Year/Month Filled	**Member Count**	**Claim Count**	**Days Supply**	**Quantity**	**Paid Amt**
April 2018	4,364	5,080	104,230	348,838	proprietary
May 2018	4,528	5,451	110,923	368,780	proprietary
June 2018	4,333	5,148	104,212	345,701	proprietary
July 2018	4,174	4,989	102,134	337,254	proprietary
August 2018	4,270	5,172	105,114	345,838	proprietary
September 2018	4,074	4,755	94,953	309,478	proprietary
October 2018	4,285	5,136	101,867	333,568	proprietary
November 2018	4,051	4,824	97,513	320,786	proprietary
December 2018	3,922	4,606	93,566	305,198	proprietary
January 2019	4,069	4,852	97,411	316,620	proprietary
February 2019	3,816	4,420	89,782	292,141	proprietary
March 2019	4,040	4,767	95,853	312,913	proprietary



Top Opioid Prescribers Per Quarter

April 1, 2018 – March 31, 2019

Top 10 Opioid Prescribers – 1Q19

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Days Supply	Quantity	Paid Amt
*586	PA	Las Vegas	NV	153	317	8,908	28,735	proprietary
*525	MD	Henderson	NV	72	280	7,765	21,595	proprietary
*121	PAC	Las Vegas	NV	164	274	7,821	26,011	proprietary
*050	PAC	Las Vegas	NV	127	269	7,702	24,557	proprietary
*647	PA	N Las Vegas	NV	96	265	7,455	24,040	proprietary
*319	MD	Henderson	NV	112	261	6,912	21,669	proprietary
*409	PA	Las Vegas	NV	133	258	7,275	22,911	proprietary
*127	MD	Las Vegas	NV	103	254	7,326	21,840	proprietary
*305	PAC	Las Vegas	NV	112	251	7,308	24,130	proprietary
*740	MD	Las Vegas	NV	100	209	5,567	16,346	proprietary

Top 10 Opioid Prescribers – 4Q18

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Days Supply	Quantity	Paid Amt
*586	PA	Las Vegas	NV	186	459	13,086	41,997	proprietary
*525	MD	Henderson	NV	76	323	9,486	26,463	proprietary
*121	PAC	Las Vegas	NV	158	300	8,455	26,299	proprietary
*305	PAC	Las Vegas	NV	128	297	8,129	26,295	proprietary
*050	PAC	Las Vegas	NV	132	258	7,082	22,643	proprietary
*319	MD	Henderson	NV	97	248	6,732	21,855	proprietary
*190	NP	Las Vegas	NV	112	238	6,439	20,363	proprietary
*647	PA	N Las Vegas	NV	84	231	6,533	20,846	proprietary
*237	NP	Las Vegas	NV	104	229	6,796	20,556	proprietary
*127	MD	Las Vegas	NV	99	220	6,365	20,105	proprietary

Top 10 Opioid Prescribers – 3Q18

Prescriber ID	Prescriber Type	Physician City	Physician State	Member Count	Claim Count	Days Supply	Quantity	Paid Amt
*586	PA	Las Vegas	NV	209	485	14,073	45,665	proprietary
*305	PAC	Las Vegas	NV	159	375	10,311	33,933	proprietary
*525	MD	Henderson	NV	82	305	9,034	25,542	proprietary
*127	MD	Las Vegas	NV	112	257	7,473	22,123	proprietary
*319	MD	Henderson	NV	111	254	6,641	20,624	proprietary
*409	PA	Las Vegas	NV	135	233	6,704	19,930	proprietary
*121	PAC	Las Vegas	NV	136	231	6,591	20,061	proprietary
*237	NP	Las Vegas	NV	96	222	6,612	19,998	proprietary
*635	MD	Las Vegas	NV	125	214	5,241	16,889	proprietary
*740	MD	Las Vegas	NV	91	196	5,575	17,228	proprietary

Top 10 Opioid Prescribers – 2Q18								
Prescriber ID	**Prescriber Type**	**Physician City**	**Physician State**	**Member Count**	**Claim Count**	**Days Supply**	**Quantity**	**Paid Amt**
***305**	PAC	Las Vegas	NV	158	380	34,165	10,225	proprietary
***121**	PAC	Las Vegas	NV	172	370	33,573	10,418	proprietary
***586**	PA	Las Vegas	NV	171	347	35,182	9,928	proprietary
***525**	MD	Henderson	NV	82	324	26,873	9,563	proprietary
***127**	MD	Las Vegas	NV	140	311	26,059	8,715	proprietary
***871**	MD	Las Vegas	NV	116	236	20,280	6,297	proprietary
***237**	NP	Las Vegas	NV	95	221	20,250	6,616	proprietary
***050**	PAC	Henderson	NV	102	219	20,587	6,328	proprietary
***229**	MD	Las Vegas	NV	94	210	19,145	6,250	proprietary
***647**	PA	N Las Vegas	NV	69	181	16,327	5,132	proprietary

Top 10 Opioid Utilizers with Prescriber Breakdown

April 1, 2018 – March 31, 2019

Member	Claim Count	Quantity	Days Supply
Prescriber			
*674	**53**	**1,813**	**371**
***650**	4	133	28
***731**	1	28	7
***154**	48	1,652	336
*513	**39**	**3,900**	**1,170**
***121**	12	1,200	360
***310**	6	600	180
***978**	21	2,100	630
*405	**39**	**3,120**	**1,170**
***121**	3	240	90
***978**	36	2,880	1,080
*677	**37**	**1,500**	**1,110**
***335**	3	120	90
***286**	34	1,380	1,020
*061	**34**	**2,790**	**994**
***547**	2	180	60
***586**	18	1,440	540
***127**	2	180	60
***310**	5	420	150
***978**	7	570	184
*392	**34**	**2,457**	**913**
***078**	1	56	14
***623**	2	98	28
***569**	25	1,703	691
***647**	4	400	120
***677**	2	200	60
*950	**33**	**640**	**160**

***965**	2	36	10
***767**	1	20	5
***822**	30	584	145
*020	**33**	**1,980**	**990**
***229**	12	720	360
***126**	6	360	180
***237**	15	900	450
*628	**33**	**2,042**	**665**
***635**	5	324	118
***871**	4	360	120
***580**	11	510	165
***504**	2	148	44
***249**	2	180	60
***305**	4	168	56
***050**	3	204	58
***190**	2	148	44
*408	**32**	**1,704**	**821**
***057**	3	187	73
***635**	6	295	170
***871**	2	130	60
***305**	20	1,036	504
***050**	1	56	14

Top 10 Opioid Utilizers with Drug Breakdown

April 1, 2018 – March 31, 2019

Member	Claim Count	Quantity	Days Supply
Drug			
***674**	**53**	**1,813**	**371**
HYDROCODONE-ACETAMIN 7.5-325	53	1,813	371
***513**	**39**	**3,900**	**1,170**
HYDROMORPHONE 4 MG TABLET	13	2,340	390
MORPHINE SULF ER 15 MG TABLET	13	780	390
MORPHINE SULF ER 30 MG TABLET	13	780	390
***405**	**39**	**3,120**	**1,170**
HYDROCODONE-ACETAMIN 10-325 MG	13	1,560	390
MORPHINE SULF ER 15 MG TABLET	13	780	390
MORPHINE SULF ER 30 MG TABLET	13	780	390
***677**	**37**	**1,500**	**1,110**
OXYCODONE HCL 10 MG TABLET	13	780	390
OXYCONTIN ER 60 MG TABLET	12	360	360
OXYCONTIN ER 80 MG TABLET	12	360	360
***061**	**34**	**2,790**	**994**
MORPHINE SULF ER 15 MG TABLET	9	510	254
MORPHINE SULF ER 30 MG TABLET	12	720	360
OXYCODONE HCL 10 MG TABLET	4	480	120

	OXYCODONE-ACETAMINOPHEN 10-325	9	1,080	260
***392**		**34**	**2,457**	**913**
	HYDROCODONE-ACETAMIN 10-325 MG	1	56	14
	METHADONE HCL 10 MG TABLET	3	360	90
	METHADONE HCL 5 MG TABLET	1	21	7
	OXYCODONE HCL 15 MG TABLET	12	1,072	328
	OXYCODONE HCL 30 MG TABLET	2	120	60
	OXYCODONE HCL ER 40 MG TABLET	5	268	134
	OXYCONTIN ER 30 MG TABLET	7	388	194
	OXYCONTIN ER 60 MG TABLET	3	172	86
***950**		**33**	**640**	**160**
	ACETAMINOPHEN-COD #3 TABLET	1	20	5
	HYDROCODONE-ACETAMIN 5-325 MG	2	36	10
	TRAMADOL HCL 50 MG TABLET	30	584	145
***020**		**33**	**1,980**	**990**
	ASCOMP WITH CODEINE CAPSULE	1	45	30
	BUTALBITAL COMP-CODEINE #3 CAP	10	450	300
	OXYCODON-ACETAMINOPHEN 7.5-325	11	990	330
	TRAMADOL HCL 50 MG TABLET	11	495	330
***628**		**33**	**2,042**	**665**
	OXYCODONE-ACETAMINOPHEN 10-325	10	824	206
	OXYCONTIN ER 10 MG TABLET	16	618	309
	PRIMLEV 10-300 MG TABLET	7	600	150
***408**		**32**	**1,704**	**821**
	FENTANYL 12 MCG/HR PATCH	3	45	90
	FENTANYL 50 MCG/HR PATCH	13	165	330
	FENTANYL 75 MCG/HR PATCH	1	10	30
	OXYCODONE HCL 30 MG TABLET	15	1,484	371

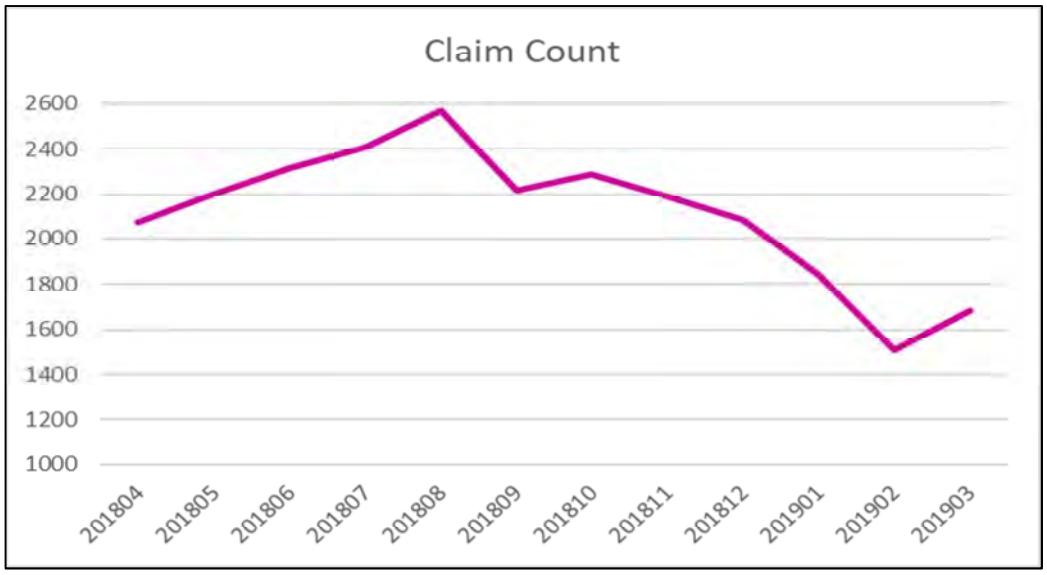
Opioid Utilization

Overall Summary

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Year Month Filled	Member Count	Claim Count	Claims per Member	Sum of Qty	Sum of Days Supply	Qty per Member
201804	1,430	2,072	1.45	125,855.5	40,815	88.01
201805	1,446	2,202	1.52	136,531.5	44,572	94.42
201806	1,503	2,314	1.54	142,563	46,714	94.85
201807	1,563	2,412	1.54	156,047	50,010	99.84
201808	1,665	2,569	1.54	166,011	51,919	99.71
201809	1,492	2,218	1.49	142,654	45,809	95.61
201810	1,532	2,291	1.50	150,087	48,327	97.97
201811	1,495	2,191	1.47	144,211	46,967	96.46
201812	1,446	2,087	1.44	134,275.5	43,576	92.86
201901	1,520	1,844	1.21	116,357	38,304	76.56
201902	1,302	1,507	1.16	97,902	31,852	75.19
201903	1,416	1,683	1.19	109,497	35,710	77.33



Top 10 Opioid Prescribers by Count of Claims

SilverSummit Healthplan

Current Quarter

Encryped ID	Specialty	Degree	City	Member Count	Claim Count	Sum of Days Supply	Sum of Qty
PP	Pain Management	PA	Las Vegas	106	230	6,767	21,831
NN	Pain Management	PA	Las Vegas	121	212	6,321	18,947
J	Pain Management	PA	Las Vegas	58	190	5,506	18,122
V	Anesthesiology	MD	Las Vegas	56	162	3,639	7,787
CC	Pain Management	MD	Las Vegas	110	160	4,476	13,783
P	Pain Management	PA	Las Vegas	111	145	4,238	13,130
EE	Psychiatry & Neurology Psychiatry	MD	Las Vegas	33	139	2,269	4,162
F	Pain Management	PA	Las Vegas	34	110	3,210	9,904
QQ	Anesthesiology	MD	Henderson	45	98	2,817	8,975
RR	Anesthesiology	MD	Las Vegas	44	93	2,185	6,450

Previous Quarter

Encryped ID	Specialty	Degree	City	Member Count	Claim Count	Sum of Days Supply	Sum of Qty
P	Pain Management	PA	Las Vegas	128	249	7,390	22,852
NN	Pain Management	PA	Las Vegas	116	246	7,344	22,386
J	Pain Management	PA	Las Vegas	68	188	5,422	17,877
PP	Pain Management	PA	Las Vegas	94	183	5,400	17,855
EE	Psychiatry & Neurology Psychiatry	MD	Las Vegas	38	168	2,549	4,408
CC	Pain Management	MD	Las Vegas	103	155	4,425	12,949
V	Anesthesiology	MD	Las Vegas	52	150	3,613	7,823
F	Pain Management	PA	Las Vegas	31	109	3,202	9,887
Y	Pain Management	MD	Las Vegas	43	109	3,254	9,478
QQ	Anesthesiology	MD	Henderson	41	100	2,957	9,643

Opioid Utilization by Member

Top 25 Members by Claim Count

April 1, 2018 - March 31, 2019

Silversummit Healthplan

Member Enc ID	Enc NPI	Count of Claim	Sum of Qty	Sum of Days
1		39	793	557
	X	39	793	557
2		36	732	366
	EE	36	732	366
3		34	275	209
	W	34	275	209
4		29	1,537	652
	NN	15	1,110	450
	EE	11	187	112
	Y	2	150	60
	CC	1	90	30
5		28	808	419
	EE	26	748	389
	SS	1	30	15
	TT	1	30	15
6		28	2,434	704
	V	20	1,995	570
	UU	4	180	60
	J	2	210	60
	VV	2	49	14
7		27	1,946	733
	E	8	670	230
	M	7	480	180
	Y	4	196	83
	G	3	300	90
	CC	2	90	60
	WW	2	150	60
	NN	1	60	30
8		26	2,488	764
	J	26	2,488	764
9		26	1,530	765
	R	16	930	465
	F	6	360	180
	AA	2	120	60
	GG	2	120	60
10		26	1,699	682
	XX	1	42	14
	P	4	212	84
	YY	11	695	284
	NN	10	750	300

Opioid Utilization by Member

Top 25 Members by Claim Count

April 1, 2018 - March 31, 2019

Silversummit Healthplan

Member Enc ID	Enc NPI	Count of Claim	Sum of Qty	Sum of Days
11		26	780	420
	EE	26	780	420
12		26	1,815	745
	J	26	1,815	745
13		26	2,319	769
	WW	12	1,080	360
	M	6	540	180
	ZZ	4	360	120
	AAA	4	339	109
14		26	2,730	780
	KK	13	1,170	390
	AA	8	960	240
	J	5	600	150
15		26	1,560	780
	P	12	720	360
	NN	10	600	300
	CC	4	240	120
16		26	2,340	780
	C	2	180	60
	L	10	900	300
	BBB	2	180	60
	FF	10	900	300
	II	2	180	60
17		25	2,670	750
	LL	25	2,670	750
18		25	2,204	727
	J	14	1,290	420
	A	8	720	240
	GG	3	194	67
19		25	2,130	750
	F	21	1,800	630
	J	2	180	60
	AA	2	150	60
20		25	2,415	735
	F	11	1,050	330
	R	8	840	240
	A	2	210	60
	UU	2	135	45
	AA	2	180	60

Opioid Utilization by Member

Top 25 Members by Claim Count

April 1, 2018 - March 31, 2019

Silversummit Healthplan

Member Enc ID	Enc NPI	Count of Claim	Sum of Qty	Sum of Days
21		25	2,280	750
	J	15	1,380	450
	A	10	900	300
22		25	2,356	686
	J	12	1,036	296
	A	7	720	210
	R	3	300	90
	GG	2	210	60
	AA	1	90	30
23		25	364	183
	DD	23	322	162
	BB	2	42	21
24		25	3,049	609
	CCC	24	3,009	603
	DDD	1	40	6
25		25	2,880	720
	J	23	2,640	660
	R	2	240	60

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

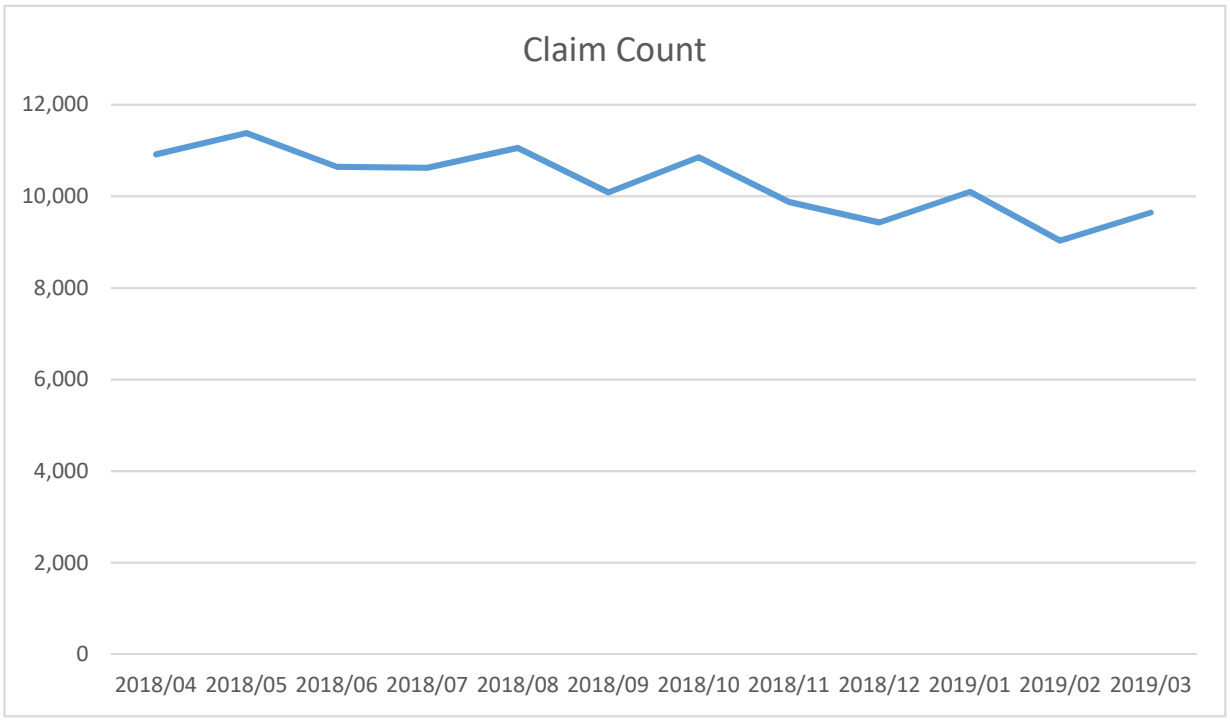
Opioid Utilization

Overall Summary

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Year/Month Filled	Member Count	Claim Count	Claims Per Member	Sum of Days Supply	Sum of Quantity	Qty Per Member
2018/04	9,313	10,918	1.17	245,148	822,394	88.31
2018/05	9,440	11,384	1.21	254,968	850,249	90.07
2018/06	8,980	10,646	1.19	235,066	791,575	88.15
2018/07	8,864	10,627	1.20	233,676	783,145	88.35
2018/08	9,077	11,054	1.22	239,958	800,098	88.15
2018/09	8,583	10,086	1.18	218,157	724,588	84.42
2018/10	8,927	10,857	1.22	236,217	780,822	87.47
2018/11	8,310	9,880	1.19	219,782	728,027	87.61
2018/12	7,979	9,432	1.18	208,540	690,257	86.51
2019/01	8,368	10,100	1.21	220,629	728,149	87.02
2019/02	7,740	9,032	1.17	197,880	650,047	83.99
2019/03	8,137	9,644	1.19	211,241	691,771	85.02



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top 10 Opioid Prescribers by Count of Claims

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Top 10 Opioid Prescribers by Claim Count					Q1 2019 - 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	480	1,190	99	107,956	NA
B	PAIN MANAGEMENT	LAS VEGAS	NEVADA	384	909	162	85,729	NA
C	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	338	868	73	81,223	NA
D	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	166	542	231	58,600	NA
E	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	345	522	212	39,334	NA
F	PHYSICAL MEDICINE REHAB	LAS VEGAS	NEVADA	186	432	136	36,646	NA
G	PAIN MANAGEMENT	LAS VEGAS	NEVADA	181	422	105	40,423	NA
H	PAIN MANAGEMENT	LAS VEGAS	NEVADA	175	398	91	38,437	NA
I	PAIN MANAGEMENT	LAS VEGAS	NEVADA	257	396	106	37,192	NA
J	PAIN MANAGEMENT	HENDERSON	NEVADA	174	375	153	34,412	NA

Top 10 Opioid Prescribers by Claim Count					Q4 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
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
E	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	335	632	189	52,354	NA
H	PAIN MANAGEMENT	LAS VEGAS	NEVADA	239	567	114	56,184	NA
D	ANESTHESIOLOGY & PAIN MGT	RENO	NEVADA	178	565	170	63,634	NA
I	PAIN MANAGEMENT	LAS VEGAS	NEVADA	314	516	83	49,067	NA
C	ANESTHESIOLOGY & PAIN MGT	LAS VEGAS	NEVADA	266	503	105	45,906	NA
F	PHYSICAL MEDICINE REHAB	LAS VEGAS	NEVADA	188	418	160	35,568	NA
K	GENERAL PRACTICE	LAS VEGAS	NEVADA	117	395	82	37,635	NA
L	PAIN MANAGEMENT & ER MEDICINI	LAS VEGAS	NEVADA	255	347	142	32,426	NA

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

Top 25 Members by Claim Count

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Encrypted Member ID	Encrypted Prescriber ID	Claim Count	Sum of Days Supply	Sum of Quantity
M1	AA	51	1,047	1,780
	AB	3	18	122
	AC	3	21	142
	AD	1	30	30
Total		58	1,116	2,074
M2	AE	46	306	1,831
	AF	6	35	210
Total		52	341	2,041
M3	AG	48	296	1,157
	AH	2	14	60
	AI	2	6	20
Total		52	316	1,237
M4	AJ	44	306	1,118
	AK	4	28	119
Total		48	334	1,237
M5	AL	41	811	6,983
	AM	2	38	245
Total		43	849	7,228
M6	D	41	1,180	4,690
	AN	1	3	10
Total		42	1,183	4,700
M7	AO	39	1,170	4,050
Total		39	1,170	4,050
M8	AP	35	705	4,170
	AQ	2	53	206
	AR	1	28	140
Total		38	786	4,516
M9	AS	33	990	4,350
	AT	5	150	690
Total		38	1,140	5,040
M10	D	34	997	4,317
	AU	3	90	390
Total		37	1,087	4,707

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

Top 25 Members by Claim Count

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Encrypted Member ID	Encrypted Prescriber ID	Claim Count	Sum of Days Supply	Sum of Quantity
M11	E	20	408	1,176
	B	15	427	1,274
	AV	2	10	50
Total		37	845	2,500
M12	D	31	930	1,920
	AU	6	180	360
Total		37	1,110	2,280
M13	D	36	1,034	2,733
	AW	1	30	60
Total		37	1,064	2,793
M14	AX	13	390	855
	AY	12	360	720
	AZ	9	270	480
	BA	1	30	135
	BB	1	30	120
Total		36	2,310	1,080
M15	BC	36	1,080	6,480
Total		36	1,080	6,480
M16	D	30	873	2,923
	AU	5	150	420
Total		35	1,023	3,343
M17	BD	14	400	1,704
	BE	11	50	627
	BF	4	11	100
	BG	2	8	60
	BH	1	3	13
	BI	1	7	84
	BJ	1	5	10
Total		34	484	2,598
M18	B	17	505	1,560
	E	17	435	1,290
Total		34	940	2,850
M19	BK	18	375	2,490
	BL	14	310	928
	BM	2	22	72
Total		34	707	3,490
M20	BN	18	480	1,170
	B	11	161	387
	BO	4	56	140
Total		33	697	1,697

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

Top 25 Members by Claim Count
April 1, 2018 - March 31, 2019
Health Plan of Nevada

Encrypted Member ID	Encrypted Prescriber ID	Claim Count	Sum of Days Supply	Sum of Quantity
M21	AR	17	496	951
	BP	8	236	434
	AQ	4	118	249
	BQ	2	60	150
	AH	1	30	15
Total		32	940	1,799
M22	BR	11	127	390
	BS	2	12	62
	BT	2	8	8
	BU	2	6	18
	BV	1	5	30
	BW	1	5	30
	BX	1	3	6
	BY	1	3	12
	BZ	1	5	15
	CA	1	5	30
	CB	1	6	40
	CC	1	4	16
	CD	1	7	42
	CE	1	4	12
	CF	1	7	28
	CG	1	7	40
	CH	1	10	30
	CI	1	3	12
Total		31	227	821
M23	CJ	26	690	2,250
	CK	2	60	180
	CL	2	60	180
	CM	1	30	45
Total		31	840	2,655
M24	D	31	930	4,630
Total		31	930	4,630
M25	CN	23	690	1,410
	CO	7	210	660
Total		30	900	2,070
Grand Total		**508**	**14,097**	**41,086**

Correlation between Top Prescribers and Top Recipients:
Prescriber B - Member M11, M18 & M20
Prescriber D - Member M6, M10, M12, M13, M16 & M24
Prescriber E - Member M11 & M18

Board Requested Reports

Opioid Use Disorder and Opioid Use

OPTUMRx®

Opioid Use Disorder

April 1, 2018 - March 31, 2019

Fee for Service Medicaid

Summary	
Members with a diagnosis of Opioid Use Disorder	10805
Members with diagnosis getting an opioid	4592
Members with diagnosis getting treatment	193

Top 25 Member Utilization of Opioid

Member ID Encrypted	Drug Label Name	Count of Claims	Sum of Qty	Days Supply
00000032537	MORPHABOND TAB 60MG ER	1	60	30
00000032537	MORPHINE SUL TAB 15MG ER	8	480	270
00000032537	MORPHINE SUL TAB 60MG ER	11	660	360
00000032537	OXYCODONE TAB 10MG	8	720	240
00000032537	PRIMLEV TAB 10-300MG	5	450	150
00000032537	**Total**	**33**	**2370**	**1050**
00000048459	SUBOXONE MIS 8-2MG	36	758	379
00000048459	**Total**	**36**	**758**	**379**
00004135313	BUPREN/NALOX MIS 12-3MG	1	14	14
00004135313	BUPREN/NALOX MIS 8-2MG	1	14	14
00004135313	EMBEDA CAP 30-1.2MG	1	30	15
00004135313	OXYCODONE TAB 15MG	2	180	45
00004135313	SUBLOCADE INJ 300/1.5	1	1.5	28
00004135313	SUBOXONE MIS 12-3MG	10	186	186
00004135313	SUBOXONE MIS 8-2MG	17	358	268
00004135313	**Total**	**33**	**783.5**	**570**
02091966667	SUBOXONE MIS 8-2MG	42	570	285
02091966667	**Total**	**42**	**570**	**285**
11113124107	HYDROCO/APAP TAB 10-325MG	13	1560	390
11113124107	MORPHINE SUL TAB 15MG ER	10	600	300
11113124107	MORPHINE SUL TAB 30MG ER	11	660	330
11113124107	**Total**	**34**	**2820**	**1020**
11114210759	METHADONE TAB 10MG	3	298	74
11114210759	METHADONE TAB 5MG	5	600	150
11114210759	OXYCODONE TAB 10MG	5	268	112
11114210759	OXYCODONE TAB 15MG	1	90	30
11114210759	OXYCODONE TAB 5MG	3	180	90
11114210759	SUBOXONE MIS 8-2MG	19	296	148
11114210759	**Total**	**36**	**1732**	**604**
12276655556	BUPRENORPHIN DIS 20MCG/HR	3	12	84
12276655556	BUTRANS DIS 20MCG/HR	5	20	140
12276655556	OXYCOD/APAP TAB 10-325MG	3	390	90
12276655556	PERCOCET TAB 10-325MG	32	1255	266
12276655556	**Total**	**43**	**1677**	**580**
22220385424	SUBOXONE MIS 8-2MG	42	580	297
22220385424	**Total**	**42**	**580**	**297**
26351900103	MORPHINE SUL TAB 15MG ER	12	920	355
26351900103	MORPHINE SUL TAB 30MG ER	12	1080	420
26351900103	OXYCODONE TAB 10MG	12	810	360
26351900103	**Total**	**36**	**2810**	**1135**
33333487769	METHADONE TAB 10MG	1	60	30

33333487769	SUBOXONE MIS 4-1MG	2	60	60
33333487769	SUBOXONE MIS 8-2MG	50	575	286
33333487769	**Total**	**53**	**695**	**376**
33336598709	MORPHINE SUL TAB 30MG ER	25	700	350
33336598709	OXYCOD/APAP TAB 10-325MG	23	1486	321
33336598709	OXYCOD/APAP TAB 7.5-325	2	112	28
33336598709	**Total**	**50**	**2298**	**699**
44444608969	SUBLOCADE INJ 100/0.5	4	2	112
44444608969	SUBLOCADE INJ 300/1.5	3	4.5	84
44444608969	SUBOXONE MIS 12-3MG	2	34	34
44444608969	SUBOXONE MIS 4-1MG	4	59	42
44444608969	SUBOXONE MIS 8-2MG	24	334	173
44444608969	**Total**	**37**	**433.5**	**445**
44447584413	MORPHINE SUL TAB 15MG ER	17	894	298
44447584413	OXYCODONE TAB 15MG	19	1284	328
44447584413	**Total**	**36**	**2178**	**626**
49291822223	MORPHINE SUL TAB 15MG ER	11	660	330
49291822223	MORPHINE SUL TAB 30MG ER	11	660	330
49291822223	OXYCOD/APAP TAB 10-325MG	12	2160	360
49291822223	**Total**	**34**	**3480**	**1020**
49291822322	MORPHINE SUL TAB 15MG ER	12	720	360
49291822322	MORPHINE SUL TAB 30MG ER	12	720	360
49291822322	OXYCODONE TAB 20MG	12	1080	360
49291822322	**Total**	**36**	**2520**	**1080**
53055655556	METHADONE TAB 10MG	12	2160	360
53055655556	OXYCODONE TAB 10MG	5	600	150
53055655556	OXYCODONE TAB 15MG	2	240	60
53055655556	OXYCODONE TAB 20MG	5	600	150
53055655556	TRAMADOL HCL TAB 50MG	12	1440	360
53055655556	**Total**	**36**	**5040**	**1080**
55552607564	MORPHINE SUL TAB 15MG ER	18	555	217
55552607564	NUCYNTA ER TAB 50MG	5	300	150
55552607564	OXYCOD/APAP TAB 10-325MG	23	1876	365
55552607564	**Total**	**46**	**2731**	**732**
55554574244	HYDROMORPHON TAB 4MG	12	1080	420
55554574244	MORPHINE SUL TAB 30MG ER	12	720	390
55554574244	MORPHINE SUL TAB 60MG ER	12	720	360
55554574244	**Total**	**36**	**2520**	**1170**
55555689066	HYDROCO/APAP TAB 10-325MG	46	2716	323
55555689066	**Total**	**46**	**2716**	**323**
66666706306	HYDROMORPHON TAB 8MG	11	88	94
66666706306	MORPHINE SUL TAB 15MG ER	12	720	360
66666706306	OXYCODONE TAB 10MG	12	1440	360
66666706306	**Total**	**35**	**2248**	**814**
77779762011	FENTANYL DIS 12MCG/HR	1	10	30
77779762011	HYDROMORPHON TAB 2MG	13	1379	344
77779762011	MORPHINE SUL TAB 15MG	12	718	344
77779762011	MORPHINE SUL TAB 15MG ER	10	822	284
77779762011	MORPHINE SUL TAB 30MG ER	1	90	30
77779762011	OXYCOD/APAP TAB 10-325MG	1	60	30
77779762011	**Total**	**38**	**3079**	**1062**
77779999712	FENTANYL DIS 75MCG/HR	20	120	359
77779999712	HYDROCO/APAP TAB 10-325MG	15	1342	358

77779999712	**Total**	**35**	**1462**	**717**
88882873004	SUBOXONE MIS 8-2MG	40	552	301
88882873004	**Total**	**40**	**552**	**301**
94228200003	BUPRENORPHIN DIS 20MCG/HR	4	16	112
94228200003	BUTRANS DIS 20MCG/HR	10	40	296
94228200003	HYSINGLA ER TAB 40 MG	8	240	240
94228200003	HYSINGLA ER TAB 60 MG	4	120	120
94228200003	OXYCODONE TAB 20MG	2	44	8
94228200003	OXYCODONE TAB 30MG	12	1830	360
94228200003	**Total**	**40**	**2290**	**1136**
97868944445	HYDROCO/APAP TAB 10-325MG	4	360	120
97868944445	HYSINGLA ER TAB 40 MG	9	270	270
97868944445	OXYCODONE TAB 10MG	13	1680	390
97868944445	TRAMADOL HCL TAB 50MG	13	1170	390
97868944445	**Total**	**39**	**3480**	**1170**
99994944326	BUT/APAP/CAF CAP CODEINE	12	1440	360
99994944326	METHADONE TAB 10MG	12	1228	344
99994944326	OXYCODONE TAB 15MG	13	1496	374
99994944326	**Total**	**37**	**4164**	**1078**

Top 25 Member Claim Detail on MAT

Member ID Encrypted	Drug Label Name	Count of Claims	Sum of Qty	Days Supply
00000002369	BUPREN/NALOX MIS 8-2MG	2	120	60
00000002369	SUBOXONE MIS 8-2MG	42	1184	592
00000002369	**Total**	**44**	**1304**	**652**
00000048459	SUBOXONE MIS 8-2MG	72	1516	758
00000048459	**Total**	**72**	**1516**	**758**
00001144802	SUBOXONE MIS 2-0.5MG	6	60	90
00001144802	SUBOXONE MIS 4-1MG	16	346	270
00001144802	SUBOXONE MIS 8-2MG	28	614	420
00001144802	**Total**	**50**	**1020**	**780**
00004135313	BUPREN/NALOX MIS 12-3MG	2	28	28
00004135313	BUPREN/NALOX MIS 8-2MG	2	28	28
00004135313	SUBLOCADE INJ 300/1.5	1	1.5	28
00004135313	SUBOXONE MIS 12-3MG	20	372	372
00004135313	SUBOXONE MIS 8-2MG	34	716	536
00004135313	**Total**	**59**	**1145.5**	**992**
02091966667	SUBOXONE MIS 8-2MG	84	1140	570
02091966667	**Total**	**84**	**1140**	**570**
11115361995	SUBOXONE MIS 8-2MG	44	1340	670
11115361995	**Total**	**44**	**1340**	**670**
18103400102	SUBLOCADE INJ 100/0.5	2	1	56
18103400102	SUBLOCADE INJ 300/1.5	2	3	56
18103400102	SUBOXONE MIS 8-2MG	52	752	376
18103400102	**Total**	**56**	**756**	**488**
22220385424	SUBOXONE MIS 8-2MG	84	1160	594
22220385424	**Total**	**84**	**1160**	**594**
22222264138	SUBLOCADE INJ 100/0.5	1	0.5	28
22222264138	SUBLOCADE INJ 300/1.5	2	3	56
22222264138	SUBOXONE MIS 12-3MG	4	68	68
22222264138	SUBOXONE MIS 4-1MG	14	420	420
22222264138	SUBOXONE MIS 8-2MG	70	1528	794

22222264138	**Total**		**91**	**2019.5**	**1366**
22224228406	SUBOXONE	MIS 8-2MG	56	1468	734
22224228406	**Total**		**56**	**1468**	**734**
33333487769	SUBOXONE	MIS 4-1MG	4	120	120
33333487769	SUBOXONE	MIS 8-2MG	100	1150	572
33333487769	**Total**		**104**	**1270**	**692**
33333499658	SUBOXONE	MIS 8-2MG	44	1284	698
33333499658	**Total**		**44**	**1284**	**698**
33334340175	SUBOXONE	MIS 8-2MG	56	876	494
33334340175	**Total**		**56**	**876**	**494**
33336596143	SUBLOCADE	INJ 300/1.5	1	1.5	28
33336596143	SUBOXONE	MIS 12-3MG	42	744	740
33336596143	SUBOXONE	MIS 2-0.5MG	20	488	488
33336596143	SUBOXONE	MIS 8-2MG	28	734	734
33336596143	**Total**		**91**	**1967.5**	**1990**
44443493616	BUPREN/NALOX	MIS 12-3MG	4	120	60
44443493616	SUBOXONE	MIS 12-3MG	46	1440	720
44443493616	**Total**		**50**	**1560**	**780**
44444608969	SUBLOCADE	INJ 100/0.5	4	2	112
44444608969	SUBLOCADE	INJ 300/1.5	3	4.5	84
44444608969	SUBOXONE	MIS 12-3MG	4	68	68
44444608969	SUBOXONE	MIS 4-1MG	8	118	84
44444608969	SUBOXONE	MIS 8-2MG	48	668	346
44444608969	**Total**		**67**	**860.5**	**694**
55558583925	BUPREN/NALOX	MIS 8-2MG	4	112	56
55558583925	SUBOXONE	MIS 8-2MG	54	1124	576
55558583925	**Total**		**58**	**1236**	**632**
55559504183	SUBOXONE	MIS 8-2MG	48	1456	728
55559504183	**Total**		**48**	**1456**	**728**
58764033334	SUBOXONE	MIS 8-2MG	58	916	468
58764033334	**Total**		**58**	**916**	**468**
66667678127	SUBOXONE	MIS 8-2MG	48	990	626
66667678127	**Total**		**48**	**990**	**626**
66669855551	SUBOXONE	MIS 8-2MG	44	920	460
66669855551	**Total**		**44**	**920**	**460**
69350344545	SUBLOCADE	INJ 300/1.5	1	1.5	28
69350344545	SUBOXONE	MIS 4-1MG	32	448	406
69350344545	SUBOXONE	MIS 8-2MG	76	944	474
69350344545	**Total**		**109**	**1393.5**	**908**
77779814158	SUBOXONE	MIS 8-2MG	120	1436	718
77779814158	**Total**		**120**	**1436**	**718**
88880062655	BUPREN/NALOX	MIS 8-2MG	2	60	30
88880062655	SUBOXONE	MIS 8-2MG	70	1500	752
88880062655	**Total**		**72**	**1560**	**782**
88882873004	SUBOXONE	MIS 8-2MG	80	1104	602
88882873004	**Total**		**80**	**1104**	**602**
99994060912	SUBOXONE	MIS 8-2MG	46	1376	688
99994060912	**Total**		**46**	**1376**	**688**

Anthem

Members with Opioid Use Disorder Diagnosis Summary

Summary of Utilization

April 1, 2018 – March 31, 2019

Member Totals			
OUD Dx	**OUD Dx + Opioid**	**OUD Dx + Substance Abuse Agent**	**OUD Dx + Opioid + Substance Abuse Agent**
2634	476	522	0

Opioid Claims: Top 25 Members

Drug	Claim Count	Total Quantity	Total Days Supply
METHADONE HCL 10 MG	58	4686	1662
HYDROCODONE-ACETAMINOPHEN 7.5-325 MG	55	1885	404
MORPHINE SULFATE ER 30 MG	54	2918	1549
HYDROMORPHONE HCL 4 MG	45	5337	1302
OXYCODONE HCL 10 MG	44	3983	1261
OXYCODONE-ACETAMINOPHEN 10MG-325MG	40	4088	1098
MORPHABOND ER 30 MG	38	2230	1115
HYDROCODONE-ACETAMINOPHEN 10MG-325MG	35	3504	968
TRAMADOL HCL 50 MG	33	4392	919
OXYCODONE HCL 15 MG	26	2270	725
MORPHINE SULFATE 15 MG	22	1424	637
OXYCODONE HCL 30 MG	22	2254	575
OXYCONTIN 30 MG	21	1014	507
OXYCODONE HCL 20 MG	20	2390	550
MORPHINE SULFATE ER 15 MG	17	1020	510
FENTANYL 75MCG/HR	13	390	390
FENTANYL 100 MCG/HR	13	160	390
OXYMORPHONE HCL ER 10 MG	12	720	360
OXYMORPHONE HCL 10 MG	12	1410	360
OXYMORPHONE HCL ER 30 MG	12	688	344
BUTRANS 20 MCG/HR	8	32	230
NUCYNTA ER 100 MG	7	288	165
OXYCONTIN 20 MG	6	360	180
OXYCODONE HCL ER 40 MG	5	268	134
OXYCONTIN 60 MG	3	172	86
BUPRENORPHINE 20 MCG/HR	3	12	88
OXYCODONE-ACETAMINOPHEN 5 MG-325MG	3	62	15
FENTANYL 25 MCG/HR	2	30	60
ACETAMINOPHEN-CODEINE 300MG-30MG	2	29	12
OXYMORPHONE HCL ER 20 MG	1	60	30
BUPRENORPHINE 10 MCG/HR	1	4	30
HYDROCODONE-ACETAMINOPHEN 5 MG-325MG	1	12	4
METHADONE HCL 5 MG	1	21	7
OXYCODONE HCL 5 MG	1	20	5
Grand Total	**636**	**48133**	**16672**

Substance Abuse Agent Claims: Top 25 Members

Drug	Claim Count	Total Quantity	Total Days Supply
SUBOXONE 8 MG-2 MG SL FILM	250	4,926	3,163
BUPRENORPHIN-NALOXON 8-2 MG SL	155	3,571	1,907
BUPRENORPHINE 8 MG TABLET SL	64	1,663	888
SUBOXONE 4 MG-1 MG SL FILM	51	1,786	672
BUPRENORP-NALOX 8-2 MG SL FILM	19	380	265
BUPRENORPHINE 2 MG TABLET SL	8	82	75
SUBOXONE 2 MG-0.5 MG SL FILM	8	245	84
BUPRENO-NALOX 2-0.5 MG SL FILM	4	129	73
SUBOXONE 12 MG-3 MG SL FILM	4	120	60
BUPRENORP-NALOX 4-1 MG SL FILM	2	70	28
ZUBSOLV 5.7-1.4 MG TABLET SL	1	14	7
Grand Total	**566**	**12,986**	**7,222**

Opioid Use Disorder and Opioid Use

Opioid Use Disorder Summary

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Members With an OUD Diagnosis	Members Receiving an Opioid	Members Receiving Treatment	Members Receiving an Opioid and Treatment
801	167	312	106

Opioid Use Disorder and Opioid Use

Opioids Claims for Top 25 Utilizers

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Rank	Drug	Claim Count	Quantity	Days Supply
1				
	FENTANYL DIS 25MCG/HR	12	10	30
	OXYCODONE TAB 5MG	12	90	30
2				
	OXYCODONE TAB 15MG	12	180	30
	FENTANYL DIS 100MCG/H	11	15	30
3				
	MORPHINE SUL TAB 60MG ER	12	90	30
	HYDROCO/APAP TAB 10-325MG	9	120	30
4				
	HYDROCO/APAP TAB 10-325MG	10	90	30
	MORPHINE SUL TAB 15MG ER	10	60	30
5				
	MORPHINE SUL TAB 30MG ER	10	90	30
	OXYCODONE TAB 10MG	10	120	30
6				
	METHADONE TAB 10MG	11	90	30
	HYDROCO/APAP TAB 10-325MG	8	120	30
7				
	MORPHINE SUL TAB 15MG ER	9	60	30
	OXYCOD/APAP TAB 10-325MG	7	90	30
8				
	OXYCODONE TAB 15MG	7	120	30
	HYSINGLA ER TAB 40 MG	6	30	30
9				
	OXYCOD/APAP TAB 10-325MG	12	90	30
10				
	OXYCODONE TAB 10MG	10	120	30
11			90	30
	METHADONE TAB 10MG	10	90	30
12				
	OXYCOD/APAP TAB 5-325MG	9	90	30
13				
	OXYCODONE TAB 10MG	9	120	30
14				
	HYDROCO/APAP TAB 10-325MG	9	120	30

Opioid Use Disorder and Opioid Use

Opioids Claims for Top 25 Utilizers

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

15				
	MORPHINE SUL TAB 30MG ER	8	60	30
16				
	OXYCODONE TAB 15MG	8	120	30
17				
	OXYCOD/APAP TAB 10-325MG	8	90	30
18				
	OXYCOD/APAP TAB 5-325MG	8	120	30
19				
	OXYCOD/APAP TAB 10-325MG	7	90	30
20				
	OXYCOD/APAP TAB 10-325MG	7	120	30
21				
	OXYCOD/APAP TAB 7.5-325	7	90	30
22				
	HYDROCO/APAP TAB 10-325MG	6	90	30
23				
	OXYCODONE TAB 15MG	6	120	30
24				
	OXYCOD/APAP TAB 7.5-325	6	90	30
25				
	TRAMADOL HCL TAB 50MG	6	180	30

Opioid Use Disorder and Opioid Use

Opioid Use Disorder Drug Claims for Top 25 Utilizers

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Rank	Drug		Claim Count	Quantity	Days Supply
1					
	SUBOXONE	MIS 8-2MG	24	30	15
2					
	SUBOXONE	MIS 8-2MG	23	30	15
3					
	SUBOXONE	MIS 8-2MG	23	30	15
4					
	SUBOXONE	MIS 8-2MG	22	30	15
5					
	SUBOXONE	MIS 8-2MG	20	30	15
6					
	SUBOXONE	MIS 8-2MG	20	30	15
7					
	SUBOXONE	MIS 8-2MG	19	30	15
8					
	BUPRENORPHIN SUB 8MG		19	14	7
9					
	SUBOXONE	MIS 8-2MG	18	7	7
10					
	SUBOXONE	MIS 8-2MG	17	30	15
11					
	SUBOXONE	MIS 8-2MG	15	30	15
12					
	SUBOXONE	MIS 8-2MG	14	22	15
13					
	BUPRENORPHIN SUB 8MG		14	30	15
14					
	SUBOXONE	MIS 8-2MG	13	60	30
15					
	SUBOXONE	MIS 8-2MG	13	60	30
16					
	SUBOXONE	MIS 8-2MG	13	60	30
17					
	SUBOXONE	MIS 8-2MG	13	60	30
18					
	SUBOXONE	MIS 8-2MG	13	30	15

Opioid Use Disorder and Opioid Use

Opioid Use Disorder Drug Claims for Top 25 Utilizers

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

19					
	SUBOXONE	MIS 8-2MG	12	60	30
20					
	SUBOXONE	MIS 8-2MG	12	60	30
21					
	SUBOXONE	MIS 8-2MG	12	60	30
22					
	SUBOXONE	MIS 8-2MG	12	7	7
23					
	SUBOXONE	MIS 8-2MG	12	60	30
24					
	SUBOXONE	MIS 8-2MG	12	30	15
25					
	SUBOXONE	MIS 8-2MG	12	10	30

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

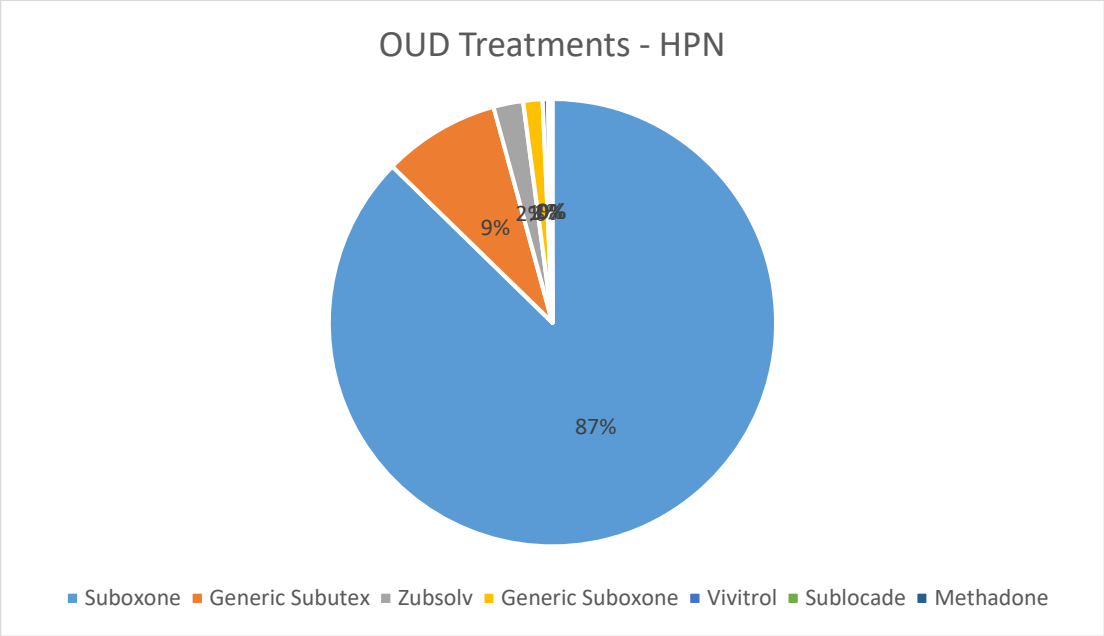
Opioid Use Disorder

Summary

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Summary	Member Count
Member with OUD Diagnosis	583
OUD Members with non-OUD treatment opioids	11
OUD Members with OUD treatment scripts	573
OUD Members with OUD treatments AND opioids	1



HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

Top 25 Members by Claim Count

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Encrypted Member ID	Claim Count	Sum of Days Supply	Sum of Quantity
M1			
BUT/APAP/CAF CAP CODEINE	13	390	420
BUTORPHANOL SOL 10MG/ML	28	357	70
HYDROCO/APAP TAB 5-325MG	1	4	24
OXYCOD/APAP TAB 10-325MG	2	14	112
OXYCOD/APAP TAB 5-325MG	14	351	1,448
Total	58	1,116	2,074
M2			
HYDROCO/APAP TAB 10-325MG	52	341	2,041
Total	52	341	2,041
M3			
HYDROCO/APAP TAB 5-325MG	2	6	20
OXYCOD/APAP TAB 10-325MG	14	101	420
OXYCOD/APAP TAB 7.5-325	36	209	797
Total	52	316	1,237
M4			
HYDROCO/APAP TAB 10-325MG	1	7	42
HYDROCO/APAP TAB 5-325MG	2	14	70
OXYCOD/APAP TAB 10-325MG	2	14	116
OXYCOD/APAP TAB 5-325MG	40	278	869
OXYCOD/APAP TAB 7.5-325	3	21	140
Total	48	334	1,237
M5			
BUT/APAP/CAF CAP CODEINE	4	120	360
HYDROMORPHON TAB 8MG	13	368	2,225
OXYCODONE TAB 5MG	26	361	4,643
Total	43	849	7,228
M6			
ASCOMP/COD CAP 30MG	13	390	1560
HYDROCO/APAP TAB 10-325MG	1	3	10
MORPHINE SUL TAB 30MG ER	13	390	1,140
OXYCOD/APAP TAB 5-325MG	1	30	150
OXYCOD/APAP TAB 7.5-325	12	360	1,800
OXYCODONE TAB 10MG	2	10	40
Total	42	1,183	4,700
M7			
HYDROMORPHON TAB 4MG	13	390	390
MORPHINE SUL TAB 15MG ER	13	390	1,710
OXYCODONE TAB 5MG	13	390	1,950
Total	39	1,170	4,050
M8			
MORPHINE SUL TAB 100MG ER	13	388	776
OXYCOD/APAP TAB 10-325MG	23	345	3,450
OXYCODONE TAB 15MG	2	53	290
Total	38	786	4,516

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

Top 25 Members by Claim Count

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Encrypted Member ID	Claim Count	Sum of Days Supply	Sum of Quantity
M9			
HYDROMORPHON TAB 8MG	13	390	1,560
MORPHINE SUL TAB 60MG ER	12	360	1,680
OXYCOD/APAP TAB 10-325MG	13	390	1,800
Total	38	1,140	5,040
M10			
HYDROMORPHON TAB 2MG	13	367	2,202
HYDROMORPHON TAB 4MG	11	330	630
OXYCOD/APAP TAB 5-325MG	2	60	240
OXYCODONE TAB 15MG	11	330	1,635
Total	37	1,087	4,707
M11			
ENDOCET TAB 10-325MG	1	30	120
HYDROCO/APAP TAB 10-325MG	9	55	110
HYDROMORPHON TAB 2MG	1	5	30
OXYCOD/APAP TAB 10-325MG	13	365	1460
OXYMORPHONE TAB 10MG ER	13	390	780
Total	37	845	2,500
M12			
MORPHINE SUL SOL 100/5ML	11	330	330
MORPHINE SUL TAB 15MG ER	13	390	780
OXYCOD/APAP TAB 10-325MG	13	390	1,170
Total	37	1,110	2,280
M13			
OXYCODONE TAB 15MG	5	150	200
OXYCODONE TAB 30MG	10	277	1304
OXYCODONE TAB HCL 30MG	4	120	315
OXYMORPHONE TAB 20MG ER	5	150	240
OXYMORPHONE TAB 40MG ER	13	367	734
Total	37	1,064	2,793
M14			
BUT/APAP/CAF CAP CODEINE	13	390	510
HYSINGLA ER TAB 40 MG	11	330	330
OXYCOD/APAP TAB 10-325MG	12	360	1,470
Total	36	1,080	2,310
M15			
HYDROCO/APAP TAB 10-325MG	12	360	1,440
METHADONE TAB 10MG	12	360	3600
MORPHINE SUL TAB 60MG ER	12	360	1,440
Total	36	1,080	6,480
M16			
BUTORPHANOL SOL 10MG/ML	3	63	43
HYDROCO/APAP TAB 10-325MG	6	180	960
MORPHINE SUL TAB 100MG ER	13	390	780
OXYCODONE TAB 30MG	13	390	1560
Total	35	1,023	3,343

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

Top 25 Members by Claim Count
April 1, 2018 - March 31, 2019
Health Plan of Nevada

Encrypted Member ID	Claim Count	Sum of Days Supply	Sum of Quantity
M17			
MORPHINE SUL TAB 15MG ER	3	90	240
MORPHINE SUL TAB 30MG ER	3	65	130
OXYCOD/APAP TAB 10-325MG	3	90	540
OXYCODONE TAB 10MG	3	90	360
OXYCODONE TAB 15MG	1	10	84
OXYCODONE TAB 5MG	21	139	1244
Total	34	484	2,598
M18			
BUT/APAP/CAF CAP CODEINE	4	120	240
BUT/ASA/CAF/ CAP COD 30MG	2	60	120
MORPHINE SUL TAB 30MG ER	9	270	540
OXYCOD/APAP TAB 10-325MG	9	240	960
OXYCODONE TAB 15MG	5	130	750
ZOHYDRO ER CAP 30MG	5	120	240
Total	34	940	2,850
M19			
HYDROCO/APAP TAB 10-325MG	19	327	2,310
MORPHINE SUL TAB 100MG ER	6	156	312
MORPHINE SUL TAB 200MG ER	9	224	868
Total	34	707	3,490
M20			
METHADONE TAB 10MG	16	339	986
OXYCOD/APAP TAB 10-325MG	16	328	651
OXYCOD/APAP TAB 7.5-325	1	30	60
Total	33	697	1,697
M21			
FENTANYL DIS 100MCG/H	13	390	285
FENTANYL DIS 25MCG/HR	1	30	15
FENTANYL DIS 50MCG/HR	4	120	60
FENTANYL DIS 75MCG/HR	1	30	15
OXYCODONE TAB 30MG	13	370	1,424
Total	32	940	1,799
M22			
APAP/CODEINE TAB 300-30MG	2	6	18
APAP/CODEINE TAB 300-60MG	1	7	40
HYDROCO/APAP TAB 10-325MG	3	12	24
HYDROCO/APAP TAB 5-325MG	15	109	379
HYDROCO/APAP TAB 7.5-325	1	7	28
HYDROMORPHON TAB 2MG	3	17	102
OXYCOD/APAP TAB 5-325MG	6	69	230
Total	31	227	821

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Opioid Utilization By Member

Top 25 Members by Claim Count
April 1, 2018 - March 31, 2019
Health Plan of Nevada

Encrypted Member ID	Claim Count	Sum of Days Supply	Sum of Quantity
M23			
ASCOMP/COD CAP 30MG	4	60	120
BUT/ASA/CAF/ CAP COD 30MG	3	60	105
HYDROCO/APAP TAB 10-325MG	13	390	1,560
MORPHINE SUL TAB 15MG ER	11	330	870
Total	31	840	2,655
M24			
FENTANYL DIS 50MCG/HR	1	30	10
HYSINGLA ER TAB 80 MG	2	60	60
OXYCODONE TAB 30MG	12	360	3,600
ZOHYDRO ER CAP 20MG	3	90	180
ZOHYDRO ER CAP 30MG	4	120	240
ZOHYDRO ER CAP 40MG	9	270	540
Total	31	930	4,630
M25			
MORPHINE SUL TAB 30MG ER	11	330	420
OXYCODONE TAB 30MG	12	360	1350
OXYCODONE TAB HCL 30MG	1	30	120
TRAMADOL HCL TAB 50MG	6	180	180
Total	30	900	2,070
Grand Total	**955**	**21,189**	**79,146**

Board Requested Reports

Specialty Drug Utilization

OPTUMRx®

Specialty Drug Utilization

April 1, 2018 - March 31, 2019
Fee for Service Medicaid

Top 25 Drugs by Claim Count

Drug Name	Count of Members	Count of Claims	Days Supply	Sum of Qty
LOVENOX	2,113	4,818	21,860	17,128
PARSABIV	94	2,019	2,019	85,819
AVASTIN	587	1,800	2,000	6,283
PROGRAF	261	1,633	50,033	204,920
GENVOYA	160	1,258	28,517	28,518
CELLCEPT	253	1,146	38,216	141,129
TIVICAY	190	993	28,704	29,646
TRUVADA	139	938	18,623	18,628
DESCOVY	159	888	26,730	26,745
SYNAGIS	247	839	23,173	865
HUMIRA	182	797	23,221	1,948
PULMOZYME	109	763	22,162	67,550
BOTOX	335	721	5,997	65,966
CARBOPLATIN	195	702	907	23,588
ARANESP	187	637	831	444
BIKTARVY	143	597	17,910	17,910
PACLITAXEL	127	567	804	17,022
TRIUMEQ	76	532	16,184	16,184
NEULASTA	193	486	741	295
XOLAIR	57	461	9,312	2,102
GAMMAGARD	99	401	1,979	135,170
REVATIO	68	396	11,575	36,243
TOBI	107	391	11,590	102,285
PREZCOBIX	74	390	11,537	11,561
GAMUNEX	71	390	4,272	196,800

Top 25 Drugs by Paid Amount

Drug Name	Count of Members	Count of Claims	Days Supply	Sum of Qty
ADVATE	17	85	1,995	13,681,724
NOVOSEVEN	3	23	630	5,560,002
HELIXATE	3	38	1,085	3,490,951
EPCLUSA	94	223	6,122	6,118
HUMIRA	182	797	23,221	1,948
PARSABIV	94	2,019	2,019	85,819
PULMOZYME	109	763	22,162	67,550
NEULASTA	193	486	741	295
GAMUNEX	71	390	4,272	196,800
GENVOYA	160	1,258	28,517	28,518
HARVONI	46	105	2,695	2,695
SOLIRIS	6	107	107	11,310
SYNAGIS	247	839	23,173	865
MAVYRET	93	182	5,124	15,372
OPDIVO	72	318	530	9,364
TECFIDERA	51	259	7,950	15,900
GENOTROPIN	56	369	10,989	2,468
KEYTRUDA	41	203	303	1,672
EXONDYS 51	4	35	931	2,150
OCREVUS	38	70	659	1,340
ORFADIN	2	20	600	2,880
BIKTARVY	143	597	17,910	17,910
LETAIRIS	26	173	5,319	5,243
RITUXAN	140	358	1,169	17,882
AFINITOR	18	90	2,550	3,004

Anthem

Specialty Drug Utilization

April 1, 2018 – March 31, 2019

Top 25 By Claim Count

Drug	Claim Count	Total Quantity	Total Days Supply
GENVOYA TABLET	1,218	36,427	36,427
TRUVADA 200 MG-300 MG TABLET	975	29,167	29,167
TIVICAY 50 MG TABLET	964	29,572	28,852
DESCOVY 200-25 MG TABLET	866	25,904	25,904
TRIUMEQ 600-50-300 MG TABLET	662	19,860	19,860
BIKTARVY 50-200-25 MG TABLET	602	18,060	18,060
XOLAIR 150 MG VIAL	437	1,260	12,250
HUMIRA PEN 40 MG/0.8 ML	425	942	11,770
MYCOPHENOLATE 500 MG TABLET	364	36,521	11,009
PREZCOBIX 800 MG-150 MG TABLET	296	8,880	8,880
ODEFSEY TABLET	253	7,537	7,537
TACROLIMUS 1 MG CAPSULE	231	35,088	6,827
STRIBILD TABLET	229	6,845	6,845
MAVYRET 100-40 MG TABLET	222	16,044	5,348
SYNAGIS 100 MG/1 ML VIAL	222	258	6,216
BOTOX 200 UNIT VIAL	201	202	17,226
VIVITROL 380 MG VIAL + DILUENT	199	199	5,732
ENOXAPARIN 40 MG/0.4 ML SYR	193	1,596	3,772
TENOFOVIR DISOP FUM 300 MG TB	189	5,490	5,670
ENBREL 50 MG/ML SURECLICK SYR	156	690	4,368
RITONAVIR 100 MG TABLET	155	5,100	4,650
JULUCA 50-25 MG TABLET	152	4,544	4,544
COMPLERA TABLET	149	4,470	4,470
VEMLIDY 25 MG TABLET	142	4,260	4,260
MERCAPTOPURINE 50 MG TABLET	135	6,211	3,659
PREZISTA 800 MG TABLET	133	3,990	3,990
ATRIPLA TABLET	127	3,810	3,810
MYCOPHENOLATE 250 MG CAPSULE	120	18,604	3,517

Top 25 By Paid Amount

Drug	Claim Count	Total Quantity	Total Days Supply
GENVOYA TABLET	1,218	36,427	36,427
MAVYRET 100-40 MG TABLET	222	16,044	5,348
HUMIRA PEN 40 MG/0.8 ML	425	942	11,770
TRIUMEQ 600-50-300 MG TABLET	662	19,860	19,860
BIKTARVY 50-200-25 MG TABLET	602	18,060	18,060
TIVICAY 50 MG TABLET	964	29,572	28,852
TRUVADA 200 MG-300 MG TABLET	975	29,167	29,167
DESCOVY 200-25 MG TABLET	866	25,904	25,904
XOLAIR 150 MG VIAL	437	1,260	12,250
HP ACTHAR GEL 80 UNIT/ML VIAL	19	115	419
ENBREL 50 MG/ML SURECLICK SYR	156	690	4,368
TECFIDERA DR 240 MG CAPSULE	113	6,780	3,390
STRIBILD TABLET	229	6,845	6,845
SYNAGIS 100 MG/1 ML VIAL	222	258	6,216
ODEFSEY TABLET	253	7,537	7,537
IMATINIB MESYLATE 400 MG TAB	69	1,995	1,995
TAKHZYRO 300 MG/2 ML VIAL	11	44	308
PREZCOBIX 800 MG-150 MG TABLET	296	8,880	8,880
AUBAGIO 14 MG TABLET	80	2,240	2,240
REVLIMID 25 MG CAPSULE	36	644	903
COMPLERA TABLET	149	4,470	4,470
ORKAMBI 200 MG-125 MG TABLET	17	1,904	476
JULUCA 50-25 MG TABLET	152	4,544	4,544
EPCLUSA 400 MG-100 MG TABLET	21	448	448
SPRYCEL 100 MG TABLET	31	900	900
ATRIPLA TABLET	127	3,810	3,810
HUMIRA(CF) PEN 40 MG/0.4 ML	56	132	1,568
XYREM 500 MG/ML ORAL SOLUTION	23	11,160	688

Specialty Drug Utilization

Top 25 Specialty Medications by Claim Count

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Medication Name	Count of Claims	Sum of Quantity	Sum of Days Supply
GENVOYA TAB	480	14,335	14,335
TRUVADA TAB 200-300	460	13,763	13,765
TIVICAY TAB 50MG	395	12,128	11,828
DESCOVY TAB 200/25	382	11,460	11,460
TRIUMEQ TAB	206	6,180	6,180
BIKTARVY TAB	178	5,338	5,338
PREZCOBIX TAB 800-150	120	3,600	3,600
MAVYRET TAB 100-40MG	112	9,408	3,136
MYCOPHENOLAT TAB 500MG	103	9,800	3,064
TACROLIMUS CAP 1MG	100	15,180	2,955
BOTOX INJ 200UNIT	83	84	5,476
ODEFSEY TAB	80	2,373	2,373
STRIBILD TAB	67	1,980	1,980
RITONAVIR TAB 100MG	65	2,100	1,935
HUMIRA PEN INJ 40MG/0.8	59	118	1,652
TECFIDERA CAP 240MG	56	3,360	1,680
TACROLIMUS CAP 0.5MG	56	3,210	1,680
COMPLERA TAB	54	1,620	1,620
PREZISTA TAB 800MG	52	1,560	1,560
ATRIPLA TAB	47	1,410	1,410
MYCOPHENOLIC TAB 360MG DR	46	4,208	1,339
SYNAGIS INJ 100MG/ML	45	48	1,260
ATAZANAVIR CAP 300MG	44	1,320	1,320
ENBREL SRCLK INJ 50MG/ML	43	169	1,204
ISENTRESS TAB 400MG	42	2,512	1,256
Total	**3,375**	**127,264**	**103,406**

Specialty Drug Utilization

Top 25 Specialty Medications by Amount Paid

April 1, 2018 - March 31, 2019

SilverSummit Healthplan

Medication Name	Count of Claims	Sum of Quantity	Sum of Days Supply
MAVYRET TAB 100-40MG	112	9,408	3,136
GENVOYA TAB	480	14,335	14,335
TRUVADA TAB 200-300	460	13,763	13,765
TIVICAY TAB 50MG	395	12,128	11,828
DESCOVY TAB 200/25	382	11,460	11,460
TRIUMEQ TAB	206	6,180	6,180
BIKTARVY TAB	178	5,338	5,338
TECFIDERA CAP 240MG	56	3,360	1,680
EPCLUSA TAB 400-100	16	448	448
HUMIRA PEN INJ 40MG/0.8	59	118	1,652
PREZCOBIX TAB 800-150	120	3,600	3,600
ODEFSEY TAB	80	2,373	2,373
ENBREL SRCLK INJ 50MG/ML	43	169	1,204
STRIBILD TAB	67	1,980	1,980
CERDELGA CAP 84MG	8	448	224
LETAIRIS TAB 10MG	19	570	570
GILENYA CAP 0.5MG	22	660	660
HUMIRA PEN INJ 40/0.4ML	26	68	719
ILARIS INJ 150MG/ML	10	10	280
REVLIMID CAP 25MG	14	231	329
COMPLERA TAB	54	1,620	1,620
TASIGNA CAP 150MG	11	1,232	308
NUTROPIN AQ INJ 20MG/2ML	11	110	298
SYNAGIS INJ 100MG/ML	45	48	1,260
PROMACTA TAB 50MG	5	450	150
Total	**2,879**	**90,107**	**85,397**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top 25 Specialty Drugs by Count of Claims

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Product Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
TRUVADA TAB 200-300	691	1,489	44,539	44,539	NA
DESCOVY TAB 200/25	521	1,155	34,578	34,578	NA
HUMIRA PEN INJ 40MG/0.8	469	1,135	31,766	2,428	NA
TRIUMEQ TAB	471	1,102	32,999	32,999	NA
BIKTARVY TAB	302	635	19,019	19,019	NA
MYCOPHENOLAT TAB 500MG	223	494	14,600	55,356	NA
ODEFSEY TAB	177	409	12,270	12,270	NA
MAVYRET TAB 100-40MG	256	408	11,424	34,272	NA
PREZCOBIX TAB 800-150	181	404	12,104	12,104	NA
ENOXAPARIN INJ 40/0.4ML	254	352	6,376	2,678	NA
COMPLERA TAB	119	259	7,711	7,711	NA
ATRIPLA TAB	108	257	7,710	7,710	NA
HUMIRA PEN INJ 40/0.4ML	113	251	7,038	556	NA
ISENTRESS TAB 400MG	107	239	7,043	14,072	NA
RITONAVIR TAB 100MG	110	233	6,921	7,416	NA
MERCAPTOPUR TAB 50MG	83	192	5,380	9,753	NA
ZOMACTON INJ 10MG	65	140	3,742	743	NA
HUMIRA KIT 40MG/0.8	55	132	3,698	276	NA
ATAZANAVIR CAP 300MG	52	121	3,610	3,610	NA
SILDENAFIL TAB 20MG	53	117	3,469	13,204	NA
CAPECITABINE TAB 500MG	52	110	2,442	10,556	NA
JULUCA TAB 50-25MG	52	109	3,270	3,270	NA
DUPIXENT INJ 300/2ML	45	107	2,815	428	NA
MYCOPHENOLAT CAP 250MG	54	107	3,121	17,680	NA
ENOXAPARIN INJ 80/0.8ML	71	102	1,358	1,867	NA
Grand Total	**4,684**	**10,059**	**289,003**	**349,095**	**NA**

HEALTH PLAN OF NEVADA
A UnitedHealthcare Company

Top 25 Specialty Drugs by Paid Amount

April 1, 2018 - March 31, 2019

Health Plan of Nevada

Product Name	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
HUMIRA PEN INJ 40MG/0.8	469	1,135	31,766	2,428	NA
MAVYRET TAB 100-40MG	256	408	11,424	34,272	NA
TRIUMEQ TAB	471	1,102	32,999	32,999	NA
TRUVADA TAB 200-300	691	1,489	44,539	44,539	NA
DESCOVY TAB 200/25	521	1,155	34,578	34,578	NA
BIKTARVY TAB	302	635	19,019	19,019	NA
HUMIRA PEN INJ 40/0.4ML	113	251	7,038	556	NA
ODEFSEY TAB	177	409	12,270	12,270	NA
TASIGNA CAP 150MG	29	79	2,191	7,672	NA
PREZCOBIX TAB 800-150	181	404	12,104	12,104	NA
COMPLERA TAB	119	259	7,711	7,711	NA
ATRIPLA TAB	108	257	7,710	7,710	NA
HUMIRA KIT 40MG/0.8	55	132	3,698	276	NA
ZOMACTON INJ 10MG	65	140	3,742	743	NA
REBIF REBIDO INJ 44/0.5	23	54	1,512	324	NA
ISENTRESS TAB 400MG	107	239	7,043	14,072	NA
NUTROPIN AQ INJ 20MG/2ML	21	55	1,283	270	NA
HUMIRA INJ 40/0.4ML	21	51	1,428	130	NA
DUPIXENT INJ 300/2ML	45	107	2,815	428	NA
HUMIRA PEN INJ CD/UC/HS	20	20	560	120	NA
ILARIS INJ 150MG/ML	7	18	504	18	NA
JULUCA TAB 50-25MG	52	109	3,270	3,270	NA
IBRANCE CAP 100MG	8	24	672	504	NA
IBRANCE CAP 125MG	11	24	672	504	NA
AFINITOR DIS TAB 3MG	4	12	252	504	NA
Grand Total	**3,876**	**8,568**	**250,800**	**237,021**	**NA**

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):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	

Top 10 Drug Classes by Paid Amount - Current Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTIHEMOPHILIC	118	$ 89,747,137.34
METABOLIC MODIFIERS	4,167	$ 27,412,039.13
INSULIN	4,592	$ 22,661,071.09
ANTICONVULSANTS - MISC	27,200	$ 20,781,612.46
ANTIRETROVIRALS	1,854	$ 18,037,331.46
SYMPATHOMIMETICS	22,995	$ 17,643,612.56
BENZISOXAZOLES	5,860	$ 15,504,246.24
ANTINEOPLASTIC	368	$ 15,214,870.30
MS AGENTS	269	$ 14,566,040.37
LOCAL ANESTHETICS - TOPICAL	2,144	$ 14,133,862.13

Top 10 Drug Classes by Paid Amount - Previous Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTIHEMOPHILIC	81	$ 66,415,042.89
INSULIN	4,368	$ 21,136,381.63
METABOLIC MODIFIERS	3,476	$ 20,257,800.36
ANTICONVULSANTS - MISC	26,546	$ 19,036,910.62
ANTINEOPLASTIC	493	$ 18,103,401.19
SYMPATHOMIMETICS	21,765	$ 17,568,693.17
ANTIRETROVIRALS	1,881	$ 17,488,092.00
BENZISOXAZOLES	5,715	$ 13,939,579.99
HEPATITIS AGENTS	156	$ 13,867,923.56
ANTIPSYCHOTICS - MISC	2,628	$ 12,598,081.16

Top 10 Drug Classes by Claim Count - Current Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTICONVULSANTS - MISC	27,200	$ 20,781,612.46
SYMPATHOMIMETICS	22,995	$ 17,643,612.56
NSAIDS	19,727	$ 2,107,066.42
OPIOID COMBINATIONS	17,930	$ 2,283,354.40
SSRIs	16,156	$ 1,500,979.34
OPIOID AGONISTS	15,349	$ 4,634,501.83
GLUCOCORTICOSTEROIDS	14,042	$ 3,043,291.98
CENTRAL MUSCLE RELAXANTS	12,673	$ 1,547,370.16
5-HT3 RECEPTOR ANTAGONISTS	12,318	$ 871,757.67
BENZODIAZEPINES	11,308	$ 775,209.89

Top 10 Drug Classes by Claim Count - Previous Quarter		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
ANTICONVULSANTS - MISC	26,546	$ 19,036,910.62
SYMPATHOMIMETICS	21,765	$ 17,568,693.17
NSAIDS	19,185	$ 1,950,808.59
OPIOID COMBINATIONS	18,048	$ 2,203,652.65
SSRIs	15,833	$ 1,542,462.32
OPIOID AGONISTS	15,440	$ 4,572,347.01
GLUCOCORTICOSTEROIDS	13,077	$ 2,581,710.42
CENTRAL MUSCLE RELAXANTS	12,452	$ 1,591,051.14
5-HT3 RECEPTOR ANTAGONISTS	11,966	$ 1,039,199.21
BENZODIAZEPINES	11,541	$ 891,373.56

Anthem

Top 10 Drug Classes

1Q19 vs 4Q18

Top 10 Drug Classes by Paid Amount - Current Quarter (Jan – Mar 2019)		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
Antiretrovirals	1,765	proprietary
Insulin	4,757	proprietary
Sympathomimetics	20,424	proprietary
Antineoplastic Enzyme Inhibitors	80	proprietary
Anti-TNF-alpha - Monoclonal Antibodies	142	proprietary
Anticonvulsants - Misc.	14,660	proprietary
Multiple Sclerosis Agents	113	proprietary
Hepatitis Agents	114	proprietary
Incretin Mimetic Agents (GLP-1 Receptor Agonists)	921	proprietary
Quinolinone Derivatives	2,010	proprietary

Top 10 Drug Classes by Paid Amount - Previous Quarter (Oct – Dec 2018)		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
Antiretrovirals	1,903	proprietary
Insulin	4,491	proprietary
Sympathomimetics	17,841	proprietary
Hepatitis Agents	138	proprietary
Antineoplastic Enzyme Inhibito	74	proprietary
Anticonvulsants - Misc.	14,402	proprietary
Anti-TNF-alpha - Monoclonal Antibodies	133	proprietary
Multiple Sclerosis Agents	111	proprietary
Incretin Mimetic Agents (GLP-1 Receptor Agonists)	878	proprietary
Quinolinone Derivatives	1,831	proprietary

Top 10 Drug Classes by Claim Count - Current Quarter (Jan – Mar 2019)		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
Nonsteroidal Anti-inflammatory Agents (NSAIDs)	23,494	proprietary
Sympathomimetics	20,424	proprietary
Anticonvulsants - Misc.	14,660	proprietary
HMG CoA Reductase Inhibitors	12,666	proprietary
Selective Serotonin Reuptake Inhibitors (SSRIs)	12,245	proprietary
Aminopenicillins	11,766	proprietary
Antihistamines - Non-Sedating	9,972	proprietary
Central Muscle Relaxants	9,781	proprietary
Opioid Combinations	9,506	proprietary
Glucocorticosteroids	9,356	proprietary

Top 10 Drug Classes by Claim Count - Previous Quarter (Oct – Dec 2018)		
Drug Class Name	**Count of Claims**	**Pharmacy Paid**
Nonsteroidal Anti-inflammatory	21,455	proprietary
Sympathomimetics	17,841	proprietary
Anticonvulsants - Misc.	14,402	proprietary
HMG CoA Reductase Inhibitors	12,540	proprietary
Selective Serotonin Reuptake I	12,163	proprietary
Opioid Combinations	9,950	proprietary
Central Muscle Relaxants	9,563	proprietary
Aminopenicillins	9,393	proprietary
Antihistamines - Non-Sedating	9,361	proprietary
ACE Inhibitors	8,944	proprietary

Nevada Medicaid

Quarterly DUR Report

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan K. Bitton, PharmD, MBA
Report Quarter (Calendar Year):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	6/3/2019

Top 10 Drug Classes by Paid Amount - Q1 2019 - Current Quarter

Drug Class Name	Count of Claims	Pharmacy Paid
ANTIRETROVIRALS	2,429	NA
INSULIN	8,255	NA
ANTI-TNF-ALPHA - MONOCLONAL ANTIBODIES	443	NA
SYMPATHOMIMETICS	29,432	NA
HEPATITIS AGENTS	149	NA
ANTINEOPLASTIC ENZYME INHIBITORS	137	NA
INCRETIN MIMETIC AGENTS (GLP-1 RECEPTOR AGONISTS)	1,638	NA
ANTICONVULSANTS - MISC.	22,900	NA
MULTIPLE SCLEROSIS AGENTS	153	NA
DIAGNOSTIC TESTS	8,918	NA

Top 10 Drug Classes by Paid Amount - Q4 2018 - Previous Quarter

Drug Class Name	Count of Claims	Pharmacy Paid
ANTIRETROVIRALS	2,631	NA
INSULIN	8,886	NA
ANTI-TNF-ALPHA - MONOCLONAL ANTIBODIES	427	NA
SYMPATHOMIMETICS	27,053	NA
ANTINEOPLASTIC ENZYME INHIBITORS	136	NA
HEPATITIS AGENTS	148	NA
MULTIPLE SCLEROSIS AGENTS	182	NA
INCRETIN MIMETIC AGENTS (GLP-1 RECEPTOR AGONISTS)	1,490	NA
ANTICONVULSANTS - MISC.	23,525	NA
DIAGNOSTIC TESTS	9,246	NA

Top 10 Drug Classes by Claim Count - Q1 2019 - Current Quarter

Drug Class Name	Count of Claims	Pharmacy Paid
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)	35,992	NA
SYMPATHOMIMETICS	29,432	NA
ANTICONVULSANTS - MISC.	22,900	NA
HMG COA REDUCTASE INHIBITORS	20,831	NA
OPIOID COMBINATIONS	18,377	NA
SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)	18,352	NA
AMINOPENICILLINS	16,664	NA
ANTIHISTAMINES - NON-SEDATING	15,544	NA
CENTRAL MUSCLE RELAXANTS	14,956	NA
GLUCOCORTICOSTEROIDS	14,861	NA

Top 10 Drug Classes by Claim Count - Q4 2018 - Previous Quarter

Drug Class Name	Count of Claims	Pharmacy Paid
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)	34,798	NA
SYMPATHOMIMETICS	27,053	NA
ANTICONVULSANTS - MISC.	23,525	NA
HMG COA REDUCTASE INHIBITORS	21,231	NA
OPIOID COMBINATIONS	19,271	NA
SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)	18,982	NA
CENTRAL MUSCLE RELAXANTS	15,235	NA
ACE INHIBITORS	14,866	NA
ANTIHISTAMINES - NON-SEDATING	14,105	NA
PROTON PUMP INHIBITORS	13,977	NA

Top 10 Drug Classes by Claim Count

SilverSummit Healthplan

Q1 2019

Class	Drug Class Name	Count of Claims	Pharmacy Paid
6610	Nonsteroidal Anti-inflammatory Agents (NSAIDs)	5,912	SSHP Confidential
7260	Anticonvulsants - Misc.	4,514	SSHP Confidential
4420	Sympathomimetics	4,469	SSHP Confidential
5816	Selective Serotonin Reuptake Inhibitors (SSRIs)	4,081	SSHP Confidential
3940	HMG CoA Reductase Inhibitors	3,762	SSHP Confidential
6599	Opioid Combinations	3,156	SSHP Confidential
7510	Central Muscle Relaxants	2,612	SSHP Confidential
0120	Aminopenicillins	2,567	SSHP Confidential
2210	Glucocorticosteroids	2,320	SSHP Confidential
4927	Proton Pump Inhibitors	2,203	SSHP Confidential

Q4 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
6610	Nonsteroidal Anti-inflammatory Agents (NSAIDs)	5,877	SSHP Confidential
7260	Anticonvulsants - Misc.	4,485	SSHP Confidential
4420	Sympathomimetics	4,108	SSHP Confidential
5816	Selective Serotonin Reuptake Inhibitors (SSRIs)	4,094	SSHP Confidential
3940	HMG CoA Reductase Inhibitors	3,848	SSHP Confidential
6599	Opioid Combinations	3,274	SSHP Confidential
7510	Central Muscle Relaxants	2,752	SSHP Confidential
4927	Proton Pump Inhibitors	2,147	SSHP Confidential
3610	ACE Inhibitors	2,099	SSHP Confidential
0120	Aminopenicillins	2,092	SSHP Confidential

Top 10 Drug Classes by Claim Count

SilverSummit Healthplan

Q3 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
4420	Sympathomimetics	5,877	SSHP Confidential
5816	Selective Serotonin Reuptake Inhibitors (SSRIs)	4,488	SSHP Confidential
4927	Proton Pump Inhibitors	4,108	SSHP Confidential
6599	Opioid Combinations	4,095	SSHP Confidential
6610	Nonsteroidal Anti-inflammatory Agents (NSAIDs)	3,848	SSHP Confidential
3940	HMG CoA Reductase Inhibitors	3273	SSHP Confidential
7510	Central Muscle Relaxants	2752	SSHP Confidential
7260	Anticonvulsants - Misc.	2,147	SSHP Confidential
0120	Aminopenicillins	2,100	SSHP Confidential
3610	ACE Inhibitors	2,092	SSHP Confidential

Q2 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
6610	Nonsteroidal Anti-inflammatory Agents (NSAIDs)	5,890	SSHP Confidential
7260	Anticonvulsants - Misc.	4,495	SSHP Confidential
5816	Selective Serotonin Reuptake Inhibitors (SSRIs)	4,129	SSHP Confidential
3940	HMG CoA Reductase Inhibitors	3,682	SSHP Confidential
6599	Opioid Combinations	3,526	SSHP Confidential
4420	Sympathomimetics	3489	SSHP Confidential
7510	Central Muscle Relaxants	2775	SSHP Confidential
3610	ACE Inhibitors	2,279	SSHP Confidential
4927	Proton Pump Inhibitors	2,146	SSHP Confidential
2725	Biguanides	1,873	SSHP Confidential

Top 10 Drug Classes by Paid Amount

SilverSummit Healthplan

Q1 2019

Class	Drug Class Name	Count of Claims	Pharmacy Paid
1210	ANTIRETROVIRALS**	689	SSHP Confidential
2710	INSULIN**	1,344	SSHP Confidential
1235	HEPATITIS AGENTS**	43	SSHP Confidential
4420	SYMPATHOMIMETICS**	4,469	SSHP Confidential
5940	ANTIPSYCHOTICS - MISC.**	295	SSHP Confidential
6240	MULTIPLE SCLEROSIS AGENTS**	34	SSHP Confidential
6627	ANTI-TNF-ALPHA - MONOCLONAL ANTIBODIES**	35	SSHP Confidential
7260	ANTICONVULSANTS - MISC.**	4,514	SSHP Confidential
5925	QUINOLINONE DERIVATIVES**	556	SSHP Confidential
2717	INCRETIN MIMETIC AGENTS (GLP-1 RECEPTOR AGONISTS)**	237	SSHP Confidential

Q4 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	92	SSHP Confidential
1210	ANTIRETROVIRALS**	2,019	SSHP Confidential
2710	INSULIN**	6,311	SSHP Confidential
4420	SYMPATHOMIMETICS**	25,641	SSHP Confidential
7260	ANTICONVULSANTS - MISC.**	32,833	SSHP Confidential
1235	HEPATITIS AGENTS**	160	SSHP Confidential
2135	ANTINEOPLASTIC - ANTIBODIES**	413	SSHP Confidential
5907	BENZISOXAZOLES**	6,888	SSHP Confidential
5940	ANTIPSYCHOTICS - MISC.**	3,009	SSHP Confidential
3090	METABOLIC MODIFIERS**	2,683	SSHP Confidential

Top 10 Drug Classes by Paid Amount

SilverSummit Healthplan

Q3 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	92	SSHP Confidential
1210	ANTIRETROVIRALS**	2,019	SSHP Confidential
2710	INSULIN**	6,311	SSHP Confidential
4420	SYMPATHOMIMETICS**	25,641	SSHP Confidential
7260	ANTICONVULSANTS - MISC.**	32,833	SSHP Confidential
1235	HEPATITIS AGENTS**	160	SSHP Confidential
2135	ANTINEOPLASTIC - ANTIBODIES**	413	SSHP Confidential
5907	BENZISOXAZOLES**	6,888	SSHP Confidential
5940	ANTIPSYCHOTICS - MISC.**	3,009	SSHP Confidential
3090	METABOLIC MODIFIERS**	2,683	SSHP Confidential

Q2 2018

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	112	SSHP Confidential
1210	ANTIRETROVIRALS**	2,147	SSHP Confidential
4420	SYMPATHOMIMETICS**	27,680	SSHP Confidential
2710	INSULIN**	6,747	SSHP Confidential
7260	ANTICONVULSANTS - MISC.**	33,994	SSHP Confidential
1235	HEPATITIS AGENTS**	179	SSHP Confidential
5907	BENZISOXAZOLES**	7,173	SSHP Confidential
6240	MULTIPLE SCLEROSIS AGENTS**	266	SSHP Confidential
3090	METABOLIC MODIFIERS**	2,609	SSHP Confidential
2135	ANTINEOPLASTIC - ANTIBODIES**	423	SSHP Confidential

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): Q1 2019
Report Period Start Date: 1/1/2019
Report Period End Date: 3/31/2019
Submission Date of Report:

Prospective DUR

What percentage of claims denied at Point of Sale for the following DUR edits?	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)	150,134	42,914	29%	5,666	4%	13,376	9%
Ingredient duplication (ID)	73,868	19,367	26%	5,186	7%	46,851	63%
Late Refill (LR)	25,167	20,116	80%	2,821	11%	-	0%
Total High Dose (HD)	87,750	50,172	57%	5,648	6%	302	0%
Drug-Pregnancy (PG)							
Total Low Dose (LD)							
Drug-Drug (DD)	476,776	134,532	28%	14,096	3%	5,702	1%
Drug-Disease (MC)							
Drug-Allergy (DA)							
Drug-Age (PA)	47	39	83%	7	15%	-	0%

Top 10 Drugs by Therapeutic Problem Type - Overutilization

ER	TD	ID	LR	HD	PG	LD	DD	MC	DA	PA
	MORPHINE SULFATE	AMLODIPINE BESYLATE	GABAPENTIN	CYCLOBENZAPRINE HYDROCHLORIDE			ATORVASTATIN CALCIUM			PROMETHAZINE-DM
	KETOROLAC TROMETHAMINE	GABAPENTIN	PROVENTIL HFA	ONDANSETRON ODT			ALPRAZOLAM			NITROFURANTOIN
	QUETIAPINE FUMARATE	HYDROCODONE/ACETAMINOPHEN	PROVENTIL HFA	SENSIPAR			HYDROCODONE/ACETAMINOPHEN			PROMETHAZINE HCL PLAIN
	RISPERIDONE	SENSIPAR	PROVENTIL HFA	IPRATROPIUM BROMIDE/ALBUTEROL SULFATE			ALPRAZOLAM			PROMETHAZINE /CODEINE
	GABAPENTIN	SODIUM CHLORIDE	PROVENTIL HFA	SENSIPAR			AMLODIPINE BESYLATE			COMPOUND CLAIM
	HYDROCODONE/ACETAMINOPHEN	SENSIPAR	PROVENTIL HFA	IPRATROPIUM BROMIDE/ALBUTEROL SULFATE			TRAZODONE HYDROCHLORIDE			VIRTUSSIN A/C
	LORAZEPAM	PROVENTIL HFA	PROVENTIL HFA	FAMOTIDINE			GABAPENTIN			GUAIATUSSIN AC
	HYDROMORPHONE HCL	PARSABIV	GABAPENTIN	PARSABIV			HYDROCODONE/ACETAMINOPHEN			NITROFURANTOIN
	DEXAMETHASONE SODIUM PHOSPHATE	SENSIPAR	LEVOTHYROXINE SODIUM	ALBUTEROL SULFATE			ALPRAZOLAM			ACETAMINOPHEN/CODEINE
	GABAPENTIN	ONDANSETRON HCL	PROVENTIL HFA	PANTOPRAZOLE SODIUM			CLOPIDOGREL			NITROFURANTOIN MONOHYDRATE /MACROCRYSTALS

Anthem

CDUR Summary

April 1, 2018 – March 31, 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)	46862	46613	99.47%	n/a	n/a	249	0.53%
Therapeutic duplication (TD)	74465	39341	52.83%	n/a	n/a	35124	47.17%
Ingredient duplication (ID)	14341	1716	11.97%	n/a	n/a	12625	88.03%
Late Refill (LR)	23482	3849	16.39%	n/a	n/a	19633	83.61%
Total High Dose (HD)	34193	15092	44.14%	n/a	n/a	19101	55.86%
Drug-Pregnancy (PG)	386	96	24.87%	n/a	n/a	290	75.13%
Total Low Dose (LD)	7420	1799	24.25%	n/a	n/a	5621	75.75%
Drug-Drug (DD)	14341	1716	11.97%	n/a	n/a	12625	88.03%
Drug-Disease (MC)	18741	18621	99.36%	n/a	n/a	120	0.64%
Drug-Allergy (DA)	122	24	19.67%	n/a	n/a	98	80.33%
Drug-Age (PA)	12260	2728	22.25%	n/a	n/a	9532	77.75%

Top 10 Drugs by Therapeutic Problem Type - Overutilization

ER	TD	ID	LR	HD
ATORVASTATIN CALCIUM	ALBUTEROL SULFATE	GABAPENTIN	LISINOPRIL	AMOXICILLIN
LEVOTHYROXINE SODIUM	VENTOLIN HFA	HYDROCODONE-ACETAMINOPHEN	GABAPENTIN	OSELTAMIVIR PHOSPHATE
LISINOPRIL	QUETIAPINE FUMARATE	OXYCODONE-ACETAMINOPHEN	METFORMIN HCL	VENTOLIN HFA
BUSPIRONE HCL	FLUOXETINE HCL	ESCITALOPRAM OXALATE	AMLODIPINE BESYLATE	PREDNISOLONE
AMLODIPINE BESYLATE	SERTRALINE HCL	HYDROXYZINE PAMOATE	LEVOTHYROXINE SODIUM	POLYMYXIN B SUL-TRIMETHOPRIM
METOPROLOL TARTRATE	DULOXETINE HCL	ALPRAZOLAM	RANITIDINE HCL	ONDANSETRON ODT
SERTRALINE HCL	VENLAFAXINE HCL ER	FLUCONAZOLE	PREDNISONE	IBUPROFEN
GABAPENTIN	TRAZODONE HCL	AZITHROMYCIN	METOPROLOL TARTRATE	PREDNISOLONE SODIUM PHOSPHATE
METFORMIN HCL	GABAPENTIN	OXYCODONE HCL	TOPIRAMATE	AMOXICILLIN-CLAVULANATE POTASS
TRAZODONE HCL	LEVOTHYROXINE SODIUM	HYDROXYZINE HCL	METHYLPREDNISOLONE	ALBUTEROL SULFATE

Top 10 Drugs by Therapeutic Problem Type - Overutilization

PG	LD	DD	MC	DA	PA
PRENATAL VITAMINS	JANUVIA	GABAPENTIN	HYDROCODONE-ACETAMINOPHEN	OXYCODONE-ACETAMINOPHEN	TRIAMCINOLONE ACETONIDE
ASPIRIN EC	BUPROPION HCL	HYDROCODONE-ACETAMINOPHEN	IBU	HYDROCODONE-ACETAMINOPHEN	ALBUTEROL SULFATE
CLASSIC PRENATAL	IPRATROPIUM BROMIDE	OXYCODONE-ACETAMINOPHEN	OXYCODONE-ACETAMINOPHEN	AMOXICILLIN-CLAVULANATE POTASS	ONDANSETRON ODT
PRENATAL VITAMIN	MONTELUKAST SODIUM	ESCITALOPRAM OXALATE	IBUPROFEN	MELOXICAM	CHILDREN'S LORATADINE
MEDROXYPROGESTERONE ACETATE	PROPRANOLOL HCL	HYDROXYZINE PAMOATE	MELOXICAM	TRAMADOL HCL	PROMETHAZINE-DM
ALPRAZOLAM	ACYCLOVIR	ALPRAZOLAM	NAPROXEN	CEPHALEXIN	GUAIFENESIN
CLONAZEPAM	HYDROXYZINE HCL	FLUCONAZOLE	OXYCODONE HCL	IBU	HYDROXYZINE HCL
ATORVASTATIN CALCIUM	DULOXETINE HCL	AZITHROMYCIN	TRAMADOL HCL	NITROGLYCERIN PATCH	BUDESONIDE
OB COMPLETE PETITE	ALBUTEROL SULFATE	OXYCODONE HCL	AZITHROMYCIN	MORPHABOND ER	MONTELUKAST SODIUM
DOXYCYCLINE MONOHYDRATE	NARCAN	HYDROXYZINE HCL	BUPROPION HCL SR	BASAGLAR KWIKPEN U-100	VENTOLIN HFA

Nevada Medicaid

Quarterly DUR Report

Health Plan Name: SilverSummit Healthplan
Health Plan Contact: Tom Beranek, RPh

Contact Email: Thomas.L.Beranek@SilverSummitHelathPlan.com
Report Quarter (Calendar Year): Q1 2019
Report Period Start Date: 1/1/2019
Report Period End Date: 3/31/2019
Submission Date of Report: 5/28/2019

Prospective DUR							
What percentage of claims denied at Point of Sale for the following DUR edits?	Total Alerts	Total Alert Overrides	% Alert Overrides	Total Alert Cancels	% Alert Cancels	Total Alerts not adjudicated	% Alerts not adjudicated
Early Refill (ER)	12,248	0	0%	0	0%	12,248	100%
Therapeutic duplication (TD)	15,051	4,635	30.80%	1,296	9%	9,120	61%
Ingredient duplication (ID)	8,927	6	0%	2	0%	7,919	89%
Late Refill (LR)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total High Dose (HD)	2,089	1,414	68%	452	22%	223	11%
Drug-Pregnancy (PG)	160	103	64%	36	23%	21	13%
Total Low Dose (LD)	4,730	3,336	71%	823	17%	571	12%
Drug-Drug (DD)	5,244	3,854	73%	659	13%	731	14%
Drug-Disease (MC)	2,544	1,909	75%	277	11%	358	14%
Drug-Allergy (DA)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Drug-Age (PA)	28	21	75%	7	25%	0	0%

Top 10 Drugs by Therapeutic Problem Type - Overutilization										
ER	TD	ID	LR	HD	PG	LD	DD	MC	DA	PA
Gabapentin	Gabapentin	Gabapentin	N/A	Ibuprofen	Prenatal Vit W/Ferrous Fumarate- Folic Acid	Albuterol Sulfate	Trazodone	Bupropion	N/A	Promethazine-DM
Lisinopril	Lisinopril	Lisinopril	N/A	Cefdinir	Progesterone Micronized	Ondansetron Hcl	Cyclobenzaprine	Amphetamine-Dextroamphetamine	N/A	Guaifenesin-Codeine
Albuterol Sulfate	Quetiapine Fumarate	Atorvastatin	N/A	Ergocalciferol	Misoprostol	Cholecaliferol	Sertraline	Gabapentin	N/A	Nitrofurantoin
Atorvastatin	Atorvastatin	Albuterol Sulfate	N/A	Meloxicam	Norethindrone (Contraceptive)	Sumatriptan Succinate	Quetiapine Fumarate	Alprazolam	N/A	N/A
Metformin	Levothyroxine	Metformin	N/A	Montelukast	Estradiol	Potassium Chloride Microencapsulated Crystals ER	Citalopram Hydrobromide	Lamotrigine	N/A	N/A
N/A	Albuterol Sulfate	Amlodipine	N/A	Oseltamivir Phosphate	Norgestimate-Ethinyl Estradiol	Fluconazole	Atorvastatin	Warfarin Sodium	N/A	N/A
N/A	N/A	Sertraline	N/A	Amoxicillin/Potassium Clav	Norgestimate-Ethinyl Estradiol (Triphasic)	N/A	N/A	N/A	N/A	N/A
N/A	N/A	N/A	N/A	Promethazine-DM	Norethin Acet & Estrad-Fe	N/A	N/A	N/A	N/A	N/A
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Nevada Medicaid

Quarterly DUR Report

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan K. Bitton, PharmD, MBA
Report Quarter (Calendar Year):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	6/3/2019

Prospective DUR

What percentage of claims denied at Point of Sale for the following DUR edits?	Total Alerts	Total Alert Overrides	% Alert Overrides	Total Alert Cancels	% Alert Cancels	Total Alerts not adjudicated	% Alerts not adjudicated
Early Refill (ER)	63,494	N/A	N/A	N/A	N/A	63,494	100.00%
Therapeutic duplication (TD)	75,953	50,351	66.30%	16,710	22.00%	8,892	11.70%
Ingredient duplication (ID)	941	53	5.60%	57	6.10%	831	88.30%
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)	100,435	68,150	67.90%	22,755	22.70%	9,530	9.50%
Drug-Disease (MC)	200,416	167,343	83.50%	33,073	16.50%	N/A	N/A
Drug-Allergy (DA)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Drug-Age (PA)	35,074	26,472	75.50%	8,602	24.50%	N/A	N/A

Top 10 Drugs by Therapeutic Problem Type - Overutilization

ER	TD	ID	LR	HD	PG	LD	DD	MC	DA	PA
SUBOXONE	AMLODIPINE BESYLATE	SUBOXONE	ATORVASTATIN CALCIUM	OMEPRAZOLE	BUSPIRONE HCL	ALBUTEROL SULFATE	ATORVASTATIN CALCIUM	GABAPENTIN	N/A	MONTELUKAST SODIUM
PULMOZYME	LOSARTAN POTASSIUM	PULMOZYME	OMEPRAZOLE	ADDERALL XR	IBU	COMPOUND CLAIM	HYDROCHLOROTHIAZIDE	FLUTICASONE PROPIONATE	N/A	OSELTAMIVIR PHOSPHATE
KALYDECO	ALBUTEROL SULFATE	KALYDECO	METFORMIN HYDROCHLORIDE	DULOXETINE HCL	CITALOPRAM HYDROBROMIDE	FLUCONAZOLE	LISINOPRIL	PREDNISONE	N/A	IBUPROFEN
MORPHINE SULFATE ER	LISINOPRIL	MORPHINE SULFATE ER	LEVOTHYROXINE SODIUM	PANTOPRAZOLE SODIUM	OSELTAMIVIR PHOSPHATE	VITAMIN D3	TRAZODONE HYDROCHLORIDE	ALPRAZOLAM	N/A	CETIRIZINE HCL
DEXCOM G6 SENSOR	VENTOLIN HFA	DEXCOM G6 SENSOR	LISINOPRIL	OMEPRAZOLE DR	NARCAN	NORETHINDRONE ACETATE/ETHINYL ESTRADIOL	FOLIC ACID	HYDROCODONE/ACETAMINOPHEN	N/A	CLINDAMYCIN PHOSPHATE
LANTUS SOLOSTAR	HYDROCHLOROTHIAZIDE	LANTUS SOLOSTAR	AMLODIPINE BESYLATE	SUBOXONE	OXYCODONE HCL	XULANE	BUSPIRONE HCL	ATORVASTATIN CALCIUM	N/A	LORATADINE CHILDRENS
DEXCOM G6 TRANSMITTER	METOPROLOL TARTRATE	DEXCOM G6 TRANSMITTER	GABAPENTIN	AMPHETAMINE/DEXTROAMPHETAMINE	ZIPRASIDONE HCL	NYSTATIN	GABAPENTIN	ZOLPIDEM TARTRATE	N/A	AZITHROMYCIN
VITAMIN A	GABAPENTIN	VITAMIN A	MONTELUKAST SODIUM	ARIPIPRAZOLE	ALPRAZOLAM	PHENAZOPYRIDINE HCL	QUETIAPINE FUMARATE	IBUPROFEN	N/A	ONDANSETRON ODT
VITAMIN D3	CARVEDILOL	VITAMIN D3	PANTOPRAZOLE SODIUM	METHYLPHENIDATE HYDROCHLORIDE ER	ONDANSETRON ODT	ONDANSETRON ODT	FENOFIBRATE	PREDNISOLONE	N/A	POLYMYXIN B SULFATE/TRIMETHOPRIM SULFATE
ALPRAZOLAM	BASAGLAR KWIKPEN	ALPRAZOLAM	SERTRALINE HCL	TEMAZEPAM	METRONIDAZOLE	MONTELUKAST SODIUM	AMLODIPINE BESYLATE	VENTOLIN HFA	N/A	PROMETHAZINE-DM

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): Q1 2019
Report Period Start Date: 1/1/2019
Report Period End Date: 3/31/2019
Submission Date of Report:

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.)**
Antianxiety/hypnotic combo	Physician Letter	Mailing	48	Pending	Pending	Physician	OptumRx
High dose zolpidem	Physician Letter	Mailing	65	Pending	Pending	Physician	OptumRx
Suboxone and opioid use	Physician Letter	Mailing	0	N/A		Physician	OptumRx
Top 10 Opioid Prescribers	Physician Letter	Mailing	10	0	0%	Physician	OptumRx
Topical Doxepine	Physician Letter	Mailing	0	N/A	N/A	Physician	OptumRx

Anthem

Retro-DUR

Jan – March 2019

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.)**
Medication Adherence	Identifies members non-adherent to medications. Includes diabetes, HTN, cholesterol, and sickle cell	Mail/Fax	8034 (total member and provider)	N/A	N/A	Member and Provider	Internal

Nevada Medicaid

Quarterly DUR Report

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan K. Bitton, PharmD, MBA
Report Quarter (Calendar Year):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	6/3/2019

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 (9)	6	66.67%	Prescriber	OptumRx
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	3 (TBD)	TBD	TBD	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 (81)	21	25.93%	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	31 (TBD)	TBD	TBD	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 (969)	137	14.14%	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	188 (TBD)	TBD	TBD	Prescriber	OptumRx

Nevada Medicaid

Quarterly DUR Report

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan K. Bitton, PharmD, MBA
Report Quarter (Calendar Year):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	6/3/2019

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.)
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 (6552)	1740	26.56%	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	1281 (TBD)	TBD	TBD	Prescriber	OptumRx
Duplicate Therapy	This is a provider-targeted program designed to promote awareness of Therapeutic duplication concerns.	Fax/Mail	5169 (3954)	614	15.53%	Prescriber	OptumRx
Duplicate Therapy	This is a provider-targeted program designed to promote awareness of Therapeutic duplication concerns.	Fax/Mail	812 (TBD)	TBD	TBD	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 (6396)	560	8.75%	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	2761 (TBD)	TBD	TBD	Prescriber	OptumRx

Nevada Medicaid

Quarterly DUR Report

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan K. Bitton, PharmD, MBA
Report Quarter (Calendar Year):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	6/3/2019

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.)
Gaps in Care Cardiovascular	Cardiovascular Program (Atrial fibrillation):To optimize the management of atrial fibrillation (Afib) by identifying and closing the gap in medication therapy for members with Afib not on an anti-thrombin agent. Cardiovascular Program (CHD_IVD No Statin): To optimize the management of Coronary Heart Disease (CHD) and Ischemic Vascular Disease (IVD) by identifying and closing the gap in medication therapy for patients not on a statin. Cardiovascular Program (CHD_IVD Inappropriate Statin Dose): To optimize the management of Coronary Heart Disease (CHD) and Ischemic Vascular Disease (IVD) by identifying and closing the gap in medication therapy for patients not on an appropriate dose of statin. Cardiovascular Program (CHF)_Beta Blocker: To optimize the management of Congestive Heart Failure (CHF) by identifying and closing the gap in medication therapy for members with CHF not on a beta blocker or appropriate beta blocker. Cardiovascular Program (CHF)_RAAS Inhibitor: To optimize the management of Congestive Heart Failure (CHF) by identifying and closing the gap in medication therapy for members with CHF and not on an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) or angiotensin receptor-neprilysin inhibitor	Fax/Mail	403 (TBD)	TBD		Prescriber	OptumRx

Nevada Medicaid

Quarterly DUR Report

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan K. Bitton, PharmD, MBA
Report Quarter (Calendar Year):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	6/3/2019

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.)
Gaps in Care COPD	To optimize the use of long-term controller medications (LTCMs) as recommended, promote the appropriate use of short- acting beta-agonists (SABAs) in Chronic Obstructive Pulmonary Disease (COPD)	Fax/Mail	48 (TBD)	TBD		Prescriber	OptumRx
Gaps in Care Diabetes	Diabetes not on a Statin Program: To optimize the management of diabetes by identifying and closing the gap for members with diabetes not on a statin. Diabetes and Hypertension Program: To optimize the management of diabetes by identifying and closing the gap for members with diabetes and hypertension not on certain anti-hypertensive agent.	Fax/Mail	3628 (TBD)	TBD		Prescriber	OptumRx
Gaps in Care HIV	To optimize the management of by identifying and closing the gap in medication therapy for members with HIV receiving protease inhibitor but not on ritonavir.	Fax/Mail	5 (TBD)	TBD		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 (2343)	185	0.079	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	484 (TBD)	TBD	TBD	Prescriber	OptumRx

Nevada Medicaid

Quarterly DUR Report

Health Plan Name:	Health Plan of Nevada
Health Plan Contact:	Ryan K. Bitton, PharmD, MBA
Contact Email:	Ryan K. Bitton, PharmD, MBA
Report Quarter (Calendar Year):	Q1 2019
Report Period Start Date:	1/1/2019
Report Period End Date:	3/31/2019
Submission Date of Report:	6/3/2019

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.)
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	9296 (2726)	491	18.01%	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	6406 (TBD)	TBD	TBD	Prescriber	OptumRx

Nevada Medicaid

Quarterly DUR Report

Health Plan Name: SilverSummit Healthplan
Health Plan Contact: Tom Beranek, RPh

Contact Email: Thomas.L.Beranek@SilverSummitHelathPlan.com
Report Quarter (Calendar Year): Q1 2019
Report Period Start Date: 1/1/2019
Report Period End Date: 3/31/2019
Submission Date of Report: 5/28/2019

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.)
Mar - 2019, Hypertension	Outreach to members who are non-adherent on filling hypertension medications.	Mail	31	28	89%	Member	SSHP
Feb - 2019, Hypertension	Outreach to members who are non-adherent on filling hypertension medications.	Mail	12	11	90%	Member	SSHP
Jan - 2019, Hypertension	Outreach to members who are non-adherent on filling hypertension medications.	Mail	64	56	88%	Member	SSHP
Dec - 2018, Trifecta/Multiple Opioid Prescribers	Provider outreach for members who are obtaining an opioid, benzo and muscle relaxer combination	Mail	51	0	0%	Physician	SSHP
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	SSHP
Oct - 2018, Trifecta/Multiple Opioid Prescribers	Provider outreach for members who are obtaining an opioid, benzo and muscle relaxer combination	Mail	51	6	12%	Physician	SSHP