BRIAN SANDOVAL
Governor

RICHARD WHITLEY, MS
Director

MARTA JENSEN
Administrator

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

NOTICE OF PUBLIC MEETING – DRUG USE REVIEW BOARD

AGENDA

Date of Posting:	**August 7, 2017**
Date of Meeting:	**Thursday, August 24, 2017 at 5:15 PM**
Name of Organization:	**The State of Nevada, Department of Health and Human Services (DHHS), Division of Health Care Financing and Policy (DHCFP), Drug Use Review (DUR) Board.**
Place of Meeting:	**Holiday Inn Reno-Sparks** **55 East Nugget Avenue** **Sparks, NV 89431** **Phone: (775) 358-6900**

Webinar Registration
https://optum.webex.com/optum/onstage/g.php?MTID=e92eac323ab7a8132fbda47f4157cee56

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: **311 118 149**

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. No phone number is required.

A password should not be necessary, but if asked use: dvMYb222

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 27, 2017.

b. **For Possible Action:** Review and Approve Meeting Minutes from July 13, 2017.

c. 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 eteplirsen (Exondys 51®).

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

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

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

c. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria for COX-2 Inhibitors.

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

d. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for Antiemetics – Delta-9-Tetrahydrocnnabinol (THC) Derivatives.

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

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

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

f. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria and/or quantity limits for codeine and tramadol use in children.

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

5. Public Comment on any DUR Board Requested Report

6. DUR Board Requested Reports

a. Psychotropic medications used for children and adolescents.

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

b. Opioid Utilization – Top prescriber and member.

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

c. Gastroenterology studies in recipients with extended use of proton pump inhibitors.

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

d. Impact of 90-day maintenance medication requirement.

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

7. Public Comment on any Standard DUR Report

8. Standard DUR Reports

a. Review of Prescribing/Program Trends.

i. Top 10 Therapeutic Classes for Q4 2016, Q1 2017 and Q2 2017 (by Payment and by Claims).
ii. Top 50 Drugs of Q4 2016, Q1 2017 and Q2 2017 (by Payment and by Claims).

b. Concurrent Drug Utilization Review (ProDUR).

i. Review of Q4 2016, Q1 2017 and Q2 2017.
ii. Review of Top Encounters by Problem Type.

c. Retrospective Drug Utilization Review (RetroDUR).

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

9. Closing Discussion

a. Public comments on any subject.

b. Date and location of the next meeting.

i. Discussion of the time of the next meeting.

10. 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.

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

Notice of this meeting and draft copies of the changes will be available on or after the date of this notice at the DHCFP website http://dhcfp.nv.gov, the DHCFP Carson City Central office and the DHCFP Las Vegas office. The agenda posting of this meeting can be viewed at the following locations: Nevada State Library; Carson City Library; Churchill County Library; Las Vegas Library; Douglas County Library; Elko County Library; Lincoln County Library; Lyon County Library; Mineral County Library; Tonopah Public Library; Pershing County Library; Goldfield Public Library; Eureka Branch Library; Humboldt County Library; Lander County Library; Storey County Library; Washoe County Library; and White Pine County Library and may be reviewed during normal business hours.

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

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

Note: We are pleased to make accommodations for members of the public who have disabilities and wish to attend the meeting. If special arrangements are necessary, notify the Division of Health Care Financing and Policy as soon as possible and at least ten days in advance of the meeting, by e-mail at cmclach@dhcfp.nv.gov in writing, at 1100 East William Street, Suite 101, Carson City, Nevada 89701 or call Colleen McLachlan at (775) 684-3722.

STATE OF NEVADA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
DIVISION OF HEALTH CARE FINANCING AND POLICY
1100 E. William Street, Suite 101
Carson City, Nevada 89701
(775) 684-3676 • Fax (775) 687-3893

BRIAN SANDOVAL
Governor

RICHARD WHITLEY, MS
Director

MARTA JENSEN
Administrator

MEDICAID
DRUG USE REVIEW BOARD
DRAFT MEETING MINUTES

Date of Meeting: **Thursday, April 27, 2017 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: **Best Western Plus Airport Plaza Hotel**
1981 Terminal Way
Reno, NV 89502
Phone: (775) 348-6370

Committee Members Present: James Marx, MD; Paul Oesterman, Pharm.D; David England, Pharm.D; Jeffrey Zollinger, DO

Committee Members Absent: Michael Owens, MD; Chris Shea, Pharm.D.

Others Present:

DHCFP: Shannon Sprout, Deputy Administrator; Mary Griffith, RN, Pharmacy Services Specialist; Darrell Faircloth, Deputy Attorney General, Duane Young, Chief Program Services

HPES: Beth Slamowitz, Pharm.D.

OptumRx: Carl Jeffery, Pharm.D.

Others: Lisa Wilson, Biogen; Lynda Finch, Biogen; Melissa Walsh, Novartis; Ann Nelson, Vertex; Jennifer Lauper, BMS; Coleen Lawrence, Moxy Health; Tom Beranek, Silver Summit; Cheryl Donahue, Sarepta, Lisa Borland, Sarepta; Mae Kwong, Janssen; Charissa Anne, J&J; Rob Bigham, Shire; Brad Martin, Avexis; Bill White, Avexis; Robert Gustafson; Jonathan McKinnon, MD; Chris Stanfield; Deborah Profant; Helen Lee; Kyle Walker

1. Call to Order and Roll Call

Meeting called to order at 5:42 PM
Paul Oesterman, Chair: I will call the meeting to order of the drug utilization review board. As a reminder for the audience, if you choose to speak, please limit remarks to 5 minutes. We will give plenty of opportunity for public comment. We will start with roll call.

Mary Griffith
Shannon Sprout
Duane Young
Beth Slamowitz
Darrell Faircloth
Paul Oesterman, Chair
Jeff Zollinger
Dave England
James Marx
Carl Jeffery

2. Public Comment on Any Matter on the Agenda

Paul Oesterman, Chair: We have a quorum. Is there any public comment on any matter on the agenda? We will also ask for public comment before each agenda item.

3. Administrative

a. **For Possible Action:** Review and approve meeting minutes from January 26, 2017.

Paul Oesterman, Chair: We have the meeting minutes from the last meeting of January 26, 2017. Do the committee members have any comments or corrections?
James Marx: I move to approve as submitted.
Dave England: Second
Paul Oesterman, Chair: Any further comments? All those in favor of approve, say Aye.
Voting: Ayes across the board, the minutes are approved.

b. Status Update by DHCFP

Paul Oesterman, Chair: Our next item is the status update from the DHCFP.
Mary Griffith: I have a few updates on Chapter 1200. As of today we implemented new criteria the board approved in previous meetings on Lupron, irritable bowel syndrome agents, anti-asthmatic monoclonal antibody agents and Hep C agents. We deleted the criteria for Cymbalta. The seven day opioid fill limit will be implemented on May 15. This was just delayed today to allow providers more time to prepare. We are hoping to get the new criteria for Suboxone, hospice drug coverage for children, incretin mimetics, and Orkambi on the agenda for the July public hearing.

4. Board Actions

a. **For Possible Action:** Discussion and approval of Annual Drug Use Review Report.

Paul Oesterman, Chair: For our Board actions, we have to approve the Annual Drug Use Review Report. This report is pretty much consistent with what we have seen in the past standard report. Anything you wish to add?

Carl Jeffery: This is a pretty standard report with similar data as the previous data. The data and reports are about the same. CMS is trying to put more in on the fraud and abuse questions. The numbers have changed a little and those are in the back.

Paul Oesterman, Chair: Just to back up a minute, is there any public comment on this report? Does the board have any discussion?

It looks similar to what we have seen in the past. The implementation of the morphine equivalent dose, it says it will be implemented in 2017?

Carl Jeffery: Yes, because this is fiscal year 2016, so it should be included in next year's report.

Paul Oesterman, Chair: Page 26 of the report, it looks like it is a table, some of the claims reviewed by the Board.

Carl Jeffery: If you look at the very last page, that chart is listed there.

Paul Oesterman, Chair: We need a motion and a second to approve the report. We are seeing it before it needs to be submitted this year.

Dave England: I move to approve.

Paul Oesterman, Chair: We have a motion to approve the 2016 Annual DUR report and submit to CMS.

James Marx: Second.

Voting: Ayes across the board, the motion carries.

5. Clinical Presentations

Paul Oesterman, Chair: We will move to our clinical presentations. We have someone online who wishes to speak to us. Which of our clinical presentations does he wish to address?

Carl Jeffery: I think he wanted to talk about both Spinraza and Exondys 51.

Jonathan McKinnon: Hi my name is Jonathan McKinnon, I am a neurologist. We work with the muscular dystrophy kids in Las Vegas. I don't know if there are specific questions that the Board has for me. I have more experience than any other neurologist with these two drugs. I am the only neurologist that sees the muscular dystrophy kids in Las Vegas. Do you want a question and answer session? Or do you just want me to give you some information and recommendations?

Paul Oesterman, Chair: Go ahead and give us what you know and any recommendations.

Carl Jeffery: Dr. McKinnon, have you had a chance to review the proposed criteria that was in the binder?

Jonathan McKinnon: I do know there was consideration to limitation for each of the drugs, but I don't have them.

Carl Jeffery: Maybe it will help to read those to you real quick and then you can speak to the proposed criteria. For Exondys, we proposed a diagnosis of DMD, number two is documentation of the confirmed mutation of the dystopin gene amenable to the exon 51 skipping, number three is prescribed by or in consultation with a neurologist with experience treating children, and four, the dose will not exceed 30 mg per kg of body weight, once weekly.

Jonathan McKinnon: I don't hear any age limitation?

Carl Jeffery: There is no age restriction and I know some of the other plans have an ambulatory requirement, we have removed that.

Jonathan McKinnon: I would agree with that recommendation. I have five patients right now who are currently getting infusions with Exondys 51 and so far there is always access related issues that come sometime create challenges. But generally speaking, we don't have any applications from this drug. We are hoping as we get more experience with this drug, I have roughly 38 patients with Duchenne's and several of them are exon 51 amenable. I am hoping as we get more experience we can demonstrate it is efficacious for this population. I don't know if you want to hear any more. It sounds like there are not any discrepancies in criteria from the Board on the exon 51 for the Exondys 51. Should we discuss Spinraza?

Paul Oesterman, Chair: Yes, let's go ahead and cover both of them.

Carl Jeffery: For Spinraza, the criteria is a diagnosis of Spinal Muscular Atrophy and prescribed by or in consultation with a neurologist who has experience treating SMA.

Jonathan McKinnon: That sounds terrific. I am happy to hear that is the recommendation of the Board. I have four patients. This is a challenging drug to administer because it requires doing a spinal tap and then administering the drug intrathecally. As you might imagine in the pediatric population, it is challenging. So far, the data Spinraza looks very promising. I have four patients right now I am currently treating and I have 23 patients with spinal muscular atrophy. This drug has a promising efficacy. If there are no limitations on age or functional status or ambulatory status, I would recommend to the Board to keep those criteria.

Paul Oesterman, Chair: Thank you, I appreciate your input. Is there any public comment from the audience?

Lisa Borland: My name is Lisa Borland, I am with Medical Affairs at Serepta therapeutics. I will give a general background about the drug itself and a few comments about the disease. Eteplirsen was approved in September of last year. It is indicated for a subset of patients with Duchenne muscular dystrophy that is amenable to exon 51 skipping. And that indication was granted under the accelerated approval pathway and based on an increase in dystrophin production that was observed in some patients that were treated with eteplirsen under the accelerated pathway. The continual approval depends on verification of the clinical benefit from the trials. There were three studies that supported the approval, one, two and three in the prescribing information. I won't go through all the details, but I will refer the committee to the package insert on dystrophin and the safety profile. I am here for questions.

Paul Oesterman, Chair: Thank you. We are looking at the proposed prior authorization criteria for Exondys 51. Anybody on the Board have any questions or comments regarding the Exondys product? One of the comments was made about ambulatory status regarding this process. I notice on the continuation of the reauthorization there is a requirement the patient is maintaining an ambulatory status.

Carl Jeffery: I left that in there with the intent that they are maintaining their status rather than declining. Maybe we can clarify to capture that intent.

Mary Griffith: Are we talking about Exondys 51? I have a question about the testing. Typically Medicaid does not pay for genetic testing. Is there another way to get to the diagnosis without the genetic testing?

Carl Jeffery: From what I have read, this is the only way to get a definitive diagnosis of Duchenne and make sure it has the 51 skipping part, you need the genetic test.

Lisa Borland: We have programs that will pay for the testing if it is not available.

Dave England: Your program covers all members regardless of insurance?

Lisa Borland: If they don't have insurance and we go by financial need. The physicians would have details about that.

Paul Oesterman, Chair: I wonder if we should include that component in the criteria, the patient would have provided by the manufacturer.

Mary Griffith: We might have to look at that more closely. It doesn't make sense to have that as part of the criteria if we are not going to cover it.

Paul Oesterman, Chair: But if we refer people to where it can be done.

Mary Griffith: Is that the same issue for the Spinraza?

Carl Jeffery: Spinraza has gene testing too.

Lisa Borland: You heard the key opinion leader from Nevada speak. He is familiar with this process.

Paul Oesterman, Chair: Based on past history, we will approve something and others will start, if they don't have that information, it could get us into a problem. My thought would be to tentatively approve what we have here and then come back and look at the reauthorization criteria.

Shannon Sprout: Right, for those that have a diagnosis, I would not want to make this more difficult to get.

Dave England: What we also mentioned on 1.2.3, the patient has maintained ambulatory status, and do we want to change the language to state the patient has not had any decrease in status as long as they maintain at the baseline? Do they have ways to measure their status? Can we add a numeric value to this? Or do we leave it subjective?

Carl Jeffery: They don't need to be ambulatory to get this. If they are at the point where they are not ambulating, they can still get and benefit from this medication. As long as they continue to improve.

Dave England: In 1.2.5, dose will not exceed 30mg/kg. Is there any place in this discussion where there would be a need to exceed that and what would be the criteria?

Lisa Borland: Part of the reason for that, two doses where studied, the 30 and 50mg/kg. Looking at dystrophin levels, there was no difference between the 30 and 50mg/kg. It is not recommended and there would not be any reason to exceed that. For the question about ambulatory status, the studies were done in patients that were ambulatory. Maybe it makes sense to look at other functional status like lung function.

Dave England: In 1.2.2, patients that have experienced a benefit, how do we measure that? What would be the criteria for improvement?

Lisa Borland: Right, which is where it would be good to have a neurologist's input on what is measured. The six minute walk test is what was used in the studies. There are different methods for upper limb function, some do a forced air time, and some do a 10 meter walk/run.

Dave England: That is why I was asking the question. We may not need to do it now, if it comes down later there is improvement what is the status or measure of improvement to show the medication should continue. We are slowing the progression of the disease rather than a cure.

Mary Griffith: Where is says they are maintaining the ambulatory status, if they are not ambulatory, they are not a candidate?

Carl Jeffery: The studies were done in ambulatory patients and one measure was the six minute walk test, but it is approved for everyone. It has shown benefit for those not ambulatory. Some of the commercial plans have ambulatory requirements. The goal of this medication is to start it early, even before a child is walking.

Mary Griffith: How would someone continue to get this medication?

Carl Jeffery: That's what we are talking about, my intent was to put some language in there to maintain status.

Dave England: It ties into the criteria above where they are benefiting from therapy. I get the impression that we may have to go back and modify the criteria as more information becomes available.

Paul Oesterman, Chair: Our initial authorization is six months, so we have a little time to look at the reauthorization criteria.

Carl Jeffery: We have four members right now as of March, it has been steadily increasing.

Paul Oesterman, Chair: Is this a life-long medication?

Lisa Borland: Yes.

Paul Oesterman, Chair: At this point, I don't see any concerns regarding the initial authorization criteria. There are some questions regarding the reauthorization and defining documentation to show how the patient is benefiting or slowing progression. That is something that is difficult to measure. My thought would be to approve the initial authorization so that we have that and then tweak the reauthorization and bring it back

next time to add language to try to quantify some measures if possible. We need to have a motion to approve what we have here or modify what we have.

Dave England: I move to accept the initial authorization and preliminarily accept the reauthorization until we can bring that back.

Darrell Faircloth: To clarify, are we talking about two drugs together or just one?
Paul Oesterman, Chair: Just the first one right now. We have a motion to approve the criteria as presented with the ability to review it again in the near future with looking at the reauthorization criteria.

Jeff Zollinger: Second.

Voting: Ayes across the board, the motion carries.

Paul Oesterman, Chair: The second drug in the category is Spinraza. Do we have any public comment for Spinraza?

Lynda Finch: My name is Lynda Finch, I am the medical science liaison for Biogen, the manufacturer for Spinraza. You have an excellent review in front of you, I'm not going to repeat what's in there. There is some new data presented last week at the AAN meeting. Prior to that meeting, we did not have much data for the second study, CHERISH for the childhood onset, we had more data for the infantile onset. The study called CHERISH is from age 2 to 12. Spinraza demonstrated improvements in motor function vs. the sham drug on the Hammersmith motor function scale from baseline to month 15. There was an improvement of 3.9 vs a 1 point decrease in the placebo control. A 3-point improvement is considered clinically improved in this disease. Overall, Spinraza demonstrated a favorable safety profile. The majority of events appear to be due to the SMA disease itself or the lumbar function. The infantile study, ENDEER, patients presented at age less than 6 months. There were 82 patients in the study, Sprinraza group demonstrated a 40% response vs a 0% in the placebo group. This is in babies without motor control, achieving milestones with this medication. I would like to request coverage. Your criteria is broad and inclusive. This is the first and only approved treatment for this disease. We have a broad indication that is not restricted to age.

Dave England: This is recommended for all four types?

Lynda Finch: Yes, this is approved for all types and ages.

Carl Jeffery: It has not been studied in type 4 correct?

Lynda Finch: That's right. Type 4 is a very small subset of patients with this disease.

Jeff Zollinger: How often is this dosed?

Lynda Finch: In the first year, there are some loading doses, four loading doses are administered at 14 day intervals for the first three and then 40 days after the first dose and then every 4 months. The dose is the same for all patients because it is based your CFS volume.

Jeff Zollinger: And these are always administered intrathecally?

Lynda Finch: Yes. It is administered directly into the spinal fluid where the defect is. It is on oligonucleotide.

Paul Oesterman, Chair: Is there any plans to study in the adult patients?

Lynda Finch: There is a difference between child onset, we have some patients with child onset and aged into adults. We have no studies in adult onset, you don't develop symptoms until your 20s or 30s.

Paul Oesterman, Chair: I don't know if I am comfortable approving something that has not been studies in adults. I can understand if they have grown into adulthood.

Dave England: Is there literature supporting the use in adults?

Lynda Finch: What supports it is the genetic disease is exactly the same for SMA. There would not be any dosing difference since it is based on CSF volume.

Paul Oesterman, Chair: Why wasn't it studied in adults? I know it is a small percentage of the population.

Lynda Finch: Adults are only about 5% of the total population, it would be difficult to recruit for a study, which is part of the reason. We also know that by the time someone has reached adulthood, they have had a disability for a long period of time and it is not clear what benefit the drug would have. That is a lot of damage the drug would have to undo. There are patients that are being treated that are adults and we collecting that data. And we are following the adults.

Dave England: But the FDA gave approval for all types even though it was never studied?

Jeff Zollinger: But there are adults being treated?

Lynda Finch: Yes, I heard there are some patients in their 20's being treated. In terms of types, infantile onset, those babies usually don't live past age 2, but the childhood onset can live into their 20's. Type 3's usually have a normal lifespan into their 80's or 90's sometimes. The majority are going to be infantile onset.

Dave England: From a pharmacokinetic standpoint, we can't assume because it works in a child it would also work in an adult. My concern would be what could take place. You

already have several decades of damage, how could treatment now reverse several decades of damage?

Lynda Finch: Right, we don't know that. We do have some evidence with teenagers that lost their ability to walk and with treatment regained that ability. With your earlier comment regarding pharmacokinetic, this is not your typical drug in terms of absorption and distribution. It works in the CNS, we are working with the volume there that doesn't really change from children to adults. So I don't think that applies.

Dave England: It still has to be metabolized and removed somehow. Are there differences between a child and adult? I don't know the specifics here. In theory I can see where you are coming from, but without studies, we don't know for sure.
Lynda Finch: It is a limitation of the data and how the program was designed, there was more of a focus on the infants and children.

Jeff Zollinger: Based on the study, it would be nice to have similar data points and outcomes, is that published data?

Lynda Finch: Yes, our phase 2 trial is published in Lancet. In the older patients we use the 6 minute walk test. It is considered significant if they can improve by 30 meters and they often improve by 100 meters. We have had type 2 patients, who usually never walk independently. We have had two patients that gained the ability to walk. We do look at different measures in infants vs. children and ambulatory patients. We look at upper limb movement for the younger kids.

Paul Oesterman, Chair: We have the criteria in front of us for the initial authorization of a diagnosis of spinal muscular atrophy and must be prescribed by or in consultation with a neurologist who has experience treating SMA. We also have reauthorization criteria that can be looked at down the road if necessary. We need a motion to approve or recommendations to amend these criteria.

Dave England: Basically we are going to approve it but monitor it like the Exondys. So moved.

Jeff Zollinger: Second.

Voting: Ayes – 3, Nays - 1, the motion carries

Paul Oesterman, Chair: My concern is the type 4, it is minimal.

Paul Oesterman, Chair: The next item is to go back to our first clinical presentation for the prior authorization criteria and/or quantity limits for pramlintide or Symlin. Do we have any public comment?

Carl Jeffery: This is a carryover from our last meeting when we talked about and removed the criteria from Byetta and Victoza and removed the criteria except for adding

a requirement for a diagnosis on the claim. This falls in the same category, so I thought I would bring this back to the Board for discussion. This is the last of the diabetes medications that are limited by PA criteria.

Paul Oesterman, Chair: Do we have anything in our binders on this?

Carl Jeffery: I don't have any proposed criteria. There is some utilization data and we don't have many people on this. We had one member in October and in January we had three members.

Paul Oesterman, Chair: We are just recommending the removing of the prior authorization.

Carl Jeffery: Right, that was my recommendation.
Dave England: Are we removing the criteria because we have so few people on it, or because the criteria aren't applicable anymore?

Carl Jeffery: I think the criteria doesn't apply any more. I think it helps to have open access to this medication. It has a place in therapy and I don't think it is being misused.

Paul Oesterman, Chair: It seems pretty straight forward. Do we have a motion to eliminate the Prior Authorization criteria for pramlintide?

James Marx: So moved.

Jeff Zollinger: Second.

Voting: Ayes across the board, the motion carries.

6. Public Comment on any DUR Board Requested Report

Paul Oesterman, Chair: Now we are going to the DUR Board requested reports. Is there any public comment on these reports? No.

7. DUR Board Requested Reports

Paul Oesterman, Chair: The first report is psychotropic medications used for children and adolescents.

Carl Jeffery: As the Board may remember, about a year ago, we passed some rules to address polypharmacy. The rules allow one medication in the same class or one medication from up to three different classes before they require a prior authorization. The fourth medication would stop for PA or two within the same class would stop for PA. The feedback has been pretty positive. This is a checkup so you can see how things are moving. The first chart shows the number of recipients under the age of 18 receiving four or more recipients.

Paul Oesterman, Chair: It could be the same person in each month.

Carl Jeffery: Right, likely they are. I don't think that policy has any problems. We have decreased the numbers. Of those patients I broke down so you can see the number of members and what they are on. This is a years' worth of data. You can see anticonvulsants are the highest used which makes sense.

Dave England: Do the drug groups include hydroxyzine?

Carl Jeffery: Hydroxyzine falls in the anxiolytic/hypnotic class, so it does catch it.

Dave England: Ok, otherwise, those numbers don't look too bad.
Carl Jeffery: But looking at the numbers of people on hydroxyzine, I doubt they are using it for a rash, they are likely using it as an anxiolytic.

Paul Oesterman, Chair: My concern is are they using the proper salt form. The hydroxyzine hydrochloride is indicated for rash where the pamoate form is for an anxiolytic.

Carl Jeffery: There are about twice as many pamoate claims as there are hydrochloride.

Beth Slamowitz: It would be based on what the pharmacy is filling if the prescriber just writes hydroxyzine, they may not clarify.

Dave England: I think this is an interesting report.

Paul Oesterman, Chair: I think this is a good report for keeping an eye on things.

Carl Jeffery: The next report shows the trend. There was a dip in February, but that is pretty normal.

Paul Oesterman, Chair: It does look like overall the trend is increasing. It would be interesting to look at this over a longer period to see if there is a seasonal change.

Carl Jeffery: Our population has increased since last year too. We have gone from about 150,000 to 180,000 fee for service. Page 66 stars the two or more medications. You can see the number of recipients getting two or more within the same class. Most of them are anticonvulsants, but there are a lot of antipsychotics.

Mary Griffith: Are the ones on anticonvulsants, they could be using them for seizure?

Carl Jeffery: Right, we don't know for sure. We could try to pull out the diagnosis, but it isn't reliable. If you look at the atypical antipsychotics, it looks like it might be trending down.

Paul Oesterman, Chair: Is there any additional evaluation we want to look at in the future?

Dave England: I think just looking at a longer period, other than that, it looks good. Maybe we should look at this again in a year from now.

Paul Oesterman, Chair: And also look at the percentage of membership to account for the increasing population. If we could look at that in the future, that would be good.

James Marx: Are we going to look at the patients under age 4?

Carl Jeffery: Yes, that would be a good report too, looking at age 5 is the cutoff.

Paul Oesterman, Chair: Can we look at that for next time? Our next report is in regards to opioid utilization, looking at top prescriber and member.
Carl Jeffery: This is another carry over from the last couple meetings. We are trying to narrow down who these prescribers are. We have one nurse practitioner in Las Vegas that does work at a pain and spine clinic in Las Vegas. It is interesting to see this provider is far above the next person. If you look at the number of patients and you have several mid-levels in the top 10.

Jeff Zollinger: Is this nurse practitioner working independently?

Carl Jeffery: I think they are part of a group.

Jeff Zollinger: I know about 5 years ago, nurse practitioners can practice independently.

Carl Jeffery: Right, they can. PAs cannot. But they are part of a group.

Jeff Zollinger: The sum of quantity, what does that represent?

Carl Jeffery: That is the number of units, like pills.

Jeff Zollinger: What is the timeframe?

Carl Jeffery: It's a year, April 2016 to March 2017.

Dave England: Did any of these individuals show up on the State Reporting website?

Carl Jeffery: That's a good question, I'm not sure.

Dave England: This person is working in a group, and representative of 4 or 5 physicians.

Carl Jeffery: I don't know how the bigger practices work, after the initial evaluation, maybe the nurse practitioner writes the prescriptions every month for maintenance.

Jeff Zollinger: The other top 4, we don't have any background for their specialty.

Carl Jeffery: Right, they didn't have anything listed.

Jeff Zollinger: One is a dentist, number eight.

Paul Oesterman, Chair: What is interesting is if you look at the member count, the number is high, but the sum of quantities is low compared to the other.

Carl Jeffery: And the days supply is low. I think they must send everyone out the door with a prescription.

Paul Oesterman, Chair: Maybe they need to be made aware that this is not the best practice.

Jeff Zollinger: And this is just for the Medicaid population right?
Carl Jeffery: Right. I don't know where our limits are. I can't publish names, but if there is a way to provide some education to these providers.

Paul Oesterman, Chair: Could we invite someone from the Board of Pharmacy to come to one of our meetings?

Carl Jeffery: I have asked if someone could come and they have shown some interest. I think that is something we can do in the future.

James Marx: Have her bring some reports.

Paul Oesterman, Chair: Who do we need to contact?

Carl Jeffery: I can reach out to the board of pharmacy.

Paul Oesterman, Chair: And then bring this same data back, blind the names again.

Carl Jeffery: It would be interesting to see if she can pull the numbers for these prescribers. Maybe it is just a case of this one nurse practitioner gets all the Medicaid population and that is all they do.

Our next report on page 115, starts with the encrypted member ID's. The questions is of the top opioid utilizers, what other medications are they on. The pharmacy numbers are consistent as well as the prescribers so you can see if the pharmacies or prescribers matchup between members. My observation as I was getting ready for the opioid implementation, the amount of routine fills of opioids people get. I think it is just part of their normal refills. It is interesting to see how habitual their fills are. I can't tell from my data if the member has chronic pain or if they got OxyContin one time and they just keep refilling it.

Jeff Zollinger: It is my understanding that this patient here is getting oxycodone and hydromorphone, correct?

Carl Jeffery: It could be at different times. It is consolidated for the whole year.

Beth Slamowitz: I think it is interesting to see if they are on an anti-inflammatory too, there is some ibuprofen or prednisone.

Dave England: The one ending in 885, getting from pharmacy 12, pharmacy 21 provided the morphine and the alprazolam. It is the same prescriber, but that is interesting.

James Marx: A lot of the members do go to different pharmacies because of medication availability.

Carl Jeffery: Sometimes the member is just out and close to a pharmacy that day and goes there. I don't know that they are intentionally trying to evade anything.
James Marx: I think the pharmacies do interact, I don't think they are pharmacy shopping, but it is supply driven.

Beth Slamowitz: If these are paid claims, and they are putting it through Medicaid, regardless of which pharmacy they go to, it will hit a DUR edit for too soon. It will be the cash prescriptions that are harder to catch.

Paul Oesterman, Chair: There is an opportunity for lock-in.

Mary Griffith: They may be on lock-in already, we don't know.

Jeff Zollinger: The member ending in 885 has multiple prescribers.

Mary Griffith: Is there any age on this? This one member is on warfarin so they may have had a stroke.

Carl Jeffery: I didn't include age on there.

Paul Oesterman, Chair: You could have multiple prescribers in the same office too.

Jeff Zollinger: If we knew the number one prescriber fit one of these IDs, then we could match back to see other prescribers. That might be a way to get to other prescribers.

Shannon Sprout: Would it be helpful to have this report again broken down by practice location, by office, by month and if they are in lock in. Is there anything else?

Paul Oesterman, Chair: I think more information would be helpful
Shannon Sprout: We can trend line it out.

Beth Slamowitz: It would give you a good idea if you did put some indicators to show which prescribers are actually checking the PMP. If the prescribers are checking, they should know who else is also prescribing.

Carl Jeffery: In two weeks, the opioid landscape is going to look different.

Duane Young: Let's look at from the 15th of May to the 15th of June.

Shannon Sprout: I think it would be good to look at a baseline for before the change.

Paul Oesterman, Chair: That would be good, the more information, the better.
Dave England: This was for a year?

Carl Jeffery: Right. Look at how many members are on breathing medications for their asthma or COPD.

Beth Slamowitz: Also several with benzos.
Carl Jeffery: And muscle relaxants.

Jeff Zollinger: Is it possible to match back how many patients each of these prescribers are seeing? That would be interesting to see how many of prescriptions correlate to how many patients.

Dave England: Looking at this 922 member, the methadone dose seems high, 360 methadone over 30 days. That 12 per day.

Paul Oesterman, Chair: Member 592 received a 672 day supply of hydromorphone in one year.
The first patient there. Something doesn't seem right.

Carl Jeffery: It could be two different strengths.

Paul Oesterman, Chair: If we could get the drill down next time, I think that will help.

Jeff Zollinger: Is there a way to see how many patients that they see total per year?

Carl Jeffery: That would be a lot of data to go through.

Beth Slamowitz: If you broaden the number of patients from other medications. Are they seeing a large number of patients and write for a short day supply?

Jeff Zollinger: It does have the number of patients there.

Paul Oesterman, Chair: At the end of the data is a graph.

Carl Jeffery: That's the 90 day supply graph for the next report.

Paul Oesterman, Chair: The impact of the 90 days requirement for maintenance medications.

Carl Jeffery: This wasn't something from the Board, be we started a 90 day requirement for maintenance medications in February. This is the short number of prescriptions so far. Our March numbers were inflated because everyone was getting a 90 day supply, we're hoping April and May will be lower. This has been fairly well received. We get a request every once in a while without justification for why they don't want to write for 90 days.

Paul Oesterman, Chair: I would assume we would continue to see a drop in the number of 30 day supplies.

Mary Griffith: I think there would be some way to see the amount decreased for the dispensing fees.

Carl Jeffery: We should see a decrease over the next few months, they are included on the report.

James Marx: Is that the goal to decrease the dispensing fees?
Carl Jeffery: Right, the dispensing fee is $10.17, you're saving about $20 per quarter.

Beth Slamowitz: You may not see the impact for about a year until people cycle through their refills.

Paul Oesterman, Chair: I would ask that this report be replicated each time for the next few meetings. After we have been on this for six months, we should see a decrease. Any more discussion on the DUR requested reports?

8. Public Comment on any Standard DUR Report

Paul Oesterman, Chair: We will move to asking for public comment for the standard reports?

9. Standard DUR Reports

Paul Oesterman, Chair: Let's take a look at the prescribing trends.

Carl Jeffery: One of the biggest changes is Abilify is generic, it took a while for the price to come down and we changed to the generic as preferred a few months ago. That had a big impact on the top. The blood factor products are still very high. Our top drug by spend, 3 or 4 of them were blood factor products.

Paul Oesterman, Chair: Do we have any other generics coming that will be an impact?

Carl Jeffery: Zetia is coming out as generic

.

James Marx: Lyrica is coming out?

Carl Jeffery: That's not on my radar, I'll have to check. Strattera for ADHD is coming out soon. We have a couple new combination insulin products.

Jeff Zollinger: I heard there were some developments with insulin pumps.

Mary Griffith: We pay for those for children through EPSDT, but not continuous blood monitoring.

Paul Oesterman, Chair: Not too many changes. The ProDUR report now.

Carl Jeffery: I don't think there is anything out of the ordinary here either. Pretty standard compared to the last few quarters. The last quarter starts on page 158.

Paul Oesterman, Chair: Page 161, the ID report. Looking at all others, the paid Rxs is considerably less than the rejected Rxs.

Carl Jeffery: I will have to ask our report team, this is a canned report so I will send that over to them.

Paul Oesterman, Chair: The same with TD on page 168. Anybody have anything else to add?

Mary Griffith: Did we have anything on Retro-DUR?

Carl Jeffery: I did, I have something for the ED admissions and medication use for asthma and COPD. We have a list of recipients and a draft letter we will be sending out.

9. Closing Discussion

Paul Oesterman, Chair: Our next meeting is scheduled for July 27, 2017. I would like to request we look for another venue that is not so interrupted.

Carl Jeffery: I have shopped around before, I'll check it out and see what we can find.

James Marx: Are we supposed to take notice of the opioid and benzo report?

Mary Griffith: Yes, I had our data people run that separately. There is some interesting information in that too.

Paul Oesterman, Chair: It looks like it has not change from 2015 to 2016.

Mary Griffith: Right, but some of the numbers are high.

James Marx: If you follow the popular news about the botched executions, they are giving really high doses and the person isn't dying, so the combination isn't always as lethal as it is purported to be.

Paul Oesterman, Chair: With that, we will adjourn the meeting and see everyone on the 27th of July.

Meeting adjourned at 7:26 PM

Nevada Medicaid
EXONDYS 51 (eteplirsen)
Pharmacy Coverage Guideline

Brand Name	Generic Name
EXONDYS 51	eteplirsen

CRITERIA FOR COVERAGE/NONCOVERAGE

EXONDYS 51™ (eteplirsen) will be considered for coverage under the pharmacy benefit program when the following criteria are met:

1. Diagnosis of Duchenne muscular dystrophy (DMD) **AND**
2. Documentation of a confirmed mutation of the dystrophin gene amenable to exon 51 skipping **AND**
3. Prescribed by or in consultation with a neurologist who has experience treating children **AND**
4. Dose will not exceed 30 milligrams per kilogram of body weight once weekly

Initial Authorization: 6 months

Reauthorization Duration:

Authorization for continued use shall be reviewed at least every 12 months when the following criteria are met:

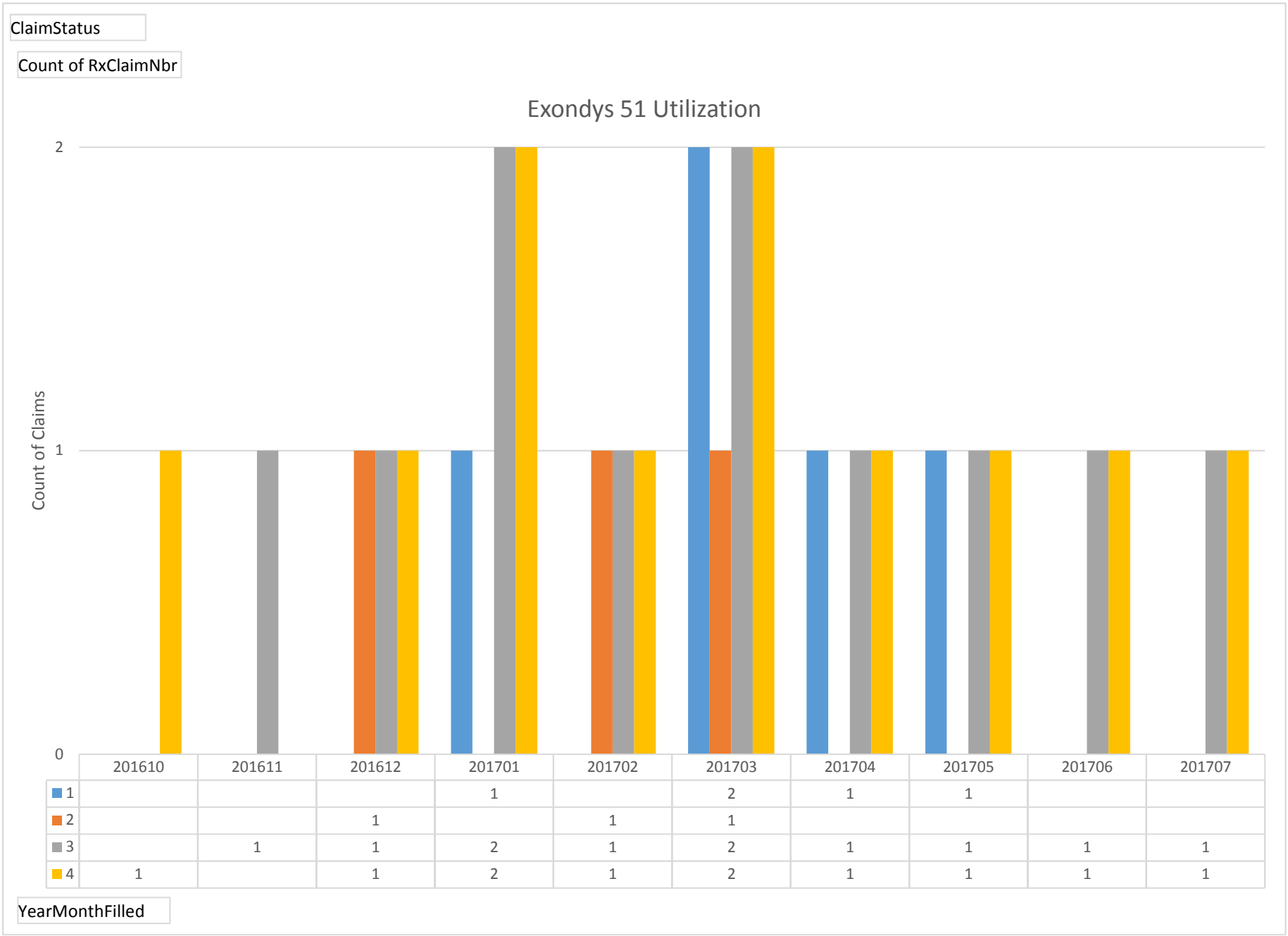
1. One of the following:
- **1.1.** All of the following:
  - **1.1.1.** Patient has been on therapy for less than 12 months **AND**
  - **1.1.2.** Patient is maintaining ambulatory status **AND**
  - **1.1.3.** Patient is tolerating therapy **AND**
  - **1.1.4.** Dose will not exceed 30 milligrams per kilogram of body weight once weekly **AND**
  - **1.1.5.** Prescribed by or in consultation with a neurologist who has experience treating children

OR

- **1.2.** All of the following:

1.2.1. Patient has been on therapy for 12 months or more **AND**
1.2.2. Patient has experienced a benefit from therapy (e.g., disease amelioration compared to untreated patients) **AND**
1.2.3. Patient is maintaining ambulatory status **AND**
1.2.4. Patient is tolerating therapy **AND**
1.2.5. Dose will not exceed 30 milligrams per kilogram of body weight once weekly **AND**
1.2.6. Prescribed by or in consultation with a neurologist who has experience treating children

Year/Mo Filled	Product Name	Count of Members	Count of Claims	Qty Total	Days Supply	Pharm Paid
201610	EXONDYS 51	1	1	32	28	$ 25,610.17
201611	EXONDYS 51	1	1	120	28	$ 96,010.17
201612	EXONDYS 51	3	3	440	84	$ 352,030.51
201701	EXONDYS 51	3	5	440	140	$ 352,050.85
201702	EXONDYS 51	3	3	440	84	$ 352,030.51
201703	EXONDYS 51	4	7	750	154	$ 600,071.19
201704	EXONDYS 51	3	3	288	84	$ 230,430.51
201705	EXONDYS 51	3	3	288	84	$ 230,430.51
201706	EXONDYS 51	2	2	152	56	$ 121,620.34
201707	EXONDYS 51	2	2	152	56	$ 121,620.34



ClaimStatus	201610	201611	201612	201701	201702	201703	201704	201705	201706	201707
1				1		2	1	1		
2			1		1	1				
3		1	1	2	1	2	1	1	1	1
4	1		1	2	1	2	1	1	1	1

Nevada Medicaid
SPINRAZA (nusinersen)
Pharmacy Coverage Guideline

Brand Name	Generic Name
SPINRAZA	nusinersen

CRITERIA FOR COVERAGE/NONCOVERAGE

SPINRAZA™ (nusinersen) will be considered for coverage under the pharmacy benefit program when the following criteria are met:

1. Diagnosis of Spinal Muscular Atrophy (SMA) **AND**
2. Prescribed by or in consultation with a neurologist who has experience treating SMA

Initial Authorization: 12 months

Reauthorization Duration:

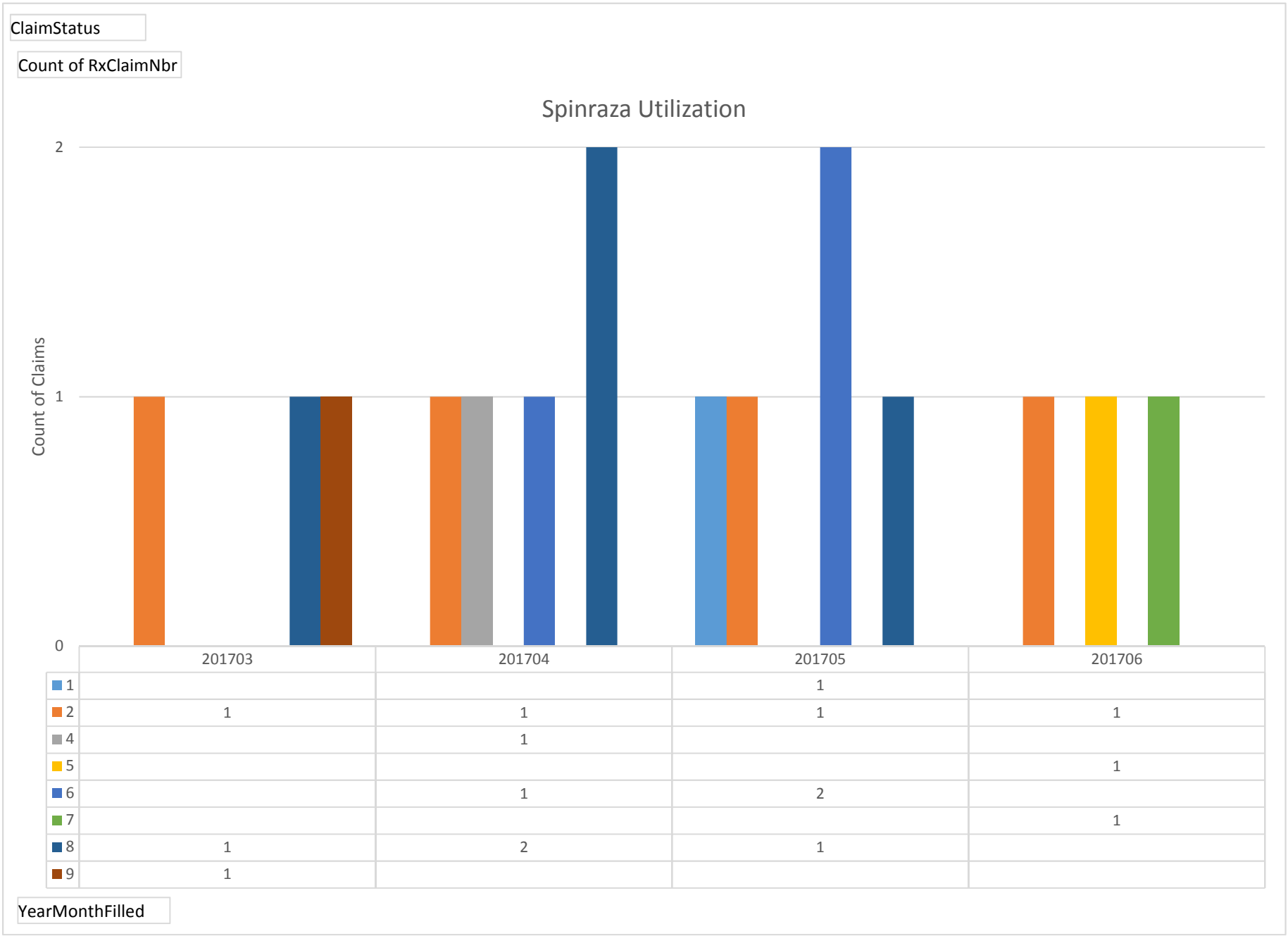
Authorization for continued use shall be reviewed at least every 12 months when the following criteria are met:

1. One of the following:
- **1.1.** All of the following:
  - **1.1.1.** Patient has been on therapy for less than 12 months **AND**
  - **1.1.2.** Patient is maintaining neurological status **AND**
  - **1.1.3.** Patient is tolerating therapy **AND**
  - **1.1.4.** Prescribed by or in consultation with a neurologist who has experience treating SMA

OR

- **1.2.** All of the following:
  - **1.2.1.** Patient has been on therapy for 12 months or more **AND**
  - **1.2.2.** Patient has experienced a benefit from therapy (e.g., disease amelioration compared to untreated patients) **AND**
  - **1.2.3.** Patient is maintaining neurological status **AND**
  - **1.2.4.** Patient is tolerating therapy **AND**
  - **1.2.5.** Prescribed by or in consultation with a neurologist who has experience treating SMA

Year/Mo Filled	Product Name	Count of Members	Count of Claims	Qty Total	Days Supply	Pharm Paid
201703	SPINRAZA	3	3	20	56	$ 500,030.51
201704	SPINRAZA	4	5	25	120	$ 625,050.85
201705	SPINRAZA	4	5	30	150	$ 750,050.85
201706	SPINRAZA	3	3	25	90	$ 625,030.51

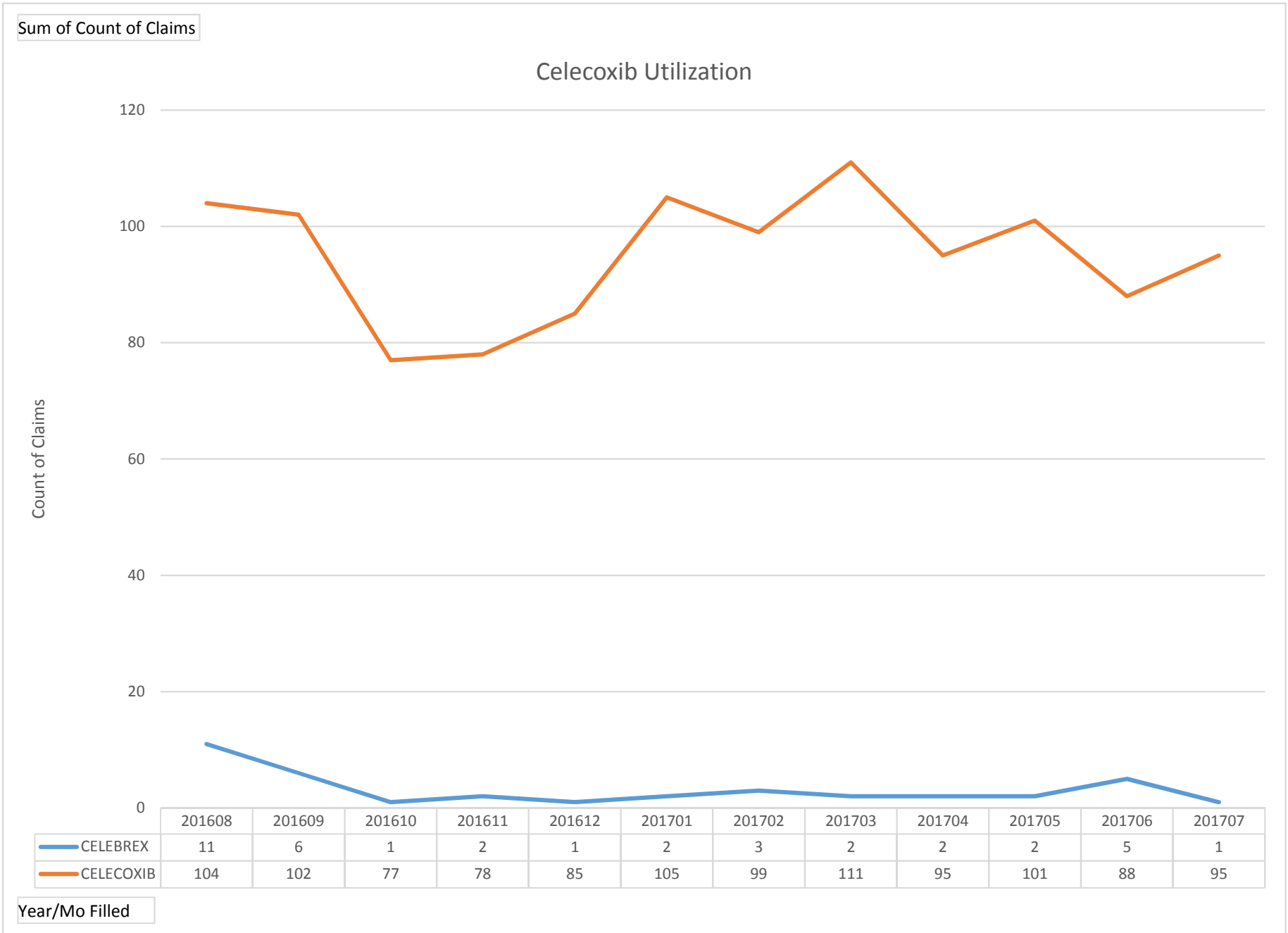


ClaimStatus	201703	201704	201705	201706
1			1	
2	1	1	1	1
4		1		
5				1
6		1	2	
7				1
8	1	2	1	
9	1			

Celecoxib Utilization

August 2016 - July 2017

Year/Month	Sum of Count of Members	Sum of Count of Claims	Sum of Qty Total	Sum of Days Supply	Sum of Pharm Paid
201608	92	115	3966	3001	$ 1,744.30
201609	99	108	4658	3285	$ 3,334.12
201610	74	78	3487	2420	$ 2,251.00
201611	78	80	3528	2452	$ 1,972.96
201612	80	86	3510	2549	$ 1,905.38
201701	102	107	5045	3379	$ 2,043.62
201702	100	102	4739	3353	$ 1,624.87
201703	110	113	5796	3985	$ 1,862.30
201704	94	97	5044	3393	$ 1,484.66
201705	92	103	5405	3588	$ 1,551.93
201706	88	93	5336	3420	$ 1,502.88
201707	86	96	4574	3218	$ 1,738.55
Grand Total	**1095**	**1178**	**55088**	**38043**	**$ 23,016.57**



	201608	201609	201610	201611	201612	201701	201702	201703	201704	201705	201706	201707
CELEBREX	11	6	1	2	1	2	3	2	2	2	5	1
CELECOXIB	104	102	77	78	85	105	99	111	95	101	88	95

B. Cox-2 Inhibitors

Therapeutic Class: NSAIDs (nonsteriodal anti-inflammatory drugs)
Last Reviewed by the DUR Board: April 28, 2011

Cox-2 Inhibitors are subject to prior authorizations and quantity limitations based on the Application of Standards in Section 1927 of the SSA and/or approved by the DUR Board. Refer for the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

Indications:

A diagnosis of osteoarthritis, rheumatoid arthritis, alkylosing spondylitis, juvenile rheumatoid arthritis, primary dysmenorrheal or acute pain in adults.

Upon documentation of a listed indication, authorization will be given if the patient meets one of the following criteria:

a. Patient is at high risk of NSAID induced adverse GI events as evidenced by any of the following:

1. Patient has a documented history or presence of peptic ulcer disease.

2. Patient has a history or presence of NSAID-related ulcer.

3. Patient has a history or presence of clinically significant GI bleeding.

b. Patient is greater than 65 years of age.

c. Patient is at risk for GI complications due to the presence of any of the following concomitant drug therapies:

1. Anticoagulants (e.g. warfarin, heparin or Low Molecular Weight (LMW) heparin).

2. Chronic use of oral corticosteroids.

d. Patient has a documented history of inability to tolerate therapy with at least two non-selective (traditional) NSAIDs.

e. The patient is not being treated daily with aspirin for cardioprophylaxis unless concurrent use of a proton pump inhibitor is documented.

f. The patient does not have a documented history of a cardiac event (e.g. stroke, myocardial infarction or has undergone coronary artery bypass graft procedure) in

the past six months.

g. The patient does not have a history of allergies to sulfonamides, aspirin or other NSAIDs.

2. Prior Authorization Guidelines

Prior authorization approval may be authorized for up to one year.

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

Therapeutic Class Overview
NSAID Gastroprotective Combination Agents and COX-2 Inhibitor

INTRODUCTION

- Non-steroidal anti-inflammatory drugs (NSAIDs) are useful in the treatment of several different types of pain. NSAIDs exert their effect through the inhibition of cyclooxygenase (COX), which impairs the transformation of arachidonic acid to prostaglandins, prostacyclin, and thromboxanes. The two isoforms of the COX enzyme are COX-1 and COX-2. COX-1 is expressed in most tissues and regulates normal cellular processes (ie, gastric cytoprotection, vascular homeostasis, platelet aggregation, and kidney function). COX-2 is expressed mainly in the brain, kidney, and bone. However, it has increased expression at other sites with inflammation (Meade et al, 1993; De Witt et al, 1993). Differences in the extent of COX-1 and COX-2 inhibition affect the activity and toxicity of individual NSAIDs.
- NSAIDs may cause gastrointestinal (GI) ulceration and bleeding. There is a 4-fold increased risk for GI bleeding or perforation in patients who use NSAIDs (Hernandez-Diaz et al, 2002; Masso et al, 2010).
    - An estimated 25% of chronic NSAID users will develop ulcer disease, and 2 to 4% will develop a GI bleed or perforation. Risk factors for an NSAID-associated GI event include high NSAID dose, advanced age, history of peptic ulcer (especially bleeding ulcer), concomitant use with corticosteroids or anticoagulants, and cardiovascular disease (Lanza et al, 2009).
- NSAIDs have been associated with an increased risk for cardiovascular events such as heart attack and stroke. Some nonselective NSAIDs, including diclofenac and ibuprofen, have demonstrated comparable cardiovascular risk to COX-2 inhibitors. Naproxen is associated with lower cardiovascular risk than other NSAIDs (Bhala et al, 2013).
- All NSAIDs carry boxed warnings for both GI and cardiovascular risks. It is important to evaluate GI and cardiovascular risk factors in patients requiring NSAID therapy (Lanza et al, 2009).
- For patients with a high risk for GI events, a selective COX-2 inhibitor may be preferred over a nonselective NSAID. Gastroprotective agents are also available to reduce the risk of NSAID-associated GI events. These agents include an exogenous prostaglandin (misoprostol), histamine-2 receptor antagonists (H2RAs), and proton pump inhibitors (PPIs).
- This review encompasses two classes: the NSAID gastroprotective combination agents and the COX-2 inhibitors.
    - NSAID gastroprotective combination agents combine a conventional NSAID with misoprostol, a PPI (esomeprazole), or an H2RA (famotidine). Available products within this class include ARTHROTEC® (diclofenac sodium/misoprostol), VIMOVO® (naproxen/esomeprazole), and DUEXIS® (ibuprofen/famotidine).
    - The only available COX-2 inhibitor is CELEBREX® (celecoxib). Previously available COX-2 inhibitors, VIOXX® (rofecoxib) and BEXTRA® (valdecoxib), were removed from the market in 2004 and 2005, respectively, due to concerns for increased cardiovascular risk (Food and Drug Administration [FDA], 2005).
- ARTHROTEC and CELEBREX are available generically. The other agents discussed in this review are available only as brand-name agents. However, it is important to note that the individual components of the NSAID gastroprotective combination products are all available as single-ingredient products at strengths similar to those included in the combination products (eg, diclofenac sodium, naproxen, esomeprazole, misoprostol, ibuprofen, and famotidine).
- The safety and efficacy of the NSAID gastroprotective combination agents have been established in randomized controlled trials; however, no head-to-head trials exist within this class. The safety and efficacy of celecoxib have been established in randomized controlled trials which compare celecoxib to placebo, conventional NSAIDs, and NSAID gastroprotective combination agents.

Table 1. Medications Included Within Class Review

Drug	Manufacturer	FDA Approval Date	Generic Availability
ARTHROTEC (diclofenac sodium/misoprostol)	GD SEARLE LLC	12/24/1997	✔
CELEBREX (celecoxib)	GD SEARLE LLC	12/31/1998	✔
DUEXIS (ibuprofen/famotidine)	HORIZON PHARMA	04/23/2011	-
VIMOVO (naproxen/esomeprazole)	HORIZON PHARMA	04/30/2010	*

Page 1 of 10

*Although generic naproxen/esomeprazole has been approved by the FDA, launch is not anticipated until 2023 based on current patent status.

(Drugs@FDA, 2017; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2017)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	ARTHROTEC (diclofenac sodium/ misoprostol)	CELEBREX (celecoxib)	DUEXIS (ibuprofen/ famotidine)	VIMOVO (naproxen/ esomeprazole)
Management of acute pain in adults		✔		
Management of primary dysmenorrhea		✔		
Management of the signs and symptoms of ankylosing spondylitis		✔		
Management of the signs and symptoms of juvenile rheumatoid arthritis in patients 2 years and older		✔		
Management of the signs and symptoms of osteoarthritis		✔		
Management of the signs and symptoms of rheumatoid arthritis		✔		
Relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers				✔
Relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper GI ulcers, which in the clinical trials was defined as a gastric and/or duodenal ulcer, in patients who are taking ibuprofen for those indications			✔	
Treatment of the signs and symptoms of osteoarthritis or rheumatoid arthritis in patients at high risk of developing NSAID-induced gastric and duodenal ulcers and their complications	✔			

(Prescribing information: ARTHROTEC, 2016; CELEBREX, 2016; DUEXIS, 2016; VIMOVO, 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 EFFICACY SUMMARY

NSAID/Gastroprotective Combination Agents

- A Cochrane meta-analysis reviewed the effectiveness of misoprostol, H2RAs, and PPIs in the prevention of NSAID-induced upper GI toxicity. The primary outcomes of endoscopic gastric ulcers (GUs) and duodenal ulcers (DUs) were evaluated in 44 randomized controlled trials with patients on traditional NSAIDs for arthritis (23 misoprostol, 12 H2RA, and 9 PPI trials). Misoprostol, double doses of H2RAs, and PPIs all demonstrated a benefit over placebo in reducing the risk for NSAID-associated GUs (relative risk [RR]=0.26, 0.44, and 0.39, respectively) and DUs (RR=0.42, 0.26, and 0.20, respectively). Standard dose H2RAs reduced the risk for DUs (RR=0.24) but not GUs (Rostom et al, 2002).
- A randomized controlled trial demonstrated that ARTHROTEC has comparable efficacy to diclofenac monotherapy for the treatment of osteoarthritis (OA) and is associated with a lower rate of GUs and DUs (Bocanegra et al, 1998). Additionally, the combination agent has demonstrated comparable efficacy to that of naproxen and piroxicam

monotherapy for the treatment of OA and is associated with a lower rate of gastric and duodenal ulcers compared to naproxen, piroxicam, and nabumetone monotherapy (Agrawal et al, 1999; Melo Gomes et al, 1993). In comparison to acetaminophen (APAP) monotherapy for the treatment of OA, diclofenac sodium/misoprostol is superior in terms of efficacy but is associated with higher GI distress and incidence of adverse events (AEs) (Pincus et al, 2001).

- The safety and efficacy of DUEXIS were evaluated in the REDUCE-1 (N=906) and REDUCE-2 (N=627) trials. Both double-blind, randomized controlled trials were 24 weeks in duration and compared ibuprofen 800 mg/famotidine 26.6 mg three times daily to ibuprofen 800 mg alone three times daily. In the pooled analysis, the incidence of GUs was 12.5% in the combination group and 20.7% in the ibuprofen group; the incidence of DUs was 1.1 and 5.1%, respectively. The risk ratio of upper GI ulcers for ibuprofen/famotidine vs ibuprofen alone was 0.46 (95% confidence interval [CI], 0.34 to 0.61). Although endoscopically-confirmed ulcers were reduced, there was no demonstrated benefit in GI complications (Laine et al, 2012). Another pooled analysis showed that DUEXIS maintained the same gastroprotective efficacy and contributed to a 51% and 59% risk reduction for GI ulcer development in patients aged < 60 years old and ≥ 60 years old, respectively, when compared to treatment with ibuprofen alone. The combination also remained effective for patients with additional risk factors for GI ulcer development (Bello et al, 2015).
- The efficacy and tolerability of VIMOVO for OA, RA, and ankylosing spondylitis were evaluated in a systematic review and network meta-analysis of 109 randomized controlled trials comparing VIMOVO, naproxen, diclofenac, ibuprofen, ketoprofen, celecoxib, or etoricoxib (Datto et al, 2013).
    - VIMOVO demonstrated comparable efficacy to all active comparators in the relief of symptoms of OA, RA, and ankylosing spondylitis.
    - Through direct meta-analysis, VIMOVO was associated with a lower risk of GU than naproxen monotherapy (odds ratio [OR]=0.17; 95% CI, 0.10 to 0.31). There was no significant difference in the incidence of GUs in direct comparisons between VIMOVO and celecoxib.
    - Through indirect mixed treatment comparison, VIMOVO-treated patients had significantly lower odds of GU occurrence compared with ibuprofen (OR=0.25; 95% credible interval [CrI], 0.10 to 0.56) and diclofenac (OR=0.43; 95% CrI, 0.18 to 0.90). No significant differences were detected in the incidence of GU between VIMOVO and ketoprofen, etoricoxib, celecoxib, or fixed-dose diclofenac sodium plus misoprostol.
- Another systematic review of 5 Phase 3 studies for VIMOVO was conducted to analyze the incidence of ulcers (gastric and duodenal), erosive gastritis, and erosive duodenitis in patients receiving concomitant low-dose aspirin (LDA) therapy (Angiolillo et al, 2014).
    - In the 2 trials with 6-month follow-up, the combined incidence of GUs was lower for the VIMOVO vs EC naproxen groups regardless of LDA use (P<0.001 for both LDA users and non-users).
    - The combined incidence of erosive gastritis from the 2 trials was also lower in VIMOVO vs EC naproxen-treated patients for both LDA users (P=0.004) and LDA non-users (P<0.001).

Celecoxib

- Celecoxib has been compared to conventional NSAIDs in several clinical trials for the treatment of OA. In general, selective COX-2 inhibitors have comparable efficacy to conventional NSAIDs such as piroxicam, naproxen, diclofenac, ibuprofen, and nabumetone. There is a difference in the reported tolerability of NSAIDs; specifically, celecoxib is associated with less GI AEs than conventional NSAIDs (Bensen et al, 1999; Chan et al, 2002; Silverstein et al, 2000; Singh et al, 2006). However, one 12-week, double-blind, parallel-group, randomized trial (N=249) failed to demonstrate noninferiority of celecoxib 200 mg daily to diclofenac 50 mg three times daily in patients with OA of the hip requiring joint replacement surgery (Emery et al, 2008).
- In the 12-week, randomized, multicenter, double-blinded SUCCESS-I study (N=13,274), the comparative efficacy and safety of celecoxib, diclofenac, and naproxen were evaluated. Celecoxib demonstrated comparable efficacy to diclofenac and naproxen in the treatment of OA. Nonselective NSAIDs were associated with significantly more ulcer complications than celecoxib (OR=7.02; 95% CI, 1.46 to 33.80; P=0.008) (Singh et al, 2006).
- Several trials have compared celecoxib with conventional NSAIDs for the relief of symptoms associated with rheumatoid arthritis (RA). Results of two studies comparing celecoxib with diclofenac and naproxen demonstrated similar efficacy (Emery et al, 1999; Simon et al, 1999). In addition, a study was conducted to compare the efficacy of celecoxib to naproxen among children with juvenile rheumatoid arthritis (JRA). Study results revealed that celecoxib was at least as effective as naproxen in treating the symptoms of JRA over 12 weeks (Foeldvari et al, 2009).
- A double-blind study compared celecoxib 200 mg twice a day to a combination of diclofenac slow-release 75 mg twice a day and omeprazole 20 mg daily in patients with either OA or RA at increased risk for GI AEs. The primary endpoint of clinically significant upper or lower GI events occurred in 0.9% of patients taking celecoxib and 3.8% of patients receiving diclofenac plus omeprazole (P<0.0001) (Chan et al, 2010).

- Several clinical trials were conducted to evaluate the use of celecoxib for the management of pain. In general, comparable analgesic effects were noted between celecoxib and other NSAIDs (ie, ibuprofen, naproxen) (Derry et al, 2012; Loo et al, 2007; Salo et al, 2003). Some trials demonstrated differences between celecoxib and ibuprofen for pain relief following minor oral surgery procedures; however, data has been inconsistent and may be dose-dependent (Doyle et al, 2002; Al-Sukhun et al, 2012).
    - One clinical trial compared the efficacy of varying doses of celecoxib to indomethacin for the treatment of acute gout. The higher dose regimen of celecoxib (800 mg for one dose, followed by 400 mg twice daily through a total of eight days of therapy) was demonstrated to have equal efficacy to indomethacin 50 mg three times daily, with improved tolerability (Schumacher et al, 2012). Although indicated for the treatment of acute pain, celecoxib is not specifically indicated for the treatment of gout, and the dose regimen in this study is higher than recommended in the celecoxib prescribing information.
- The efficacy of celecoxib for the treatment of primary dysmenorrhea was evaluated in 2 identical randomized, double-blind, active and placebo-controlled, crossover trials. Celecoxib and naproxen demonstrated a benefit over placebo in the primary outcome of time-weighted sum of total pain relief (P<0.001 for both) and the secondary outcome of time-weighted sum of pain intensity difference at 8 hours after administration (SPID[8]) (P<0.001 for both). However, naproxen established a greater improvement in SPID[8] than celecoxib (P<0.001) (Daniels et al, 2009).

Guidelines

- For moderate acute pain, NSAIDs are more effective than acetaminophen (APAP) and aspirin. Some NSAIDs have demonstrated efficacy for moderate acute pain that is equal to or greater than that of APAP/opioid combination products. Celecoxib has similar efficacy to non-selective NSAIDs for the treatment of OA and RA. Comparative efficacy among NSAIDs is not well established (Medical Letter, 2013).
- NSAIDs play an important role in the treatment of several conditions, including RA, OA, ankylosing spondylitis, juvenile idiopathic arthritis, low back pain, dysmenorrhea, and gout. Cardiovascular, GI, and renal risks should be taken into account when prescribing an NSAID (Beukelman et al, 2011; Braun et al, 2011; Chou et al, 2007; Hochberg et al, 2012; Khanna et al, 2012; Lanza et al, 2009; Medical Letter, 2013; Society of Obstetricians and Gynecologists of Canada, 2005).
- According to the American College of Gastroenterology (ACG), the selection of an appropriate NSAID therapy should consider cardiovascular and GI risk factors in addition to analgesic and anti-inflammatory potency (Lanza et al, 2009).
    - Patients at high risk for GI complications (eg, prior ulcer bleeding or multiple risk factors) are recommended alternative therapy to NSAIDs. If anti-inflammatory therapy is required, a selective COX-2 inhibitor in combination with misoprostol or a high-dose PPI should be used.
    - Patients at moderate risk for GI complications are recommended NSAID therapy with a COX-2 inhibitor or a nonselective NSAID in combination with misoprostol or a PPI.
    - Patients at low risk for GI complications are candidates for therapy with a nonselective NSAID.
    - Patients who require low-dose aspirin therapy for cardiovascular disease and NSAID therapy should receive naproxen in combination with misoprostol or a PPI.
    - Patients with a moderate risk for GI complications and high cardiovascular risk should be treated with naproxen in combination with misoprostol or a PPI.
    - Patients with high GI and high cardiovascular risk should avoid using NSAIDs, including COX-2 inhibitors.
- The American College of Rheumatology, Spondylitis Association of America, and Spondyloarthritis Research and Treatment Network recommend NSAID therapy in adults with active ankylosing spondylitis. For patients with stable ankylosing spondylitis, on demand treatment with NSAIDs is preferred over continuous treatment (Ward et al, 2016).
- In 2015, the International NSAID Consensus Group released recommendations for NSAID use in patients with OA (Scarpignato et al, 2015).
    - COX-2 inhibitors and non-selective NSAIDs have the same efficacy for pain management in patients with RA or OA.
    - NSAID-related AEs are not prevented by PPIs in the lower GI areas (beyond the duodenum). Celecoxib causes less AEs than nonselective NSAIDs throughout the entire GI system.
    - The risk for cardiovascular events is similar between celecoxib and most non-selective NSAIDs. The literature shows that naproxen causes the least amount of cardiovascular AEs among non-selective NSAIDs.

SAFETY SUMMARY

- Key contraindications to all NSAID-containing products include:

  - Treatment of peri-operative pain in the setting of coronary artery bypass graft surgery
  - History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs
- Celecoxib is contraindicated in patients with a history of allergic-type reactions to sulfonamides.
- ARTHROTEC is contraindicated in patients with active GI bleeding.
- ARTHROTEC is also contraindicated throughout pregnancy; DUEXIS, VIMOVO, and celecoxib should be avoided in late pregnancy because NSAIDs can cause premature closure of the ductus arteriosus in the fetus.
- All NSAIDs, including celecoxib, have boxed warnings for the risk of serious and potentially fatal cardiovascular and GI events.
  - Serious cardiovascular thrombotic reactions (ie, myocardial infarction and stroke) may occur as early as the first weeks of treatment. The risk may increase with higher dosage and longer duration of use. NSAIDs are contraindicated in the setting of coronary artery bypass graft (CABG) surgery.
  - Serious GI adverse reactions (ie, bleeding, ulceration, and perforation of the stomach or intestines) may occur without warning symptoms at any time during therapy. The risk is higher for elderly patients and patients with a history of PUD or GI bleeding.
- ARTHROTEC labeling also includes a boxed warning for the risk of uterine rupture, abortion, premature birth, and birth defects in pregnant women caused by misoprostol.
- Additional key warnings and precautions for NSAIDs include:
  - New onset or worsening of hypertension
  - Congestive heart failure and edema
  - Renal injury and renal papillary necrosis with long-term use
  - Serious skin reactions
  - Elevated liver enzymes, hepatotoxicity, and rare severe hepatic reactions
  - Anemia
  - Inhibition of platelet aggregation
- Key warnings with prolonged use of PPI's (VIMOVO) include:
  - Increased risk of osteoporosis-related fractures
  - Acute interstitial nephritis
  - Potential for anemia, hypomagnesemia, and hypocalcemia
  - Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE)
- The most commonly reported adverse drug events, reported in at least 5% of patients in clinical trials, include:
  - ARTHROTEC: abdominal pain, diarrhea, dyspepsia, nausea, and flatulence
  - Celecoxib: abdominal pain, diarrhea, dyspepsia, nausea, cough, fever, headache, hypertension, nasopharyngitis, and upper respiratory tract infection
  - DUEXIS: nausea, diarrhea, and dyspepsia
  - VIMOVO: erosive gastritis, gastritis, dyspepsia, upper abdominal pain, diarrhea, gastric ulcer, nausea, and upper respiratory tract infection
- Key drug interactions with NSAIDs include:
  - The effects of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, furosemide, and thiazide diuretics may be diminished by concurrent NSAID therapy.
  - Plasma lithium levels may be increased by NSAIDs.
  - Patients on warfarin or other anticoagulants are at an increased risk of bleeding complications.
- The 2015 American Geriatrics Society (AGS) Beers Criteria recommends avoiding chronic use of non-selective NSAIDs in older adults. NSAIDs increase the risk of GI bleeding and peptic ulcer disease in high-risk groups (ie, age >75, concomitant use of anticoagulants or systemic corticosteroids). While the addition of gastroprotective agents reduces GI risk, it does not eliminate it (AGS, 2015).
- The Prospective Randomized Evaluation of Celecoxib Integrated Safety versus Ibuprofen Or Naproxen (PRECISION) trial evaluated the cardiovascular safety of celecoxib 200 mg twice daily compared with ibuprofen 800 mg three times daily and naproxen 500 mg twice daily. The randomized, multicenter, double-blind, noninferiority trial included 24,081 patients with increased cardiovascular risk who required NSAID therapy for OA or RA. The primary outcome measure was a composite of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke. Secondary outcome measures included GI and renal safety (Nissen et al, 2016).
  - Celecoxib was noninferior to ibuprofen and naproxen with regards to cardiovascular safety. In the intent-to-treat population, a primary outcome event occurred in 2.3% of the celecoxib group, 2.5% of the naproxen group, and 2.7% of the ibuprofen group (hazard ratio [HR]=0.93 vs naproxen, HR=0.85 vs ibuprofen; P<0.001 for noninferiority to both).

- Celecoxib was associated with a lower incidence of GI adverse events compared to naproxen (P=0.01) and ibuprofen (P=0.002).
- Celecoxib was also associated with a significantly lower incidence of renal adverse events compared with ibuprofen (P=0.004). Statistical significance was not reached when compared with naproxen (P=0.19).

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
ARTHROTEC (diclofenac sodium/ misoprostol)	Film-coated tablet: 50 mg/200 mcg 75 mg/200 mcg	OA 50 mg/200 mcg three times daily; alternative regimens due to intolerance*: 75 mg/200 mcg tablet twice daily or 50 mg/200 mcg twice daily RA 50 mg/200 mcg three or four times daily; alternative regimens due to intolerance*: 75 mg/200 mcg or 50 mg/200 mcg twice daily	Dosages may be individualized using the separate products (misoprostol and diclofenac), after which the patient may be changed to the appropriate dose of ARTHROTEC. If clinically indicated, the concomitant use of misoprostol and ARTHROTEC, or the use of individual components, may be appropriate to optimize the misoprostol dose and/or frequency of administration.
CELEBREX (celecoxib)	Capsule: 50 mg 100 mg 200 mg 400 mg	OA 200 mg once daily or 100 mg twice daily RA 100 to 200 mg twice daily JRA (Pediatric patients ≥ 2 years) Patients ≥10 kg to ≤25 kg: 50 mg twice daily Patients >25 kg: 100 mg twice daily Ankylosing spondylitis 200 mg once daily in a single dose or 100 mg twice daily; if no effect is observed after 6 weeks, a trial of 400 mg (single or divided doses) may be of benefit Acute pain and primary dysmenorrhea 400 mg initially, followed by 200 mg dose if needed on first day; on subsequent days, 200 mg twice daily as needed	For patients who have difficulty swallowing capsules, the contents of a CELEBREX capsule can be added to applesauce. The entire capsule contents are carefully emptied onto a level teaspoon of cool or room temperature applesauce and ingested immediately with water. The sprinkled capsule contents on applesauce are stable for up to 6 hours under refrigerated conditions (2 to 8° C; 35 to 45° F).
DUEXIS (ibuprofen/ famotidine)	Film-coated tablets: 800 mg/26.6 mg	RA and OA 800 mg/26.6 mg administered orally three times per day	DUEXIS tablets should be swallowed whole. Do not chew, divide, or crush tablets.
VIMOVO (naproxen/ esomeprazole)	Delayed-release tablet: 375 mg/20 mg 500 mg/20 mg	OA, RA, and ankylosing spondylitis 375 mg/20 mg or 500 mg/20 mg twice daily	Tablets should be swallowed whole (not split, crushed, chewed, or dissolved) with liquid and taken at least 30 minutes before meals. Use

Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
			the lowest effective dose for the shortest duration consistent with individual patient treatment goals

*Less effective in preventing ulcers.

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
ARTHROTEC (diclofenac sodium/ misoprostol)	No dosage adjustment required in the elderly.	The effectiveness and safety in pediatric patients have not been established	Not recommended in advanced renal disease unless benefits are expected to outweigh the risks	Drug-induced liver injury has been reported with diclofenac; use the lowest effective dose for the shortest possible duration	Pregnancy category X Excreted in breast milk; use with caution
CELEBREX (celecoxib)	Dose adjustment is usually not necessary in elderly patients. Elderly patients < 50 kg: initiate therapy at the lowest recommended dosage	Safety and efficacy have been established in children 2 years of age or older and for a maximum of 6 months of treatment in JRA.	Not recommended in patients with severe renal insufficiency If treatment with celecoxib is necessary, monitor patients renal function closely	The daily dose of celecoxib should be reduced by 50% in patients with moderate hepatic impairment. Celecoxib is not recommended for patients with severe hepatic impairment.	Pregnancy category C Pregnancy category D (starting at 30 weeks gestation) Limited data shows low levels in breast milk; use with caution
DUEXIS (ibuprofen/ famotidine)	No dosage adjustment required; initiate dose at the lower end of the dosing range and monitor for adverse reactions	The effectiveness and safety in pediatric patients have not been established	Not recommended in patients with creatinine clearance <50 mL/min	The effects of hepatic dysfunction have not been evaluated.	Avoid use in pregnant women starting at 30 weeks of gestation (3rd trimester) Excreted in breast milk; use with caution
VIMOVO (naproxen/ esomeprazole)	Use caution when high doses are required and some adjustment of dosage may be required in elderly patients	The effectiveness and safety in pediatric patients have not been established	Not recommended for use in moderate to severe or severe renal insufficiency	Not recommended for use in patients with severe hepatic impairment Dosage adjustment should be considered in mild or moderate hepatic impairment	Avoid use in pregnant women starting at 30 weeks of gestation Limited data shows levels in

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
					breast milk; use with caution

*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 D = Positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may justify the 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.

(Clinical Pharmacology, 2017)

CONCLUSION

- NSAIDs are useful in the treatment of several different types of pain; however, potential GI and cardiovascular adverse events must be considered when selecting an NSAID for drug therapy (Lanza et al, 2009).
- Due to COX-1 inhibition, NSAIDs are associated with GI adverse reactions, including dyspepsia, bleeding, and peptic ulcer disease. To decrease GI risk, clinicians may select a COX-2 selective NSAID (celecoxib) or add a gastroprotective agent to NSAID therapy. The gastroprotective agent may be given separately or as a fixed-dose combination product. ARTHROTEC (diclofenac sodium/misoprostol), VIMOVO (naproxen/esomeprazole), and DUEXIS (ibuprofen/famotidine) are the currently available NSAID gastroprotective combination agents.
- Clinical trials have demonstrated that the combination NSAID gastroprotective combination agents produce comparable anti-inflammatory effects to NSAIDs alone and are associated with a lower incidence of gastric and duodenal ulcers. The individual components of the NSAID gastroprotective combination products are all available as single-ingredient products at strengths similar to those included in the combination products.
- Placebo and active-controlled trials with celecoxib have demonstrated comparable efficacy to nonselective NSAIDs for its approved indications. The PRECISION trial established the noninferiority of celecoxib with regards to cardiovascular safety compared to ibuprofen and naproxen. Additionally, it confirmed a lower incidence of GI adverse events with celecoxib than with both nonselective NSAID comparators (Nissen et al, 2016).
- Considerations for the selection of an NSAID include analgesic and anti-inflammatory potency as well as GI and cardiovascular risk. In general, patients with moderate GI risk may receive therapy with a COX-2 inhibitor or a conventional NSAID plus a gastroprotective agent. Patients requiring NSAID therapy with high GI risk should receive alternative therapy. If anti-inflammatory treatment necessary, a COX-2 inhibitor may be used in combination with misoprostol or a high-dose PPI. Patients at high GI and high cardiovascular risk should avoid using NSAIDs and COX-2 inhibitors (Lanza et al, 2009).

REFERENCES

- Agrawal NM, Caldwell J, Kivitz AJ, et al. Comparison of the upper gastrointestinal safety of Arthrotec 75 and nabumetone in osteoarthritis patients at high risk for developing nonsteroidal anti-inflammatory drug-induced gastrointestinal ulcers. Clin Ther. 1999 Apr;21(4):659-74.
- Al-Sukhun J, Al,-Sukhun S, Pentilla H, et al. Preemptive analgesic effect of low doses of celecoxib is superior to low doses of traditional nonsteroidal anti-inflammatory drugs. J Craniofac Surg. 2012 Mar;23(2):526-9.
- American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015;63(11)2227-2246. doi: 10.1111/jgs.13702.
- Angiolillo DJ, Datto C, Raines S, et al. Impact of concomitant low-dose aspirin on the safety and tolerability of naproxen and esomeprazole magnesium delayed-release tablets in patients requiring chronic nonsteroidal anti-inflammatory drug therapy: an analysis from 5 Phase III studies. J Thromb Thrombolysis. 2014 Jul;38(1):11-23. doi: 10.1007/s11239-013-1035-4.
- ARTHROTEC prescribing information. Pfizer – GD Searle, New York, NY. May 2016.
- Bello AE, Kent JD, Holt RJ. Gastroprotective efficacy and safety of single-tablet ibuprofen/famotidine vs ibuprofen in older persons. Phys Sportsmed. 2015; 43(3):193-199.
- Bensen WG, Fiechtner JJ, McMillen JI, et al. Treatment of osteoarthritis with celecoxib, a cyclooxygenase-2 inhibitor: a randomized controlled trial. Mayo Clin Proc. 1999;74:1095-105.
- Beukelman T, Nivedita M, Saag K, et al. American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011 Apr;63(4):465-82. doi: 10.1002/acr.20460.

- Bhala N, Emberson J, Merhi A, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet. 2013 Aug 31;382(9894):769-79. doi: 10.1016/S0140-6736(13)60900-9.
- Bocanegra TS, Weaver AL, Tindall EA, et al. Diclofenac/ misoprostol compared with diclofenac in the treatment of osteoarthritis of the knee or hip: a randomized, placebo controlled trial. Arthrotec Osteoarthritis Study Group. J Rheumatol. 1998;25(8):1602-11.
- Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis. 2011 Jun;70(6):896-904. doi: 10.1136/ard.2011.151027.
- CELEBREX prescribing information. Pfizer. New York, NY. May 2016.
- Chan FK, Hung LC, Suen BY, et al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. N Engl J Med. 2002;347:2104-10.
- Chan FK, Lanas A, Scheiman J, et al. Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis (CONDOR): a randomized trial. Lancet. 2010 Jul 17;376(9736):173-9.
- Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. Ann Int Med. 2007 Oct 2;147(7):478-91.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/default.aspx. Accessed March 2, 2017.
- Daniels S, Robbins J, West CR, et al. Celecoxib in the treatment of primary dysmenorrhea: results from two randomized, double-blind, active- and placebo-controlled, crossover studies. Clin Ther. 2009 Jun;31(6):1192-208.
- Datto C, Hellmund R, Siddiqui MK. Efficacy and tolerability of naproxen/esomeprazole magnesium tablets compared with non-specific NSAIDs and COX-2 inhibitors: a systematic review and network analyses. Open Access Rheumatol. 2013 Feb 26;5:1-19. doi:10.2147/OARRR.S41420.
- De Witt DL, Meade EA, Smith WL. PGH synthase isoenzyme selectivity: The potential for safer nonsteroidal anti-inflammatory drugs. Am J Med. 1993;95:40S.
- Derry S, Moore RA. Single dose oral celecoxib for acute postoperative pain in adults. Cochrane Database Syst Rev. 2012, Issue 3. Art. No.: CD004233. doi: 10.1002/14651858.CD004233.pub3.
- Doyle G, Jayawardena S, Ashraf E, et al. Efficacy and tolerability of nonprescription ibuprofen versus celecoxib for dental pain. Journal of Clinical Pharmacology. 2002;49:912-19.
- Drugs@FDA [database on the Internet]. Rockville (MD): Food and Drug Administration (US), Center for Drug Evaluation and Research; 2015. Available from: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed March 2, 2017.
- DUEXIS prescribing information. Horizon Pharma USA, Inc. Northbrook, IL. May 2016.
- Emery P, Koncz T, Pan S, et al. Analgesic effectiveness of celecoxib and diclofenac in patients with osteoarthritis of the hip requiring joint replacement surgery: a 12-week, multicenter, randomized, double-blind, parallel-group, double-dummy, noninferiority study. Clin Ther. 2008 Jan;30(1):70-83.
- Emery P, Zeidler H, Kvien TK, et al. Celecoxib versus diclofenac in long-term management of rheumatoid arthritis: randomized double-blind comparison. Lancet. 1999;354:2,106-11.
- Foeldvari I, Szer IS, Zemel LS, et al. A prospective study comparing celecoxib with naproxen in children with juvenile rheumatoid arthritis. J Rheumatol. 2009 Jan;36(1):174-82.
- Food and Drug Administration. COX-2 Selective (includes Bextra, Celebrex, and Vioxx) and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). November 27, 2012. Available at: https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm429364.htm.. Accessed March 2, 2017.
- Hernandez-Diaz S, Rodriguez LA. Incidence of serious upper gastrointestinal bleeding/perforation in the general population: review of epidemiologic studies. J Clin Epidemiol 2002;55:157-63.
- Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. Arthritis Care Res (Hoboken). 2012 Apr;64(4):465-74.
- Khanna D, Khanna PP, Fitzgerald JD, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 2: therapy and anti-inflammatory prophylaxis of acute gouty arthritis. Arthritis Care Res (Hoboken). 2012;64:1447-61. doi: 10.1002/acr.21773.
- Laine L, Kivitz AJ, Bello AE, et al, on behalf of the REDUCE-1 and REDUCE-2 Study Investigators. Double-blind randomized trials of single-tablet ibuprofen/high-dose famotidine vs ibuprofen alone for reduction of gastric and duodenal ulcers. Am J Gastroenterol. 2012; 107:379-386; doi:10.1038/ajg.2011.443.
- Lanza FL, Chan FKL, Quiqley EMM. Guidelines for the prevention of NSAID-related ulcer complications. Am J Gastroenterol. 2009;104:728-38.
- Loo CY, Tan HJ, Teh HS, et al. Randomized, open label, controlled trial of celecoxib in the treatment of acute migraine. Singapore Medical Journal. 2007;48(9):834-9.
- Masso Gonzalez EL, Patrignani P, Tacconelli S, et al. Variability among nonsteroidal antiinflammatory drugs in risk of upper gastrointestinal bleeding. Arthritis Rheum 2010;62:1592-601.
- Meade EA, Smith WL, De Witt DL. Differential inhibition of prostaglandin endoperoxide synthase (cyclooxygenase) isozymes by aspirin and other non-steroidal anti-inflammatory drugs. J Biol Chem. 1993;268:6610.
- Medical Letter, Inc. Treatment guidelines from the Medical Letter: Drugs for Pain. 2013;11(128):31-42.
- Melo Gomes JA, Roth SH, Zeeh J, et al. Double-blind comparison of efficacy and gastroduodenal safety of diclofenac/misoprostol, piroxicam, and naproxen in the treatment of osteoarthritis. Ann Rheum Dis. 1993 Dec;52(12):881-5.
- Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular Safety of Celecoxib, Naproxen, or Ibuprofen for Arthritis. N Engl J Med. 2016 Dec 29;375(26):2519-29. doi: 10.1056/NEJMoa1611593.
- Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations [database on the internet]. Silver Spring (MD): Food and Drug Administration (US), Center for Drug Evaluation and Research; 2015. Available at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Accessed March 2, 2017.
- Pincus T, Koch GG, Sokka T, et al. A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. Arthritis Rheum. 2001 Jul;44(7):1587-98.
- Rostom A, Dube C, Wells G, et al. Prevention of NSAID-induced gastroduodenal ulcers. Cochrane Database Syst Rev. 2002;(4):CD002296. doi: 10.1002/14651858.CD002296.

- Salo DF, Lavery R, Varma V, et al. A randomized clinical trial comparing oral celecoxib 200 mg, celecoxib 400 mg, and ibuprofen 600 mg for acute pain. Acad Emerg Med. 2003;10(1):22-30.
- Scarpignato C, Lanas A, Blandizzi C, et al for the International NSAID Consensus Group. Safe prescribing of non-steroidal anti-inflammatory drugs in patients with osteoarthritis – an expert consensus addressing benefits as well as gastrointestinal and cardiovascular risks. BMC Medicine. 2015; 13(55):1-22.
- Schumacher HR, Berger MF, Li-Yu J, et al. Efficacy and tolerability of celecoxib in the treatment of acute gouty arthritis: a randomized controlled trial. J Rheumatol. 2012 Sep;39(9):1859-66. doi: 10.3899/jrheum.110916.Silverstein FE, Faich G, Goldstein JL, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis, the CLASS study. JAMA. 2000;284(10):1247-55.
- Simon LS, Weaver AL, Graham DY, et al. Anti-inflammatory and upper gastrointestinal effects of celecoxib in rheumatoid arthritis: a randomized controlled trial. JAMA. 1999;282(20):1,921-8.
- Singh G, Fort JG, Goldstein JL, et al. Celecoxib versus naproxen and diclofenac in osteoarthritis patients: SUCCESS-I study. American Journal of Medicine. 2006;119:255-66.
- Society of Obstetricians and Gynecologists of Canada: Primary dysmenorrhea consensus guideline. J Obstet Gynaecol Can. 2005 Dec;27(12):1117-46.
- VIMOVO prescribing information. Horizon Pharma USA. Deerfield, IL. October 2016.
- Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2016;68(2):282-98.

Publication Date: March 24, 2017

QQ. ~~Cesamet® (Nabilone) and Marinol® (Dronabinol)~~ Cannabinoid Antiemetics

Therapeutic Class: Antiemetic
Last Reviewed by DUR Board: October 25, 2012

~~Cesamet® (Nabilone) and Marinol® (Dronabinol)~~ Cannabinoid Antiemetics are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the SSA and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

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

a. ~~Cesamet® (~~Nabilone~~)~~

1. The recipient has a diagnosis of chemotherapy-induced nausea and/or vomiting; and

2. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one serotonin receptor antagonist; and

3. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one other antiemetic agent; and

4. The prescriber is aware of the potential for mental status changes associated with the use of this agent and will closely monitor the recipient.

b. ~~Marinol® (~~Dronabinol~~)~~

1. The recipient has a diagnosis of chemotherapy-induced nausea and/or vomiting; and

a. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one serotonin receptor antagonist; and

b. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one other antiemetic agent; and

c. The prescriber is aware of the potential for mental status changes associated with the use of this agent and will closely monitor the recipient; or

2. The recipient has been diagnosed with Acquired Immune Deficiency Syndrome (AIDS) and has anorexia associated with weight loss; and the

recipient has experienced an inadequate response, adverse event or has a contraindication to megestrol (Megace®); and

a. The prescriber is aware of the potential for mental status changes associated with the use of this agent and will closely monitor the recipient.

2. Prior Authorization Guidelines

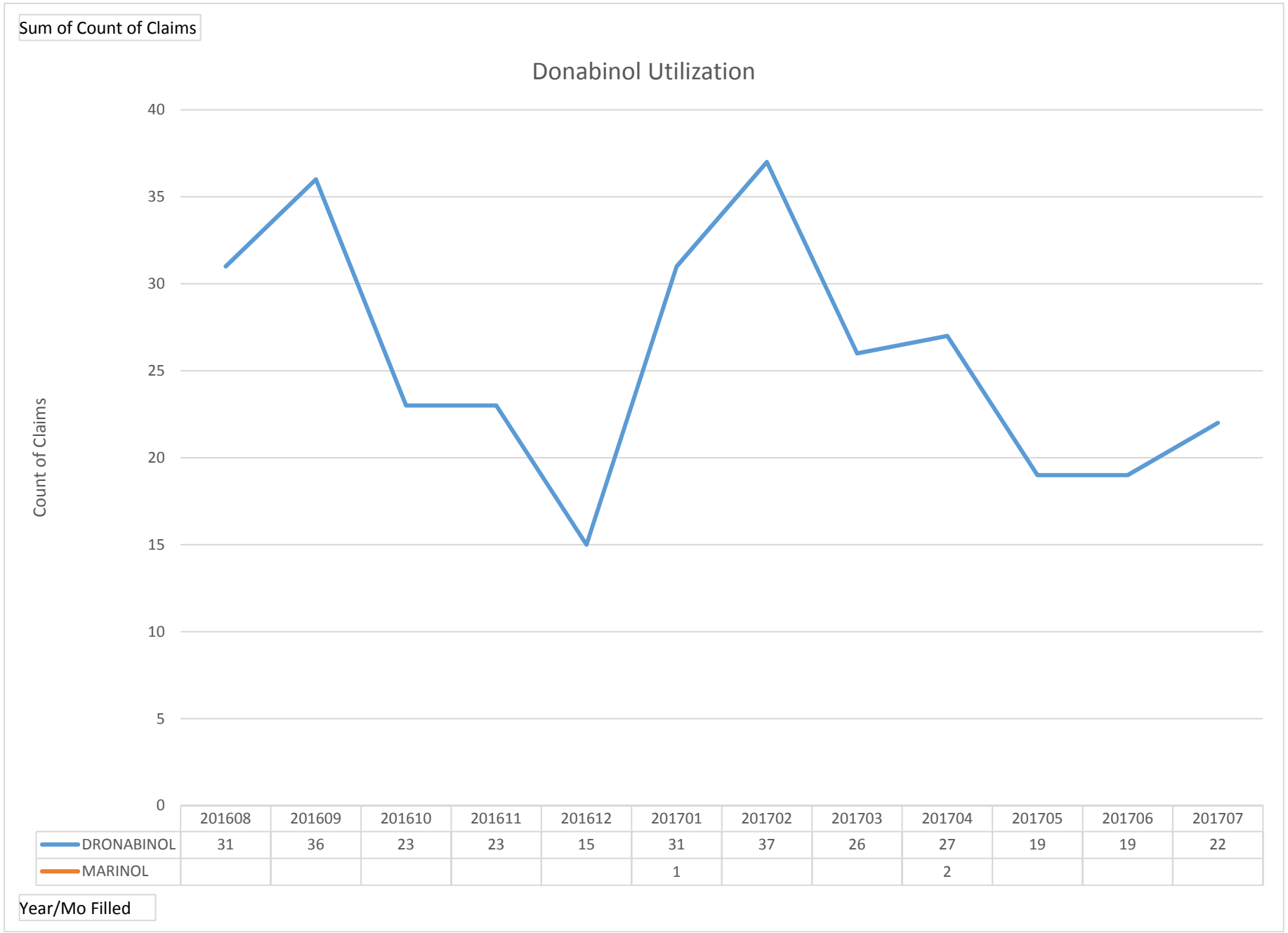
a. Prior Authorization approval will be for one year.

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

Misc. Antiemetic Utilization

August 2016 - July 2017

Year/Mo Filled	Product Name	Count of Members	Count of Claims	Qty Total	Days Supply	Pharm Paid
201608	DRONABINOL	23	31	1427	672	$ 5,595.33
201609	DRONABINOL	24	36	1420	670	$ 4,797.38
201610	DRONABINOL	20	23	1461	591	$ 7,154.25
201611	DRONABINOL	20	23	1487	573	$ 6,599.35
201612	DRONABINOL	14	15	870	440	$ 4,367.55
201701	DRONABINOL	28	31	1722	846	$ 6,519.67
201701	MARINOL	1	1	1	1	$ 3.47
201702	DRONABINOL	25	37	1358	637	$ 4,110.03
201703	DRONABINOL	24	26	1383	658	$ 6,105.72
201704	DRONABINOL	25	27	1403	695	$ 6,721.40
201704	MARINOL	1	2	2	2	$ 6.94
201705	DRONABINOL	19	19	1085	513	$ 5,777.93
201706	DRONABINOL	19	19	1170	570	$ 6,565.85
201707	DRONABINOL	19	22	1121	545	$ 6,227.57


Sum of Count of Claims
Donabinol Utilization
Count of Claims
40
35
30
25
20
15
10
5
0
201608 201609 201610 201611 201612 201701 201702 201703 201704 201705 201706 201707
DRONABINOL 31 36 23 23 15 31 37 26 27 19 19 22
MARINOL 1 2
Year/Mo Filled

QQ. Cesamet® (Nabilone) and Marinol® (Dronabinol)

Therapeutic Class: Antiemetic
Last Reviewed by DUR Board: October 25, 2012

Cesamet® (Nabilone) and Marinol® (Dronabinol) are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the SSA and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

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

a. Cesamet® (Nabilone)

1. The recipient has a diagnosis of chemotherapy-induced nausea and/or vomiting; and

2. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one serotonin receptor antagonist; and

3. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one other antiemetic agent; and

4. The prescriber is aware of the potential for mental status changes associated with the use of this agent and will closely monitor the recipient.

b. Marinol® (Dronabinol)

1. The recipient has a diagnosis of chemotherapy-induced nausea and/or vomiting; and

a. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one serotonin receptor antagonist; and

b. The recipient has experienced an inadequate response, adverse event or has a contraindication to at least one other antiemetic agent; and

c. The prescriber is aware of the potential for mental status changes associated with the use of this agent and will closely monitor the recipient; or

2. The recipient has been diagnosed with Acquired Immune Deficiency Syndrome (AIDS) and has anorexia associated with weight loss; and the

recipient has experienced an inadequate response, adverse event or has a contraindication to megestrol (Megace®); and

a. The prescriber is aware of the potential for mental status changes associated with the use of this agent and will closely monitor the recipient.

2. Prior Authorization Guidelines

a. Prior Authorization approval will be for one year.

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

Therapeutic Class Overview
Antiemetics - Delta-9-Tetrahydrocannabinol (THC) Derivatives

INTRODUCTION

- Nausea, the sensation of anticipating vomiting, may occur with or without concomitant vomiting, which is the forceful expulsion of gastric contents, dyspepsia, and other gastrointestinal (GI) symptoms (Longstreth, 2016).
- Normal function of the upper GI tract involves interactions between the gut and the central nervous system (CNS), with the motor function of the GI tract being controlled at the level of the parasympathetic and sympathetic nervous systems, enteric brain neurons, and smooth muscle cells (Longstreth, 2016).
- An undesired outcome of surgery, opiate therapy, radiation, and other external noxious stimuli, chemotherapy-induced nausea and vomiting (CINV) is often viewed as the most severe and distressing form of nausea and vomiting (N/V) (Hesketh, 2017[a]; Hesketh, 2017[b]). Additional causes of N/V include pregnancy, vestibular neuritis, gastroenteritis, gastroparesis, GI obstruction, and rumination syndrome (Longstreth, 2016).
- Three distinct types of CINV have been defined, including (Hesketh, 2017[a]; Hesketh, 2017[b]):
    - Acute emesis, which most commonly begins within one to two hours of chemotherapy and usually peaks in the first four to six hours;
    - Delayed emesis, occurring beyond 24 hours after chemotherapy; and
    - Anticipatory emesis, occurring prior to treatment as a conditioned response in patients who have developed significant N/V during previous cycles of chemotherapy.
- The precise mechanism by which chemotherapy induces emesis remains unclear; however, proposed theories include chemotherapeutic agents and their metabolites interacting directly and indirectly with receptors in the limbic forebrain (e.g., amygdala); intestinal cell wall damage caused by chemotherapy which results in 5-hydroxytryptamine (5-HT) activating the emetic cascade; as well as the release of substance P from sensory neurons after chemotherapy administration (Hesketh, 2017[a]).
- Physiologic pathways involved in the treatment of N/V primarily involve dopamine and serotonin ($5\text{-}HT_3$). Other receptors, which have a lesser role, include muscarinic, opiate, histamine H_1, cannabinoid, and neurokinin 1 (NK1) (Andrews et al, 1998; Lynch, 2005).
- Chemotherapy agents, which often cause N/V as adverse effects, are categorized based upon their emetogenicity.
    - High emetogenicity is associated with a >90% risk of emesis.
    - Moderate emetogenicity is associated with a >30 to 90% risk of emesis.
    - Low emetogenicity is associated with a 10 to 30% risk of emesis.
    - Minimal emetogenicity is associated with a <10% risk of emesis (Hesketh, 2017[a]; Hesketh, 2017[b]).
- Cannabinoid receptors have been discovered in neural tissues, and these receptors may play a role in mediating the antiemetic effects of cannabinoids such as dronabinol and nabilone. These agents, like other cannabinoids, have the potential to be abused and produce psychological dependence. Both dronabinol and nabilone may produce alterations in mood (euphoria, detachment, depression, anxiety) and alterations in reality (distorted perceptions of objects and time and hallucinations).
- Dronabinol and nabilone are Food and Drug Administration (FDA)-approved for the treatment of CINV in patients failing to respond to conventional antiemetic treatments.
- The 2016 American Society of Clinical Oncology (ASCO) antiemetic guidelines do not designate cannabinoids (e.g., nabilone, dronabinol) as appropriate first-line antiemetics for patients receiving chemotherapy of high to low emetic risk (Hesketh et al, 2016).
- Medispan Class: Antiemetics – Miscellaneous
- The scope of this review will focus on the agents outlined in Table 1 for their respective FDA-approved indications as related to CINV.

Table 1. Medications Included Within Class Review

Drug	Manufacturer	FDA Approval Date	Generic Availability
CESAMET® (nabilone)	Meda Pharms	12/26/1985	–
MARINOL® (dronabinol)	Abbvie	05/31/1985	✔
SYNDROS™*(dronabinol)	Insys	7/1/2016	–

*SYNDROS has not yet been marketed
(DRUGS@FDA.com, 2017; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2017)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	CESAMET (nabilone)	MARINOL (dronabinol)	SYNDROS (dronabinol)
Anorexia associated with weight loss in patients with AIDS.		✔	✔
N/V associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.	✔	✔	✔

(Prescribing information: MARINOL, 2016; CESAMET, 2013; SYNDROS, 2016)

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

CLINICAL EFFICACY SUMMARY

- For the management of CINV, meta-analyses and head-to-head trials have demonstrated that the cannabinoids are more effective compared to placebo and may be more effective than prochlorperazine and metoclopramide.
- In a study by Lane et al, the combination of dronabinol plus prochlorperazine significantly reduced the mean duration of vomiting per episode compared to either agent administered with placebo (Lane et al, 1991).
- In a small study, Meiri et al reported that dronabinol and ondansetron were similarly effective for the management of delayed CINV, but combination therapy with these two agents was not more effective than either agent alone (Meiri et al, 2007).
- In a large meta-analysis (13 dronabinol studies and 16 nabilone studies), treatment with cannabinoids was more effective for complete control of nausea in the first 24 hours of chemotherapy compared to alizapride, chlorpromazine, domperidone, haloperidol, metoclopramide, prochlorperazine, or thiethylperazine (relative risk [RR], 1.38; 95% confidence interval [CI], 1.18 to 1.62; number needed to treat [NNT]=6) and for complete control of vomiting (RR, 1.28; 95% CI, 1.08 to 1.51; NNT=8). Of note, cannabinoids were not more effective compared to other agents when the chemotherapy regimen was of very high- or very low-emetogenic risk (Tramèr et al, 2001).
- In a second meta-analysis, authors concluded that with regard to antiemetic efficacy, dronabinol was no more effective compared to placebo (RR, 0.47; 95% CI, 0.19 to 1.16; P=0.1) but was more effective compared to neuroleptics (RR, 0.67; 95% CI, 0.47 to 0.96; NNT=3.4). Nabilone was not more effective than neuroleptics (RR, 0.88; 95% CI, 0.72 to 1.08; P=0.21). With regard to patient preference and tolerability, cannabinoids were preferred over other study agents (RR, 0.33; 95% CI, 0.24 to 0.44; P<0.00001; NNT=1.8) (Machado Rocha et al, 2008).
- A third meta-analysis evaluated the efficacy and safety of cannabinoids in various conditions, including CINV (Whiting et al, 2015). In these indications, compared to placebo, cannabinoids were associated with a higher proportion of patients with a complete N/V response (47% vs 20%; odds ratio [OR], 3.82; 95% CI, 1.55 to 9.42). However, these results reflect the effects of cannabinoids that are not FDA-approved, which were included in the analysis.
- In a meta-analysis of 23 randomized controlled trials (11 dronabinol studies and 12 nabilone studies), compared to placebo, treatment with cannabinoids resulted in a higher chance of reporting complete absence of N/V (3 studies; RR, 2.9; 95% CI, 1.8 to 4.7); however, patients were more likely to withdraw due to an adverse event compared to placebo (2 trials; RR, 6.9; 95% CI, 1.96 to 24) and compared to prochlorperazine (5 studies; RR, 3.9; 95% CI, 1.3 to 12). The proportion of patients who reported absence of N/V was not different between cannabinoids and prochlorperazine (Smith et al, 2015).
- There are no published clinical trials comparing dronabinol to nabilone for CINV.

- The effectiveness of SYNDROS (dronabinol) oral solution for its FDA-approved indications was based on studies of dronabinol capsules.
- The 2016 ASCO antiemetic guidelines recommend the following for CINV (Hesketh et al, 2016):
    - For the prevention of N/V induced by highly emetogenic chemotherapy agents, a three drug combination of an NK_1 receptor antagonist, a 5-HT_3 receptor antagonist, and dexamethasone is recommended as first-line therapy.
    - For moderately emetogenic agents, a two-drug combination of ALOXI (palonosetron) and dexamethasone is recommended.
    - For children receiving highly or moderately emetogenic agents, a 5-HT_3 receptor antagonist plus a corticosteroid is recommended.
    - Cannabinoids (e.g., nabilone, dronabinol) are not listed as appropriate first-line antiemetics for any group of patients receiving chemotherapy of high to low emetic risk.

SAFETY SUMMARY

- Dronabinol and nabilone are synthetic, orally active cannabinoids, which have complex effects on the central nervous system, including central sympathomimetic activity.
- These agents, like other cannabinoids, have the potential to be abused and produce psychological dependence. Both dronabinol and nabilone may produce alterations in mood and alterations in reality (distorted perceptions of objects and time and hallucinations).
- Dronabinol and nabilone are contraindicated in individuals who are allergic to cannabinoids. SYNDROS is contraindicated in patients with hypersensitivity to alcohol and in patients who have received products containing disulfiram or metronidazole within 14 days. SYNDROS contains dehydrated alcohol (50%, w/w) and propylene glycol (5.5%, w/w). Disulfiram- and metronidazole-containing products should not be administered within seven days of completing SYNDROS treatment.
- In both placebo and active controlled trials, greater than 10% of patients experienced dizziness, drowsiness, dry mouth, euphoria, and coordination disturbance with either cannabinoid.
- Consider risks and benefits of using dronabinol in patients with a history of seizures. Patients with cardiac disorders may experience cardiac effects such as hypotension, hypertension, syncope, or tachycardia with cannabinoids.
- Dronabinol and nabilone may exacerbate or unmask symptoms of mania, depression, or schizophrenia.
- SYNDROS and MARINOL both contain the same active ingredient, dronabinol, and the safety of SYNDROS oral solution was based on studies using dronabinol capsules. The SYNDROS prescribing information contains updated warnings and precautions, including:
    - Avoid SYNDROS in patients with a psychiatric history or monitor patients for new or worsening psychiatric symptoms if use of SYNDROS cannot be avoided.
    - Reduce the dose or discontinue if signs and symptoms of cognitive impairment occur.
    - Consider a dose reduction or discontinue in patients who develop worsening nausea, vomiting, or abdominal pain while taking SYNDROS.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Dose	Other Dosing Considerations
MARINOL (dronabinol)	Capsule: 2.5 mg 5 mg 10 mg	**ADULT** <u>Treatment of chemotherapy-induced nausea and vomiting:</u> Capsule: initial, 5 mg/m^2 given one to three hours prior to the administration of chemotherapy; maintenance, 5 mg/m^2 every two to four hours after chemotherapy for a total of four to six doses/day; maximum, the dose may be titrated by 2.5 mg/m^2 increments to a maximum of 15 mg/m^2 per dose in the absence of significant adverse events. <u>Treatment of anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome:</u>	Capsules are not recommended for AIDS-related anorexia in pediatric patients, because safety and efficacy have not been established.

Drug	Dosage Form: Strength	Dose	Other Dosing Considerations
		Capsule, initial, 2.5 mg orally twice daily, prior to lunch and dinner; if adverse effects occur and do not resolve in one to three days with continued use, reduce dose to 2.5 mg per day before dinner or at bedtime; maximum, 20 mg per day if clinically indicated and absence of significant adverse events. **PEDIATRIC** Treatment of chemotherapy-induced nausea and vomiting: Capsule: initial, 5 mg/m^2 administered one to three hours prior to the administration of chemotherapy; maintenance, 5 mg/m^2 every two to four hours after chemotherapy for a total of four to six doses/day; maximum, the dose may be titrated by 2.5 mg/m^2 increments to a maximum of 15 mg/m^2 per dose in the absence of significant adverse events.	
SYNDROS (dronabinol)	Oral solution: 5 mg/mL	**ADULT** Treatment of chemotherapy-induced nausea and vomiting: Oral solution: initial, 4.2 mg/m^2 one to three hours prior to chemotherapy then every two to four hours after chemotherapy for a total of four to six doses per day; titrate dose to clinical response as tolerated in increments of 2.1 mg/m^2; maximum, 12.6 mg/m^2 per dose for four to six doses per day; consider decreasing dose to 2.1 mg once daily one to three hours prior to chemotherapy to reduce risk of CNS adverse reactions. In elderly, consider initiating dose at 2.1 mg/m^2 once daily one to three hours prior to chemotherapy. Treatment of anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome: Oral solution: initial, 2.1 mg twice daily to begin one hour before lunch and dinner; dosage may be increased gradually to 2.1 mg one hour before lunch and 4.2 mg one hour before dinner; the dose may be further increased to 4.2 mg one hour before lunch and dinner; maximum, 8.4 mg twice daily; reduce dose to 2.1 mg once daily one hour prior to dinner or prior to bedtime if CNS adverse reactions are severe or persistent. In elderly, consider initiating dose at 2.1 mg once daily one hour before dinner or at bedtime.	Always use calibrated oral dosing syringe for administration; the oral syringe holds a maximum of 5 mg; if the prescribed dose is greater than 5 mg, it must be divided in multiple doses. Take with 6 to 8 ounces of water. For CINV: round initial dose to nearest 0.1 mg increment; the dose may need to be rounded to the nearest 0.1 mL increment to correspond with a calibrated oral dosing syringe. Administer first dose on an empty stomach at least 30 minutes before eating. Subsequent doses can be taken without regard to meals, but timing of dose in regard to meal times should be kept consistent.

Drug	Dosage Form: Strength	Dose	Other Dosing Considerations
CESAMET (nabilone)	Capsule: 1 mg	**ADULT** Treatment of chemotherapy-induced nausea and vomiting: Capsule: initial, 1 to 2 mg twice daily to begin one to three hours prior to the administration of chemotherapy; dose of 1 or 2 mg the night before chemotherapy may be useful; may be administered two or three times daily during the entire course of each cycle and, if needed, for 48 hours after the last dose of each cycle; maximum, 2 mg three times a day.	Safety and efficacy in children <18 years of age have not been established.

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
CESAMET (nabilone)	Safety and efficacy in elderly patients have not been established.	Safety and efficacy in children <18 years of age have not been established.	Not studied in renal dysfunction.	Not studied in hepatic dysfunction.	Pregnancy Category C Unknown whether excreted in breast milk. Because many drugs including some cannabinoids are excreted in breast milk; use is not recommended in nursing mothers.
MARINOL (dronabinol)	Caution advised in the elderly as they may be more sensitive to neurological, psychoactive and hypotensive effects.	Pediatric dosage for the treatment of chemotherapy-induced emesis is the same as in adults. Not recommended for AIDS-related anorexia as it has not been studied in this population.	No dosage adjustment required.	No dosage adjustment required.	Pregnancy Category C Dronabinol is excreted in breast milk; use is not recommended in nursing mothers.
SYNDROS (dronabinol)	Caution advised in the elderly as they may be more sensitive to neurological, psychoactive and hypotensive effects; elderly patients with dementia are at an increased risk for falls.	Safety and efficacy in pediatric patients have not been established. Avoid use in preterm neonates in the immediate postnatal period due to possible propylene glycol-associated toxicities.	No dosage adjustment required.	No dosage adjustment required.	Unclassified† Women infected with HIV are advised not to breastfeed; women with CINV are advised not to breastfeed during SYNDROS treatment or for at least 9 days after the last dose.

* Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

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

CONCLUSION

- Physiologic pathways involved in the treatment of nausea and vomiting primarily involve dopamine and serotonin (5-HT_3). Other receptors, which have a lesser role, include muscarinic, opiate, histamine H_1, cannabinoid and neurokinin 1.
- Treatment of chemotherapy-induced nausea and vomiting (CINV) generally involves the use of multiple agents that affect different receptor types, such as a dopamine antagonist, a steroid, and a 5-HT_3 receptor antagonist (Basch et al, 2011).
- The choice of antiemetic therapy is generally dependent upon the relative emetogenic potential of the chemotherapy regimen. If one antiemetic regimen is ineffective, it is appropriate to use or add a different agent. General practice guidelines state, if breakthrough emesis or nausea occurs, the addition of an agent with a different mechanism of action is recommended. The American Society of Clinical Oncology (ASCO) guidelines for antiemetics in oncology do not consider cannabinoids (e.g., nabilone, dronabinol) appropriate first-line antiemetics for any group of patients receiving chemotherapy of high to low emetic risk (Hesketh et al, 2016).
- Dronabinol and nabilone are Food and Drug Administration (FDA)-approved for the treatment of CINV in patients failing to respond to conventional antiemetic treatments. Meta-analyses and placebo-controlled trials demonstrated that the cannabinoids are more effective compared to placebo and may be more effective than metoclopramide and prochlorperazine (Lane et al, 1991; Meiri et al, 2007; Machado Rocha et al, 2008; Tramer et al, 2001).
- Due to the availability of other agents that are more effective and better tolerated compared to the cannabinoids, dronabinol and nabilone are not considered first-line agents. Both of these agents have a high abuse potential and are regulated under the Controlled Substances Act.
- There are no head-to-head studies comparing dronabinol to nabilone for their FDA-approved indications. Dronabinol capsules (MARINOL) are available in a generic formulation while dronabinol oral solution (SYNDROS) and nabilone (CESAMET) are only available as branded agents.

Table 5. Advantages and Disadvantages of Delta-9-Tetrahydrocannabinol (THC) Derivatives

Drug	Advantages	Disadvantages
CESAMET (nabilone)	• Dosed twice daily	• CESAMET is a schedule II controlled substance
MARINOL (dronabinol)	• Generic formulation available. • Also indicated for anorexia associated with weight loss in adult patients with AIDS • Indicated in adult and pediatric populations for CINV	• MARINOL is a schedule III controlled substance • Requires refrigeration • Dosed three to four times daily
SYNDROS (dronabinol)	• Oral solution • Also indicated for anorexia associated with weight loss in adult patients with AIDS	• SYNDROS is a schedule II controlled substance • SYNDROS contains 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol

(Insys Therapeutics)

REFERENCES

- Andrews PLR, Naylor RJ, Joss RA. Neuropharmacology of emesis and its relevance to anti-emetic therapy. Consensus and controversies. Support Care Cancer. 1998;6:197–203.
- Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2011;29(31):4189-98.
- CESAMET prescribing information. Somerset, NJ. Meda Pharmaceuticals Inc. September 2013.
- Drugs@FDA [database on the Internet]. Rockville (MD): Food and Drug Administration (US), Center for Drug Evaluation and Research; 2017. Available from: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed March 23, 2017.
- Hesketh PJ. Pathophysiology and prediction of chemotherapy-induced nausea and vomiting. In: Post TW (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2017[a]. Available by subscription at: http://www.uptodate.com/home . Accessed March 23, 2017.
- Hesketh PJ. Prevention and treatment of chemotherapy-induced nausea and vomiting in adults. In: Post TW (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2017[b]. Available by subscription at: http://www.uptodate.com/home . Accessed March 23, 2017.
- Hesketh PJ, Bohlke K, Lyman GH, et al. Antiemetics: American Society of Clinical Oncology focused guideline update. J Clin Oncol. 2016;34(4):381-386.

- Insys Therapeutics. News release: DEA Schedules Insys Therapeutics' Syndros (dronabinol oral solution) as Schedule II drug. Available at: http://investors.insysrx.com/phoenix.zhtml?c=115949&p=irol-newsArticle&ID=2256036. Insys Therapeutics website. March 23, 2017. Accessed March 23, 2017.
- Lane M, Vogel CL, Ferguson J. Dronabinol and prochlorperazine in combination for treatment of cancer chemotherapy-induced nausea and vomiting. J Pain Symptom Manage. 1991;6(6):352-9.
- Longstreth GF. Approach to the adult with nausea and vomiting. In: Post TW (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2017. Available by subscription at: http://www.uptodate.com/home. Accessed March 23, 2017.
- Lynch ME. Preclinical science regarding cannabinoids as analgesics: an overview. Pain Res Manage 2005; 10(suppl A):7A-14A.
- Machado Rocha FC, Stéfano SC, De Cássia Haiek R, et al. Therapeutic use of Cannabis sativa on chemotherapy-induced nausea and vomiting among cancer patients: systematic review and meta-analysis. Eur J Cancer Care (Engl). 2008;17(5):431-43.
- MARINOL prescribing information. North Chicago, IL. Abbvie Inc. June 2016.
- Meiri E, Jhangiani H, Vredenburgh JJ, et al. Efficacy of dronabinol alone and in combination with ondansetron vs ondansetron alone for delayed chemotherapy-induced nausea and vomiting. Curr Med Res Opin. 2007;23(3):533-43.
- Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations [database on the internet]. Rockville (MD): U.S. Food and Drug Administration. 2017. Available from: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Accessed March 23, 2017.
- Smith LA, Azariah F, Lavender VTC, et al. Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy (Review). Cochrane Database of Systematic Reviews. 2015, Issue 11. Art. No.: CD009464.
- SYNDROS prescribing information. Chandler, AZ. Insys Therapeutics, Inc. July 2016.
- Tramèr MR, Carroll D, Campbell FA, et al. Cannabinoids for control of chemotherapy-induced nausea and vomiting: quantitative systematic review. BMJ. 2001;323(7303):16-21.
- Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. JAMA. 2015;313(24):2456-2473.

Publication date: March 24, 2017

SILIQ (brodalumab)
Pharmacy Coverage Guideline

Brand Name	Generic Name	GPI
SILIQ	brodalumab	TBD

CRITERIA FOR COVERAGE/NONCOVERAGE

SILIQ (brodalumab) will be considered for coverage under the pharmacy benefit program when the following criteria are met:

Plaque psoriasis

1. Diagnosis of moderate to severe plaque psoriasis **AND**
2. Prescribed by or in consultation with a dermatologist **AND**
3. One of the following:
  3.1 Both of the following:
    3.1.1 Trial and failure, contraindication, or intolerance to ONE of the following: [4]
      - Humira (adalimumab) **OR**
      - Stelara (ustekinumab)

      AND
    3.1.2 Trial and failure, contraindication, or intolerance to Taltz (ixekizumab)
  OR
  3.2 For continuation of prior Siliq therapy

AND

4. Patient is not receiving Siliq in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab pegol), Simponi (golimumab)] **AND**

Initial Authorization Duration: 12 months

Reauthorization Criteria and Duration:
Authorization for continued use shall be reviewed at least every 12 months when the following criteria are met:

1. Documentation of positive clinical response to Siliq therapy **AND**
2. Patient is not receiving Siliq in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab pegol), Simponi (golimumab)]

REFERENCES

1. Siliq Prescribing Information. Valeant Pharmaceuticals Int., February 2017.

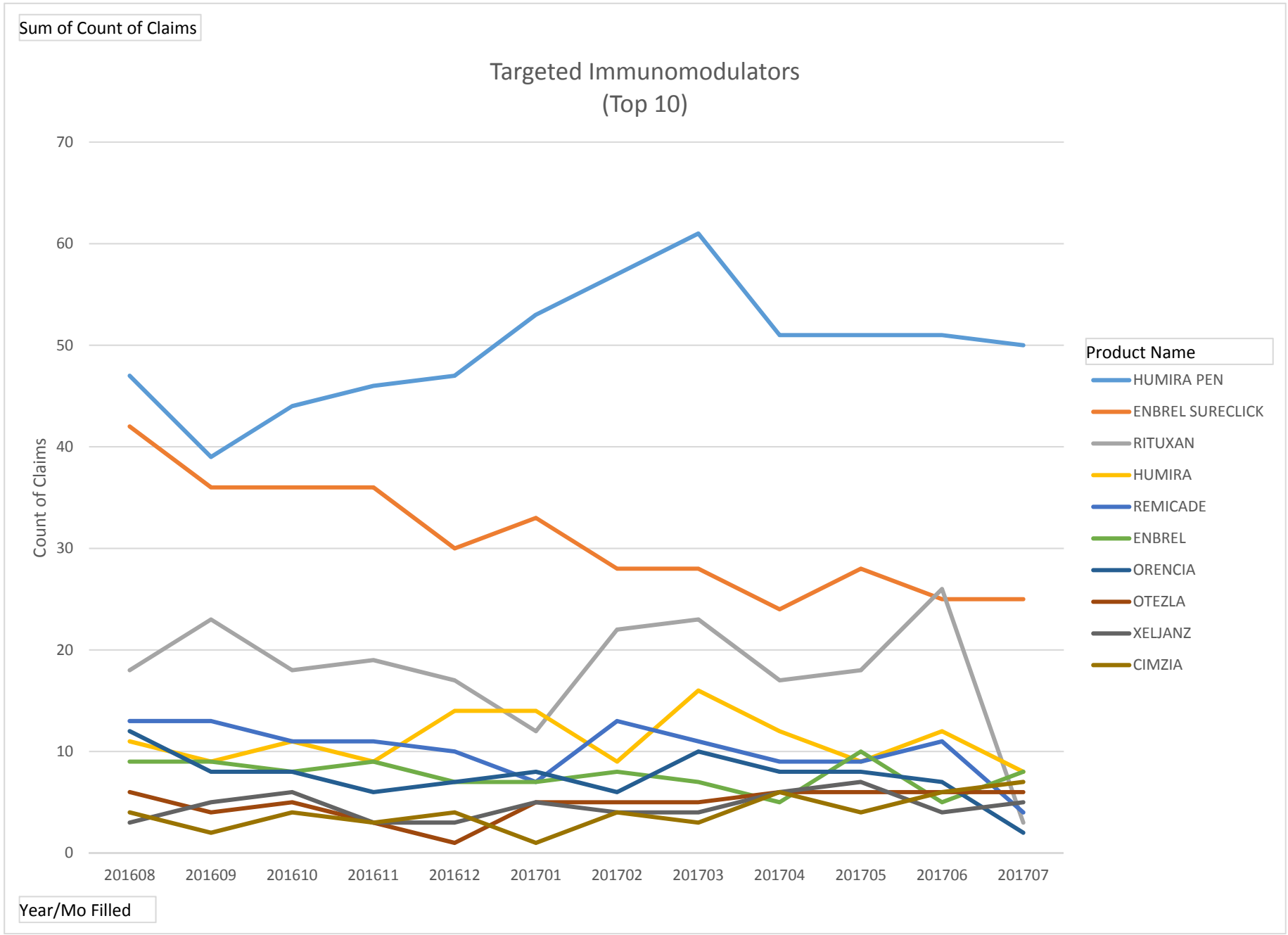
2. Lebwohl M, Strober B, Menter A et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. *N Engl J Med.* 2015; 373:1318-28.

3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011;65:137-74.

Targeted Immunomodulators

August 2016 - July 2017

Row Labels	Member Count	Claim Count	Qty	Days Supp		Total Paid
ACTEMRA	24	34	271	520	$	66,544.69
CIMZIA	38	48	50	1,404	$	165,584.12
CIMZIA STARTER KIT	4	4	12	134	$	43,689.96
COSENTYX	4	7	8	7	$	200.00
COSENTYX SENSOREADY PEN	37	44	108	1,236	$	233,353.63
ENBREL	86	92	448	2,894	$	332,145.37
ENBREL SURECLICK	341	371	1,564	10,675	$	1,574,959.43
ENTYVIO	17	20	21	210	$	110,784.83
HUMIRA	126	134	314	3,808	$	637,318.58
HUMIRA PEN	544	597	1,438	16,603	$	2,445,840.99
HUMIRA PEN-CROHNS DISEASE	10	10	60	375	$	100,685.25
HUMIRA PEN-PSORIASIS STAR	10	10	40	305	$	75,794.83
INFLECTRA	2	2	60	2	$	16,221.00
KADCYLA	25	31	75	31	$	217,860.36
KINERET	12	13	431	364	$	84,763.25
ORENCIA	87	90	305	715	$	198,791.67
ORENCIA CLICKJECT	3	3	12	84	$	11,516.22
OTEZLA	55	58	3,475	1,738	$	115,387.49
REMICADE	121	122	478	541	$	418,615.46
RITUXAN	164	216	13,120	335	$	907,344.45
SIMPONI	16	17	9	496	$	58,334.01
SIMPONI ARIA	2	2	1,012	57	$	22,108.94
STELARA	27	27	180	889	$	415,698.82
TALTZ	7	9	19	144	$	60,117.95
TREMFYA	1	1	1	1	$	20.00
XELJANZ	52	55	3,240	1,650	$	189,623.77
XELJANZ XR	15	16	480	480	$	39,945.54
Grand Total	**1,830**	**2,033**	**27,230**	**45,698**	**$**	**8,543,250.61**


Sum of Count of Claims
Targeted Immunomodulators
(Top 10)
70
60
50
40
30
20
10
0
Count of Claims
201608
201609
201610
201611
201612
201701
201702
201703
201704
201705
201706
201707
Year/Mo Filled
Product Name
HUMIRA PEN
ENBREL SURECLICK
RITUXAN
HUMIRA
REMICADE
ENBREL
ORENCIA
OTEZLA
XELJANZ
CIMZIA

L. Immunomodulator Drugs

Therapeutic Class: Immunomodulators
Last Reviewed by the DUR Board: November 5, 2015

Actemra® (tocilizumab)	Ilaris ® (canakinumab)
Amevive® (alefacept)	Kineret® (ankinra)
Arcalyst ® (rilonacept)	Orencia® (abatacept)
Cimzia® (certolizumab pegol)	Remicade® (infliximab)
Consentyx® (secukinumab)	Simponi® (golimumab)
Enbrel® (etanercept)	Simponi® ARIA™ (golimumab)
Entyvio® (vedolizumab)	Stelara® (ustekinumab)
Humira® (adalimumab)	Xeljanz® (tofacitinib)

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

1. Coverage and Limitations

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

a. For all recipients:

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

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

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

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

b. Rheumatoid Arthritis (RA):

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

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

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

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

hydroxychloroquine, leflunomide, minocycline and sulfasalazine); or

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

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

c. Psoriatic Arthritis:

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

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

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

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

d. Ankylosing Spondylitis:

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

2. The recipient is 18 years or older; and

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

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

e. Juvenile Rheumatoid Arthritis/Juvenile Idiopathic Arthritis:

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

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

a. Abatacept: Six years of age or older.

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

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

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

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

f. Plaque Psoriasis:

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

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

3. The agent is prescribed by a dermatologist; and

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

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

g. Crohn's Disease:

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

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

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

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

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

4. The recipient has fistulizing Crohn's Disease.

h. Ulcerative Colitis:

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

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

a. Infiximab: Six years of age or older.

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

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

a. Corticosteroids;

b. 5-aminosalicylic acid agents;

c. Immunosuppresants; and/or

d. Thiopurines.

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

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

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

a. Canakinumab: Four years of age or older.

b. Rilonacept: 12 years of age or older.

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

1. The recipient has a diagnosis of NOMID.

2. Prior Authorization Guidelines

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

Prior authorization approval will be for one year.

INTRODUCTION

- Immunomodulators treat a wide variety of conditions, including rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), plaque psoriasis (PsO), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC), hidradenitis suppurativa (HS), and uveitis (UV), as well as several less common conditions.
- T cells, B cells, and cytokines such as tumor necrosis factor (TNF), interleukin-1 (IL-1) and interleukin-6 (IL-6) play a key role in the inflammatory and immune process (Choy et al, 2001). This has led to the development of biologic agents to target these areas. The Food and Drug Administration (FDA) has currently approved five originator TNF inhibitors: CIMZIA® (certolizumab), ENBREL® (etanercept), HUMIRA® (adalimumab), REMICADE® (infliximab), and SIMPONI®/SIMPONI® ARIA™ (golimumab), as well as three biosimilar TNF inhibitors: AMJEVITA (adalimumab-atto), ERELZI (etanercept-szzs), and INFLECTRA (infliximab-dyyb). Other agents targeting different cells and cytokines are also FDA approved for RA treatment. These include ORENCIA® (abatacept), which inhibits CD28-B7 mediated costimulation of the T-cell; RITUXAN® (rituximab), which targets CD20, a molecule that is found on the surface of B-cells; ACTEMRA® (tocilizumab), which has activity directed against the IL-6 receptor; and KINERET® (anakinra), which targets the IL-1 receptor. An oral agent on the market, XELJANZ® and XELJANZ® XR (tofacitinib), targets Janus-associated kinase (JAK) pathways. By inhibiting the JAK pathway, the ability of cytokines to produce inflammation is reduced.
- Other immunomodulators include ILARIS® (canakinumab), which binds to the IL-1ß receptor and is approved to treat JIA; and ENTYVIO™ (vedolizumab), which binds to the α4β7 integrin and is approved to treat CD and UC. OTEZLA® (apremilast), an oral, small-molecule phosphodiesterase 4 (PDE-4) inhibitor, and STELARA (ustekinumab), which targets the IL-12 and IL-23 cytokines, are each approved for the treatment of PsA and PsO; STELARA is additionally indicated for the treatment of CD. COSENTYX™ (secukinumab) and TALTZ® (ixekizumab) bind and neutralize IL-17A and are indicated for the treatment of PsO; COSENTYX is additionally indicated to treat PsA and AS. A related agent, SILIQ™ (brodalumab), is an IL-17 receptor antagonist indicated for selected patients with PsO.
- Certain rare conditions for which immunomodulators are indicated are mentioned in this review but are not discussed in detail; these include:
    - ILARIS for the treatment of 1) cryopyrin-associated periodic syndromes (CAPS), specifically the subtypes familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS); 2) TNF receptor associated periodic syndrome (TRAPS); 3) hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD); and 4) familial Mediterranean fever (FMF)
    - KINERET for the treatment of CAPS, specifically neonatal-onset multisystem inflammatory disease (NOMID)
- RITUXAN is also approved for non–Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), and granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis) and microscopic polyangiitis (MPA). These indications will not be discussed in this review.
- TYSABRI® (natalizumab), an integrin receptor antagonist, is indicated for multiple sclerosis and CD for patients who have had an inadequate response to, or are unable to tolerate conventional therapies and TNF inhibitors; it is not included as a drug product in this review (TYSABRI prescribing information, 2016). ARCALYST (rilonacept), an interleukin-1 blocker indicated for CAPS, is also not included in this review (ARCALYST prescribing information, 2016).
- Although FDA approved, the launch plans for AMJEVITA (adalimumab-atto) and ERELZI (etanercept-szzs) are pending and may be delayed; thus, information on AMJEVITA and ERELZI is not currently included in this review.
- Medispan Classes: Antineoplastic-Monoclonal Antibodies, Antipsoriatics, Antirheumatic-Enzyme Inhibitors, Anti-TNF-Alpha-Monoclonal Antibodies, Integrin Receptor Antagonists, Interleukin-1 Receptor Antagonists, Interleukin-1beta Receptor Inhibitors, Interleukin-6 Receptor Inhibitors, PDE-4 Inhibitors, Selective Costimulation Modulators, Soluble Tumor Necrosis Factor Receptor Agents, Tumor Necrosis Factor Alpha Blockers

Table 1. Medications Included Within Class Review

Drug	Manufacturer	FDA Approval Date	Biosimilar or Generic Availability	Type of Agent
ACTEMRA (tocilizumab)	Genentech	01/08/2010	-	Human monoclonal antibody targeting the IL-6 receptor
CIMZIA (certolizumab)	UCB	04/22/2008	-	TNFα inhibitor
COSENTYX (secukinumab)	Novartis	01/21/2015	-	Human monoclonal antibody to IL-17A
ENBREL (etanercept)	Amgen	11/02/1998	-*	sTNFR fusion protein, TNFα inhibitor
ENTYVIO (vedolizumab)	Takeda Pharmaceuticals America, Inc.	05/20/2014	-	Human monoclonal antibody binds to the α4β7 integrin
HUMIRA (adalimumab)	Abbott	12/31/2002	-*	TNFα inhibitor
ILARIS (canakinumab)	Novartis	06/17/2009	-	Human monoclonal antibody that binds to IL-1ß
INFLECTRA (infliximab-dyyb)	Celltrion/ Hospira/Pfizer	04/05/2016	N/A†	TNFα inhibitor
KINERET (anakinra)	Swedish Orphan Biovitrum	11/14/2001	-	IL-1 receptor antagonist
ORENCIA (abatacept)	Bristol Myers Squibb	12/23/2005	-	sCTLA-4-Ig recombinant fusion protein
OTEZLA (apremilast)	Celgene Corporation	03/21/2014	-	Small-molecule phosphodiesterase 4 inhibitor
REMICADE (infliximab)	Janssen Biotech	8/24/1998	-†	TNFα inhibitor
RITUXAN (rituximab)	Genentech	11/26/1997	-	Anti-CD20 monoclonal antibody
SILIQ (brodalumab)‡	Valeant	02/15/2017	-	Human monoclonal antibody directed against the IL-17 receptor A (IL-17RA)
SIMPONI/ SIMPONI ARIA (golimumab)	Janssen Biotech	04/24/2009 and 07/18/2013	-	TNFα inhibitor
STELARA (ustekinumab)	Janssen Biotech	09/25/2009	-	Human monoclonal antibody targeting the IL-12 and IL-23 cytokines
TALTZ (ixekizumab)	Eli Lilly	03/22/2016	-	Human monoclonal antibody to IL-17A
XELJANZ / XELJANZ XR (tofacitinib)	Pfizer	11/06/2012 and 02/23/2016	-	Small molecule Janus kinase (JAK) inhibitor

*ERELZI (etanercept-szzs) and AMJEVITA (adalimumab-atto) have been FDA approved as biosimilars to ENBREL (etanercept) and HUMIRA (adalimumab), respectively. The specific launch dates for these products are pending and may be delayed. Further information on ERELZI and AMJEVITA will be included in this review closer to the time of launch.
†INFLECTRA (infliximab-dyyb) has been FDA approved as a biosimilar to REMICADE (infliximab). It is not an interchangeable biologic.
‡SILIQ is anticipated to be launched in the second half of 2017.

(Drugs@FDA, 2016; Prescribing information: ACTEMRA, 2016; CIMZIA, 2017; COSENTYX, 2016; ENBREL, 2016; ENTYVIO, 2014; HUMIRA, 2016; ILARIS, 2016; INFLECTRA, 2016; KINERET, 2016; ORENCIA, 2016; OTEZLA, 2015; REMICADE, 2015; RITUXAN, 2014; SILIQ, 2017; SIMPONI, 2017; SIMPONI ARIA, 2017; STELARA, 2016; TALTZ, 2016; XELJANZ/XELJANZ XR, 2016)

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

INDICATIONS

Table 2. Food and Drug Administration Approved Indications (see footnotes for less common indications: CAPS, FMF, HIDS/MKD, and TRAPS)

Drug	Rheumatoid Arthritis (RA)	Crohn's Disease (CD)	Systemic Juvenile Idiopathic Arthritis (SJIA)	Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Ulcerative Colitis (UC)	Hidradenitis Suppurativa (HS)	Uveitis (UV)
ACTEMRA (tocilizumab)	✔ *		✔ **	✔ **						
CIMZIA (certolizumab)	✔	✔				✔	✔			
COSENTYX (secukinumab)					✔ ‡	✔	✔			
ENBREL (etanercept)	✔ †			✔ **	✔ ‡	✔ †	✔			
ENTYVIO (vedolizumab)		✔						✔		
HUMIRA (adalimumab)	✔ ‡‡	✔ ⌐		✔ ∫	✔ ‡	✔ ∫∫	✔	✔	✔	✔ ▼

Drug	Rheumatoid Arthritis (RA)	Crohn's Disease (CD)	Systemic Juvenile Idiopathic Arthritis (SJIA)	Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Ulcerative Colitis (UC)	Hidradenitis Suppurativa (HS)	Uveitis (UV)
ILARIS" (canakinumab)			✔ **							
INFLECTRA (infliximab-dyyb)	✔ ⊥	✔ ⌐⌐			✔ ‡‡‡	✔	✔	✔ ⊥⊥		
KINERET▾▾ (anakinra)	✔ ∞									
ORENCIA (abatacept)	✔ ∞∞			✔ ⌂						
OTEZLA (apremilast)					✔ ‡	✔				
REMICADE (infliximab)	✔ ⊥	✔ ⌐⌐			✔ ‡‡‡	✔	✔	✔ ⊥⊥		
RITUXAN‴ (rituximab)	✔ ⫩									

Drug	Rheumatoid Arthritis (RA)	Crohn's Disease (CD)	Systemic Juvenile Idiopathic Arthritis (SJIA)	Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Ulcerative Colitis (UC)	Hidradenitis Suppurativa (HS)	Uveitis (UV)
SILIQ (brodalumab)					✓‡‡					
SIMPONI (golimumab)	✓†					✓††	✓	✓~		
SIMPONI ARIA (golimumab)	✓†									
STELARA (ustekinumab)		✓⌐⌐⌐			✓‡	✓				
TALTZ (ixekizumab)					✓‡					
XELJANZ / XELJANZ XR (tofacitinib)	✓‡‡									

*Patients with moderately to severely active RA who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).
**Patients 2 years and older.
†In combination with methotrexate (MTX) or used alone.
‡Indicated for the treatment of adult patients (18 years or older) with chronic moderate to severe PsO who are candidates for systemic therapy or phototherapy, with the exception of ENBREL, which is indicated for the treatment of patients 4 years and older with chronic moderate to severe PsO who are candidates for systemic therapy or phototherapy.
‡‡Indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA. Can be used alone or in combination with MTX or other DMARDs.

‡‡‡ Indicated for the treatment of adult patients with chronic severe (ie, extensive and/or disabling) PsO who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.
∫Indicated for reducing signs and symptoms of JIA for patients 2 years of age and older. Can be used alone or in combination with MTX.
∫∫Indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA. Can be used alone or in combination with non-biologic DMARDs.
▼Treatment of non-infectious intermediate, posterior and panuveitis in adult patients.
▼▼KINERET is also indicated for the treatment of cryopyrin-associated periodic syndromes (CAPS) including neonatal-onset multisystem inflammatory disease (NOMID).
"ILARIS also indicated for the treatment of CAPS in adults and children 4 years of age and older including: familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS); tumor necrosis factor receptor associated periodic syndrome (TRAPS) in adult and pediatric patients; hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD) in adult and pediatric patients; and familial Mediterranean fever (FMF) in adult and pediatric patients.
∞Indicated for the reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active RA, in patients 18 years of age or older who have failed one or more DMARDs. Can be used alone or in combination with DMARDs other than TNF blocking agents.
∞∞Indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA. May be used as monotherapy or concomitantly with DMARDs other than TNF antagonists.
⌂ Indicated for reducing signs and symptoms in pediatric patients 6 years and old with moderate to severely active PJIA. May be used as monotherapy or with MTX.
⌐For all patients 6 years of age and older, indicated for reducing signs and symptoms and inducing and maintaining clinical remission in patients who have had an inadequate response to conventional therapy. For adults, also indicated for reducing signs and symptoms and inducing clinical remission if patients have also lost a response to or are intolerant of infliximab.
⌐⌐Indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy and for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD. And for patients 6 years of age and older for reducing signs and symptoms and inducing and maintaining clinical remission with moderately to severely active disease who have had an inadequate response to conventional therapy.
⌐⌐⌐Indicated for treatment of adult patients with moderately to severely active CD who have: 1) failed or were intolerant to treatment with immunomodulators or corticosteroids but never failed a TNF blocker, or 2) failed or were intolerant to treatment with one or more TNF blockers
⊥In combination with MTX, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active RA.
⊥⊥For reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy. Also for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy (REMICADE only). The biosimilar INFLECTRA did not receive FDA approval for pediatric UC due to existing marketing exclusivity for Remicade for this indication (not for clinical reasons).
"'RITUXAN also indicated for Non–Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), and granulomatosis with polyangiitis (GPA) (Wegener's Granulomatosis) and microscopic polyangiitis (MPA).
╪In combination with MTX is indicated for the treatment of adult patients with moderately- to severely- active RA who have had an inadequate response to one or more TNF antagonist therapies.
╪╪Treatment of moderate to severe PsO in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies.
┤ In combination with MTX, is indicated for the treatment of adult patients with moderately to severely active RA.
┤┤ Alone or in combination with MTX, is indicated for the treatment of adult patients with active PsA.
╪╪Indicated for the treatment of adult patients with moderately to severely active RA who have had an inadequate response or intolerance to MTX. It may be used as monotherapy or in combination with MTX or other nonbiologic DMARDs. Use in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
˜Indicated in adult patients with moderately to severely active UC who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine for: inducing and maintaining clinical response; improving endoscopic appearance of the mucosa during induction; inducing clinical remission; and achieving and sustaining clinical remission in induction responders.

CLINICAL EFFICACY SUMMARY

Rheumatoid arthritis (RA)

- The approval of the subcutaneous (SQ) formulation of ORENCIA (abatacept) was based on a double-blind, double-dummy, randomized trial demonstrating noninferiority to the intravenous (IV) formulation. The trial enrolled patients with RA who had an inadequate response to methotrexate (MTX). The proportion of patients achieving American College of Rheumatology 20% improvement (ACR 20) was not significantly different between the groups (Genovese et al, 2011).
- ORENCIA (abatacept), REMICADE (infliximab), and placebo were compared in a Phase 3, randomized, double-blind trial (N=431). Enrolled patients had had an inadequate response to MTX, and background MTX was continued during the trial. Although efficacy was comparable between abatacept and infliximab after six months of treatment, some differences in favor of abatacept were evident after one year of treatment. After one year, the mean changes from baseline in disease activity score based on erythrocyte sedimentation rate (DAS28-ESR) were -2.88 and -2.25 in the abatacept and infliximab groups, respectively (estimate of difference, -0.62; 95% confidence interval [CI], -0.96 to -0.29). Abatacept demonstrated greater efficacy vs infliximab on some (but not all) secondary endpoints, including the proportion of patients with a good European League Against Rheumatism (EULAR) response (32.0% vs 18.5%), low disease activity score (LDAS) (35.3% vs 22.4%), ACR 20 responses (72.4% vs 55.8%), and improvements in the Medical Outcomes Study short-form-36 (SF-36) physical component summary (PCS) (difference of 1.93). Overall, abatacept had a relatively more acceptable safety and tolerability profile, with fewer serious adverse events (AEs) and discontinuations due to AEs than the infliximab group (Schiff et al, 2008).
- Treatment with ORENCIA (abatacept) was directly compared to treatment with HUMIRA (adalimumab), both added to MTX, in a multicenter, investigator-blind, randomized controlled trial (N=646) of RA patients with inadequate response to MTX. After two years, the proportions of patients achieving ACR 20 responses were comparable between abatacept and adalimumab treatment groups (59.7 and 60.1%, respectively; difference 1.8%; 95% CI, -5.6 to 9.2%). ACR 50 and ACR 70 responses were also similar between the two groups after two years of treatment. Rates of AEs were similar between treatment groups (Schiff et al, 2014).
- The RAPID-1 and RAPID-2 studies compared CIMZIA (certolizumab) in combination with MTX to placebo plus MTX in adults with active RA despite MTX therapy (Keystone et al, 2008; Smolen et al, 2009a). A significantly greater proportion of patients on certolizumab 400 mg plus MTX at weeks zero, two, and four then 200 or 400 mg every two weeks attained greater ACR 20, ACR 50 and ACR 70 responses over patients on placebo and MTX, respectively, after 24 weeks (P≤0.01). The response rates were sustained with active treatment over 52 weeks (Keystone et al, 2008). The Modified Total Sharp Score (mTSS) was significantly lower with certolizumab in combination with MTX compared to MTX in combination with placebo (Keystone et al, 2008; Smolen et al, 2009a). A trial evaluated CIMZIA (certolizumab) monotherapy vs placebo in patients with active disease who had failed at least one prior DMARD. After 24 weeks, ACR 20 response rates were significantly greater with active treatment (45.5%) compared to placebo (9.3%; P<0.001). Significant improvements in secondary endpoints (ACR 50, ACR 70, individual ACR component scores, and patient reported outcomes) were also associated with certolizumab therapy (Fleischmann et al, 2009).
- More CIMZIA (certolizumab)-treated patients achieved clinical disease activity index (CDAI) remission than placebo-treated patients (18.8% vs 6.1%, P≤0.05) in a randomized, double-blind, placebo-controlled trial of certolizumab over 24 weeks in 194 patients with RA who were on DMARD therapy with MTX, leflunomide, sulfasalazine and/or hydroxychloroquine for at least six months (Smolen et al, 2015a).
- A randomized, double-blind, placebo-controlled trial (N=316) conducted in Japan compared CIMZIA (certolizumab) plus MTX to placebo plus MTX in MTX-naïve patients with early RA (≤12 months persistent disease) and poor prognostic factors: high anti-cyclic citrullinated peptide (anti-CCP) antibody and either positive rheumatoid factor and/or presence of bone erosions (Atsumi et al, 2016). The primary endpoint was inhibition of radiographic progression (change from baseline in mTSS at week 52). The certolizumab plus MTX group showed significantly greater inhibition of radiographic progression vs MTX alone (mTSS change, 0.36 vs 1.58; P<0.001). Clinical remission rates were higher in patients treated with certolizumab plus MTX vs MTX alone. The authors suggest that certolizumab plus MTX could be used as possible first-line treatment in this patient population.
- The FDA approval of SIMPONI (golimumab) for RA was based on three multicenter, double-blind, randomized, controlled trials in 1,542 patients greater than or equal to18 years of age with moderate to severe active disease. A greater percentage of patients from all three trials treated with the combination of golimumab and MTX achieved ACR responses at week 14 and week 24 vs patients treated with MTX alone (Emery et al, 2009; Keystone et al, 2009; Smolen et al, 2009b). Additionally, the golimumab 50 mg groups demonstrated a greater improvement compared to the control groups in the change in mean Health Assessment Questionnaire (HAQ) Disability Index (HAQ-DI) (Keystone et al, 2009; Smolen et al, 2009b). Response with golimumab + MTX was sustained for up to five years (Keystone et al, 2013a; Smolen et al, 2015b).

- SIMPONI ARIA (golimumab) was studied in patients with RA. In one trial, 643 patients could receive golimumab 2 mg/kg or 4 mg/kg intravenously (IV) every 12 weeks with or without MTX, or placebo with MTX. The proportion of patients meeting the primary endpoint of ACR 50 response was not significantly different between the golimumab with or without MTX groups and the placebo group. However, significantly more patients receiving golimumab plus MTX achieved an ACR 20 response at week 14 compared with patients receiving placebo plus MTX (53 vs 28%; P<0.001) (Kremer et al, 2010). In the GO-FURTHER trial (N=592), golimumab 2 mg/kg IV or placebo was given at weeks zero, four and then every eight weeks. An increased percentage of patients treated with golimumab + MTX achieved ACR 20 response at week 14 (58.5% [231/395] of golimumab + MTX patients vs 24.9% [49/197] of placebo + MTX patients [P<0.001]) (Weinblatt et al, 2013). In an open-label extension period, treatment was continued through week 100, with placebo-treated patients crossing over to golimumab at week 16 (early escape) or week 24. Clinical response was maintained through week 100, with an ACR 20 response of 68.1%. There was a very low rate of radiographic progression throughout the study, and patients treated with IV golimumab plus MTX from baseline had significantly less radiographic progression to week 100 compared to patients who had initially received placebo plus MTX. No unexpected AEs occurred (Bingham et al, 2015). In the GO-MORE trial, investigators treated patients with golimumab SQ for six months. If patients were not in remission, they could be randomized to receive golimumab SQ or IV. The percentages of patients who achieved DAS28-ESR remission did not differ between the combination SQ+IV group and the SQ golimumab group (Combe et al, 2014).
- The efficacy and safety of ACTEMRA (tocilizumab) were assessed in several randomized, double-blind, multicenter studies in patients ages 18 years and older with active RA. Patients were diagnosed according to ACR criteria, with at least eight tender and six swollen joints at baseline. Tocilizumab was given every four weeks as monotherapy (AMBITION), in combination with MTX (LITHE and OPTION) or other DMARDs (TOWARD) or in combination with MTX in patients with an inadequate response to tumor necrosis factor (TNF) antagonists (RADIATE). In all studies, mild to moderate AEs were reported, occurring in similar frequencies in all study groups. The most common AEs in all studies were infections and gastrointestinal symptoms (Emery et al, 2008; Genovese et al, 2008; Jones et al, 2010; Kremer et al, 2011; Smolen et al, 2008).
    - AMBITION evaluated the safety and efficacy of tocilizumab monotherapy vs MTX in patients with active RA for whom previous treatment with MTX or biological agents had not failed. A total of 673 patients were randomized to one of three treatment arms, tocilizumab 8 mg/kg every four weeks, MTX 7.5 mg/week and titrated to 20 mg/week within eight weeks, or placebo for eight weeks followed by tocilizumab 8 mg/kg. The primary endpoint was the proportion of patients achieving ACR 20 response at week 24. The results showed that tocilizumab monotherapy when compared to MTX monotherapy produced greater improvements in RA signs and symptoms, and a favorable benefit-risk ratio in patients who had not previously failed treatment with MTX or biological agents. Additionally, more patients treated with tocilizumab achieved remission at week 24 when compared to patients treated with MTX (Jones et al, 2010).
    - LITHE evaluated 1,196 patients with moderate to severe RA who had an inadequate response to MTX. Patients treated with tocilizumab had three times less progression of joint damage, measured by Total Sharp Score, when compared to patients treated with MTX alone. Significantly more patients treated with tocilizumab 8 mg/kg were also found to achieve remission at six months as compared to MTX (33% vs 4%), and these rates continued to increase over time to one year (47% vs 8%) (Kremer et al, 2011). These benefits were maintained or improved at two years with no increased side effects (Fleishmann et al, 2013).
    - OPTION evaluated tocilizumab in 623 patients with moderate to severely active RA. Patients received tocilizumab 8 mg/kg, 4 mg/kg, or placebo IV every four weeks, with MTX at stable pre-study doses (10 to 25 mg/week). Rescue therapy with tocilizumab 8 mg/kg was offered at week 16 to patients with less than 20% improvement in swollen and tender joint counts. The primary endpoint was ACR 20 at week 24. The findings showed that ACR 20 was seen in significantly more patients receiving tocilizumab than in those receiving placebo at week 24 (P<0.001). Significantly more patients treated with tocilizumab achieved ACR 50 and ACR 70 responses at week 24 as well (P<0.001). Greater improvements in physical function, as measured by the HAQ-DI, were seen with tocilizumab when compared to MTX (-0.52 vs -0.55 vs -0.34; P<0.0296 for 4 mg/kg and P<0.0082 for 8 mg/kg) (Smolen et al, 2008).
    - TOWARD examined the efficacy and safety of tocilizumab combined with conventional DMARDs in 1,220 patients with active RA. Patients remained on stable doses of DMARDs and received tocilizumab 8 mg/kg or placebo every four weeks for 24 weeks. At week 24, significantly more patients taking tocilizumab with DMARDs achieved an ACR 20 response than patients in the control group. The authors concluded that tocilizumab, combined with any of the DMARDs evaluated (MTX, chloroquine, hydroxychloroquine, parenteral gold, sulfasalazine, azathioprine, and leflunomide), was safe and effective in reducing articular and systemic symptoms in patients with an inadequate response to these agents. A greater percentage of patients treated

with tocilizumab also had clinically meaningful improvements in physical function when compared to placebo (60% vs 30%; P value not reported) (Genovese et al, 2008).
    - RADIATE evaluated the safety and efficacy of tocilizumab in patients with RA refractory to TNF antagonist therapy. A total of 499 patients with inadequate response to one or more TNF antagonists was randomly assigned to 8 or 4 mg/kg tocilizumab or placebo every four weeks with stable MTX doses (10 to 25 mg/week) for 24 weeks. ACR 20 responses and safety endpoints were assessed. This study found that tocilizumab plus MTX is effective in achieving rapid and sustained improvements in signs and symptoms of RA in patients with inadequate response to TNF antagonists and has a manageable safety profile. The ACR 20 response in both tocilizumab groups was also found to be comparable to those seen in patients treated with HUMIRA (adalimumab) and REMICADE (infliximab), irrespective of the type or number of failed TNF antagonists (Emery et al, 2008). In the ADACTA trial, patients with severe arthritis who could not take MTX were randomized to monotherapy with tocilizumab or adalimumab. The patients in the tocilizumab group had a significantly greater improvement in DAS28 at week 24 than patients in the adalimumab group (Gabay et al, 2013).
- More recently, results of a randomized, double-blind trial evaluating ACTEMRA (tocilizumab) in early RA were published (Bijlsma et al, 2016). Patients (N=317) had been diagnosed with RA within one year, were DMARD-naïve, and had a DAS28 score of ≥2.6. Patients were randomized to 1 of 3 groups: tocilizumab plus MTX, tocilizumab plus placebo, or MTX plus placebo. Tocilizumab was given at a dose of 8 mg/kg every 4 weeks (maximum 800 mg per dose), and MTX was given at a dose of 10 mg orally per week, increased to a maximum of 30 mg per week as tolerated. Patients not achieving remission switched from placebo to active treatments, and patients not achieving remission in the tocilizumab plus MTX group switched to a standard of care group (usually a TNF inhibitor plus MTX). The primary endpoint was the proportion of patients achieving sustained remission (defined as DAS28 <2.6 with a swollen joint count ≤4, persisting for at least 24 weeks). The percentages of patients achieving a sustained remission on the initial regimen were 86%, 84%, and 44% in the tocilizumab plus MTX, tocilizumab monotherapy, and MTX monotherapy groups, respectively (P<0.0001 for both comparisons vs MTX). The percentages of patients achieving sustained remission during the entire study were 86%, 88%, and 77% in the tocilizumab plus MTX, tocilizumab monotherapy, and MTX monotherapy groups, respectively (P=0.06 for tocilizumab plus MTX vs MTX; P=0.0356 for tocilizumab vs MTX). The authors concluded that immediate initiation of tocilizumab is more effective compared to initiation of MTX in early RA.
- The FDA approval of the subcutaneous formulation of ACTEMRA (tocilizumab) was based on one multicenter, double-blind, randomized, controlled trial in patients (N=1,262) with RA. Weekly tocilizumab SQ 162 mg was found to be non-inferior to tocilizumab IV 8 mg/kg every four weeks through 24 weeks. A higher incidence of injection-site reactions were reported with the SQ formulation (Burmester et al, 2014a). In an open-label extension period, patients in both treatment arms were re-randomized to receive either IV or SQ tocilizumab through week 97. The proportions of patients who achieved ACR 20/50/70 responses, DAS28 remission, and improvement from baseline in HAQ-DI ≥0.3 were sustained through week 97 and comparable across arms. IV and SQ treatments had a comparable safety profile with the exception of higher injection-site reactions with the SQ formulation (Burmester et al, 2016). A placebo-controlled trial in 656 patients further confirmed the efficacy of SQ ACTEMRA administered every other week (Kivitz et al, 2014).
- In a Phase 3 trial, the percentage of patients who met criteria for RA disease remission was not significantly different in the XELJANZ (tofacitinib) groups (5 mg and 10 mg twice daily) vs placebo. However, significantly more patients in the tofacitinib groups did meet criteria for decrease of disease activity. The tofacitinib groups also had significant decreases in fatigue and pain (Fleishmann et al, 2012). In another Phase 3 study, XELJANZ (tofacitinib), when administered with background MTX, was superior to placebo with respect to all clinical outcomes. Although not directly compared to HUMIRA (adalimumab), the clinical efficacy of tofacitinib was numerically similar to that observed with adalimumab. Safety of tofacitinib continues to be monitored for long term effects (van Vollenhoven et al, 2012). The ORAL Scan trial showed the ACR 20 response rates at month six for patients receiving tofacitinib 5 mg and 10 mg twice daily were 51.5% and 61.8%, respectively, vs 25.3% for patients receiving placebo (P<0.0001 for both comparisons) (van der Heijde et al, 2013). The ORAL START trial evaluated tofacitinib and MTX in 956 patients with active RA over 24 months. The primary endpoint of mean change from baseline in modified total Sharp score was significantly less with tofacitinib (0.6 for 5 mg; 0.3 for 10 mg) compared to MTX (2.1; P<0.001) (Lee et al, 2014). No radiographic progression was defined as a change from baseline in the modified total Sharp score of <0.5 points. However, a minimal clinically important difference in modified total Sharp score is 4.6 points; this study did not meet this minimal clinical meaningful difference threshold.
- In the ORAL Step study, patients with RA who had an inadequate response to one or more TNF inhibitors were randomized to XELJANZ (tofacitinib) 5 mg or 10 mg twice daily or placebo; all patients were on MTX (Burmester et al, 2013a; Strand et al, 2015a). The primary outcome, ACR 20 response rate, was significantly higher with tofacitinib 5

mg (41.7%; 95% CI, 6.06 to 28.41; P=0.0024) and 10 mg (48.1%; 95% CI, 12.45 to 34.92; P<0.0001) compared to placebo (24.4%). Improvements in HAQ-DI was reported as -0.43 (95% CI, -0.36 to -0.157; P<0.0001) for tofacitinib 5 mg and -0.46 (95% CI, -0.38 to -0.17; P<0.0001) for tofacitinib 10 mg groups compared to -0.18 for placebo. Common AEs included diarrhea, nasopharyngitis, headache, and urinary tract infections in the tofacitinib groups.

- INFLECTRA (infliximab-dyyb) was evaluated and compared to REMICADE (infliximab; European Union formulation) in PLANETRA (N=606), a double-blind, multicenter, randomized trial (Yoo et al, 2013; Yoo et al, 2016; Yoo et al, 2017). The primary endpoint, ACR 20 at week 30, was achieved by 58.6% and 60.9% of patients in the REMICADE and INFLECTRA groups, respectively (treatment difference [TD], 2%; 95% CI, -6% to 10%) (intention-to-treat population). Corresponding results in the per-protocol population were 69.7% and 73.4%, respectively (TD, 4%; 95% CI, -4% to 12%). Equivalence was demonstrated between the two products.
    - Secondary endpoints included several other disease activity scales and a quality-of-life scale; no significant differences were noted in any of these endpoints at either the 30-week or 54-week assessments.
    - In the extension study (N=302) through 102 weeks, all patients received INFLECTRA. Response rates were maintained, with no differences between the INFLECTRA maintenance group and the group who switched from REMICADE to INFLECTRA.
- Two studies, one double-blind and one open-label, evaluated RITUXAN (rituximab) in patients who had failed treatment with a TNF blocker (Cohen et al, 2006, Haraoui et al, 2011). All patients continued to receive MTX. Both studies showed greater than 50% of patients achieving ACR 20 response. AEs were generally mild to moderate in severity.
- A Cochrane review (Lopez-Olivo et al, 2015) examined RITUXAN (rituximab) for the treatment of RA. Eight studies and a total of 2720 patients were included. Rituximab plus MTX, compared to MTX alone, resulted in more patients achieving ACR 50 at 24 weeks (29% vs 9%, respectively) and clinical remission at 52 weeks (22% vs 11%). In addition, rituximab plus MTX compared to MTX alone resulted in more patients having no radiographic progression (70% vs 59% at 24 weeks, with similar results at 52 through 56 and 104 weeks). Benefits were also shown for physical function and quality of life.
- In the open-label ORBIT study (N=295), adults with active, seropositive RA and an inadequate response to DMARDs who were biologic-naïve were randomized to either RITUXAN (rituximab) (n=144) or a TNF inhibitor (physician/patient choice of ENBREL [etanercept] or HUMIRA [adalimumab]; n=151) (Porter et al, 2016). Medication doses were generally consistent with FDA-approved recommendations. Patients were able to switch over to the alternative treatment due to side effects or lack of efficacy. The primary endpoint was the change in DAS28-ESR in the per-protocol population at 12 months.
    - The changes in DAS28-ESR were -2.6 and -2.4 in patients in the rituximab and TNF inhibitor groups, respectively. The difference of -0.19 (95% CI, -0.51 to 0.13) was within the prespecified non-inferiority margin of 0.6 units. The authors concluded that initial treatment with rituximab was non-inferior to initial TNF inhibitor treatment in this patient population. However, interpretation of these results is limited due to the open-label study design and the high percentage of patients switching to the alternative treatment (32% in the TNF inhibitor group and 19% in the rituximab group). The indication for rituximab is limited to patients with an inadequate response to TNF inhibitor(s).
- A randomized, open-label trial evaluated biologic treatments in patients with RA who had had an inadequate response to a TNF inhibitor (Gottenberg et al, 2016). Patients (N=300) were randomized to receive a second TNF inhibitor (n=150) or a non-TNF-targeted biologic (n=150) of the prescriber's choice. The second TNF inhibitors, in order of decreasing frequency, included HUMIRA (adalimumab), ENBREL (etanercept), CIMZIA (certolizumab), and REMICADE (infliximab), and the non-TNF biologics included ACTEMRA (tocilizumab), RITUXAN (rituximab), and ORENCIA (abatacept). The primary endpoint was the proportion of patients with a good or moderate EULAR response at week 24, defined as a decrease in DAS28-ESR of >1.2 points resulting in a score of ≤3.2.
    - At week 24, 52% of patients in the second anti-TNF group and 69% of patients in the non-TNF group achieved a good or moderate EULAR response (P=0.003 or P=0.004, depending on how missing data were handled). Secondary disease activity scores also generally supported better efficacy for the non-TNF biologics; however, HAQ scores did not differ significantly between groups. Among the non-TNF biologics, the proportion of EULAR good and moderate responders at week 24 did not significantly differ between abatacept, rituximab, and tocilizumab (67%, 61%, and 80%, respectively). There were 8 patients (5%) in the second TNF inhibitor group and 16 patients (11%) in the non-TNF biologic group that experienced serious AEs (P=0.10), predominantly infections and cardiovascular events. There were some limitations to this trial; notably, it had an open-label design, and adherence may have differed between groups because all non-TNF biologics were given as infusions under observation and most of the TNF inhibitor drugs were self-injected by patients. The authors concluded that among patients with RA inadequately treated with TNF inhibitors, a non-

TNF biologic was more effective in achieving a good or moderate disease activity response at 24 weeks; however, a second TNF inhibitor was also often effective in producing clinical improvement.

- Another recent randomized trial (Manders et al, 2015) evaluated the use of ORENCIA (abatacept) (n=43), RITUXAN (rituximab) (n=46), or a different TNF inhibitor (n=50) in patients (N=139) with active RA despite previous TNF inhibitor treatment. ACTEMRA (tocilizumab) was not included. In this trial, there were no significant differences with respect to DAS28, HAQ-DI, or SF-36 over the 1-year treatment period, and AEs also appeared similar. A cost-effectiveness analysis was also included in this publication, but results are not reported in this review.
- A Cochrane review examined ORENCIA (abatacept) for the treatment of RA. ACR 50 response was not significantly different at three months but was significantly higher in the abatacept group at six and 12 months compared to placebo (relative risk [RR], 2.47; 95% CI, 2 to 3.07 and RR, 2.21; 95% CI, 1.73 to 2.82). Similar results were seen in ACR 20 and ACR 70 (Maxwell et al, 2009).
- The safety and efficacy of HUMIRA (adalimumab) for the treatment of RA were assessed in a Cochrane systematic review. Treatment with adalimumab in combination with MTX was associated with a RR of 1.52 to 4.63, 4.63 (95% CI, 3.04 to 7.05) and 5.14 (95% CI, 3.14 to 8.41) for ACR 20, ACR 50, and ACR 70 responses at six months when compared to placebo in combination with MTX. Adalimumab monotherapy was also proven efficacious (Navarro-Sarabia et al, 2005). In another study, patients received adalimumab 20 mg or 40 mg every other week for one year, and then could receive 40 mg every other week for an additional nine years. At Year 10, 64.2%, 49%, and 17.6% of patients achieved ACR 50, ACR 70, and ACR 90 responses, respectively (Keystone et al, 2013b).
- A Phase 3, open-label study evaluated the long-term efficacy of HUMIRA (adalimumab) for RA. Patients receiving adalimumab in one of four early assessment studies could receive adalimumab for up to 10 years in the extension study. Of 846 enrolled patients, 286 (33.8%) completed 10 years of treatment. In patients completing 10 years, adalimumab led to sustained clinical and functional responses, with ACR 20, ACR 50, and ACR 70 responses being achieved by 78.6%, 55.5%, and 32.8% of patients, respectively. The authors stated that patients with shorter disease duration achieved better outcomes, highlighting the need for early treatment. No unexpected safety findings were observed. This study demonstrated that some patients with RA can be effectively treated with adalimumab on a long-term basis; however, the study is limited by its open-label design, lack of radiographic data, and the fact that only patients who continued in the study were followed (Furst et al, 2015).
- A Cochrane review was performed to compare KINERET (anakinra) to placebo in adult patients with RA. Significant improvements in both primary (ACR 20, 38% vs 23%; RR, 1.61; 95% CI, 1.32 to 1.98) and secondary (ACR 50 and ACR 70) outcomes were detected. The only significant difference in AEs noted with anakinra use was the rate of injection site reactions (71% vs 28% for placebo) (Mertens et al, 2009).
- In another Cochrane review, ENBREL (etanercept) was compared to MTX or placebo in adult patients with RA and found that at six months 64% of individuals on etanercept 25 mg twice weekly attained an ACR 20 vs 15% of patients on either MTX alone or placebo (RR, 3.8; number needed to treat [NNT], 2). An ACR 50 and ACR 70 were achieved by 39% and 15% in the etanercept group compared to 4% (RR, 8.89; NNT, 3) and 1% (RR, 11.31; NNT, 7) in the control groups. Etanercept 10 mg twice weekly was only associated with significant ACR 20 (51% vs 11% of controls; RR, 4.6; 95% CI, 2.4 to 8.8; NNT, 3) and ACR 50 responses (24% vs 5% of controls; RR, 4.74; 95% CI, 1.68 to 13.36; NNT, 5). Seventy-two percent of patients receiving etanercept had no increase in Sharp erosion score compared to 60% of MTX patients. Etanercept 25 mg was associated with a significantly reduced total Sharp score (weighted mean difference, -10.5; 95% CI, -13.33 to -7.67). The Sharp erosion scores and joint space narrowing were not significantly reduced by either etanercept dose (Blumenauer et al, 2003). In a trial of 353 patients with RA, patients received a triple therapy combination of sulfasalazine, hydroxychloroquine and MTX or etanercept and MTX. Triple therapy was shown to be noninferior to etanercept + MTX (O'Dell et al, 2013).
- A more recent Cochrane review (Singh et al, 2016a) evaluated the benefits and harms of 10 agents for the treatment of RA in patients failing treatment with MTX or other DMARDs. Agents included XELJANZ (tofacitinib) and 9 biologics (ORENCIA [abatacept], HUMIRA [adalimumab], KINERET [anakinra], CIMZIA [certolizumab], ENBREL [etanercept], SIMPONI [golimumab], REMICADE [infliximab], RITUXAN [rituximab], and ACTEMRA [tocilizumab]), each in combination with MTX or other DMARDS, compared to comparator agents such as DMARDs or placebo. Data from 79 randomized trials (total 32,874 participants) were included. Key results from this review are as follows:
    - ACR 50: Biologic plus MTX/DMARD was associated with a statistically significant and clinically meaningful improvement in ACR 50 vs comparators. TNF inhibitors did not differ significantly from non-TNF biologics. Differences between treatments in individual comparisons were small.
    - HAQ: Biologic plus MTX/DMARD was associated with a clinically and statistically significant improvement in function measured by HAQ vs comparators. TNF inhibitors did not differ significantly from non-TNF biologics.
    - Remission: Biologic plus MTX/DMARD was associated with clinically and statistically significantly greater proportion of patients achieving RA remission, defined by DAS <1.6 or DAS28 <2.6, vs comparators. TNF inhibitors did not differ significantly from non-TNF biologics.

  - Radiographic progression: Radiographic progression was statistically significantly reduced in those on biologic plus MTX/DMARD vs comparator. The absolute reduction was small and clinical relevance is uncertain.
  - Safety: Biologic plus MTX/DMARD was associated with a clinically significantly increased risk of serious AEs; statistical significance was borderline. TNF inhibitors did not differ significantly from non-TNF biologics.
- A similar Cochrane review focused on the use of biologic or XELJANZ (tofacitinib) monotherapy for RA in patients with traditional DMARD failure (Singh et al, 2016b). A total of 41 randomized trials (N=14,049) provided data for this review. Key results are as follows:
  - Biologic monotherapy was associated with a statistically significant and clinically meaningful improvement in ACR 50 and HAQ vs placebo and vs MTX or other DMARDs.
  - Biologic monotherapy was associated with a statistically significant and clinically meaningful greater proportion of patients with disease remission vs placebo.
  - Based on a single study, the reduction in radiographic progression was statistically significant for biologic monotherapy compared to active comparators, but the absolute reduction was small and of unclear clinical relevance.
- Another Cochrane review evaluated the use of biologics or XELJANZ (tofacitinib) in patients with RA who had been unsuccessfully treated with a previous biologic (Singh et al, 2017). The review included 12 randomized trials (N=3,364). Key results are as follows:
  - Biologics, compared to placebo, were associated with statistically significant and clinically meaningful improvement in RA as assessed by ACR 50 and remission rates. Information was not available for HAQ or radiographic progression.
  - Biologics plus MTX, compared to MTX or other traditional DMARDs, were associated with statistically significant and clinically meaningful improvement in ACR 50, HAQ, and RA remission rates. Information was not available for radiographic progression.
  - There were no published data for tofacitinib monotherapy vs placebo.
  - Based on a single study, tofacitinib plus MTX, compared to MTX, was associated with a statistically significant and clinically meaningful improvement in ACR 50 and HAQ. RA remission rates were not statistically significantly different, and information was not available for radiographic progression.
- Another recent Cochrane review (Hazlewood et al, 2016) compared MTX and MTX-based DMARD combinations for RA in patients naïve to or with an inadequate response to MTX; DMARD combinations included both biologic and non-biologic agents. A total of 158 studies and over 37,000 patients were included. Evidence suggested that efficacy was similar for triple DMARD therapy (MTX plus sulfasalazine plus hydroxychloroquine) and MTX plus most biologic DMARDs or XELJANZ (tofacitinib). MTX plus some biologics were superior to MTX in preventing joint damage in MTX-naïve patients, but the magnitude of effects was small.
- A meta-analysis evaluated the efficacy of REMICADE (infliximab) in combination with MTX compared to placebo plus MTX. There was a higher proportion of patients in the infliximab group that achieved an ACR 20 at 30 weeks compared to patients in the placebo group (RR, 1.87; 95% CI, 1.43 to 2.45). These effects were similar in the proportion of patients achieving ACR 50 and ACR 70 (RR, 2.68; 95% CI, 1.79 to 3.99 and RR, 2.68; 95% CI, 1.78 to 4.03) (Wiens et al, 2009).
- Another meta-analysis of randomized controlled trials included HUMIRA (adalimumab), KINERET (anakinra), ENBREL (etanercept), and REMICADE (infliximab) with or without MTX. The odds ratio (OR) for an ACR 20 was 3.19 (95% CI, 1.97 to 5.48) with adalimumab, 1.7 (95% CI, 0.9 to 3.29) with anakinra, 3.58 (95% CI, 2.09 to 6.91) with etanercept and 3.47 (95% CI, 1.66 to 7.14) with infliximab compared to placebo. The OR to achieve an ACR 50 with adalimumab was 3.97 (95% CI, 2.73 to 6.07), 2.13 (95% CI, 1.27 to 4.22) with anakinra, 4.21 (95% CI, 2.74 to 7.43) and with etanercept 4.14 (95% CI, 2.42 to 7.46) compared to placebo. Further analysis of each agent against another was performed, and no significant difference was determined between individual agents in obtaining an ACR 20 and ACR 50. However, the TNF-blockers as a class showed a greater ACR 20 and ACR 50 response compared to anakinra (OR, 1.96; 95% CI, 1.03 to 4.01 and OR, 1.93; 95% CI,1.05 to 3.5; P<0.05) (Nixon et al, 2007).
- The Agency for Healthcare Research and Quality published a review of drug therapy to treat adults with RA (Donahue et al, 2012). They concluded that there is limited head to head data comparing the biologics. Studies that are available are generally observational in nature or mixed treatment comparison meta-analysis. At this time, there appears to be no significant differences amongst the agents. Clinical trials have shown better efficacy with combination biologics and MTX and no additional increased risk of AEs. However, combinations of two biologic agents showed increased rate of serious AEs with limited or no increase in efficacy.
- A meta-analysis of six trials (N=1,927) evaluated the efficacy of withdrawing biologics from patients with RA who were in sustained remission or had low disease activity (Galvao et al, 2016). The biologics in the identified trials were TNF inhibitors, most commonly ENBREL (etanercept) or HUMIRA (adalimumab). Compared to withdrawing the

medication, continuing the biologic increased the probability of having low disease activity (RR, 0.66; 95% CI, 0.51 to 0.84) and remission (RR, 0.57; 95% CI, 0.44 to 0.74). Although outcomes were worse in patients withdrawing the biologic, the investigators noted that almost half of the patients maintained a low disease activity after withdrawal. The authors suggested that further research is necessary to identify subgroups for which withdrawal may be more appropriate.

Ankylosing spondylitis (AS)

- The FDA-approval of HUMIRA (adalimumab) for the treatment of AS was based on one randomized, double-blind, placebo-controlled study (N=315) in which a significantly greater proportion of patients achieved a 20% improvement in the Assessment of SpondyloArthritis International Society criteria (ASAS 20) (primary endpoint) with adalimumab (58% vs 21% with placebo; P<0.001). A greater than 50% improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score, a measure of fatigue severity, spinal and peripheral joint pain, localized tenderness, and morning stiffness which is considered clinically meaningful, was detected in 45% of adalimumab-treated patients compared to 16% of placebo-treated patients (P<0.001) at week 12. This response was sustained through week 24, with 42% in the adalimumab group achieving a greater than or equal to 50% improvement in BASDAI score compared to 15% in the placebo group (P<0.001) (van der Heijde et al, 2006).
- In two double-blind, randomized, placebo-controlled trials, the efficacy of ENBREL (etanercept) was evaluated in patients with AS (Calin et al, 2004; Gorman et al, 2002). Etanercept had a significantly greater response to treatment compared to placebo (P<0.001)(Gorman et al, 2002). More patients achieved an ASAS 20 response compared to placebo (P<0.001)(Calin et al, 2004). An open-label extension study, evaluating the long-term safety and efficacy of etanercept in patients with AS, was conducted. Safety endpoints included AEs, serious AEs, serious infection, and death while efficacy endpoints included ASAS 20 response, ASAS 5/6 response and partial remission rates. After up to 192 weeks of treatment, the most common AEs were injection site reactions, headache and diarrhea. A total of 71% of patients were ASAS 20 responders at week 96 and 81% of patients were responders at week 192. The ASAS 5/6 response rates were 61% at week 96 and 60% at week 144, and partial remission response rates were 41% at week 96 and 44% at week 192. Placebo patients who switched to etanercept in the open-label extension trial showed similar patterns of efficacy maintenance (Davis et al, 2008). A multicenter, randomized, double-blind trial compared etanercept and sulfasalazine in adult patients with active AS that failed treatment with nonsteroidal anti-inflammatory drugs (NSAIDs). A significantly greater proportion of patients treated with etanercept compared to patients treated with sulfasalazine achieved the primary outcome of ASAS 20 at week 16 (P<0.0001). There were also significantly more patients that achieved ASAS 40 and ASAS 5/6 in the etanercept group compared to the sulfasalazine group (P<0.0001 for both) (Braun et al, 2011).
- The FDA-approval of SIMPONI (golimumab) for AS was based on a multicenter, randomized, double-blind, placebo-controlled trial in adult patients with active disease for at least three months (N=356). Golimumab with or without a DMARD was compared to placebo with or without a DMARD and was found to significantly improve the signs and symptoms of AS as demonstrated by the percentage of patients achieving an ASAS 20 response at week 14 (Inman et al, 2008). Sustained improvements in ASAS 20 and ASAS 40 response rates were observed for up to five years in an open-label extension trial (Deodhar et al, 2015). Safety profile through five years was consistent with other TNF inhibitors.
- The efficacy of REMICADE (infliximab) in the treatment of AS was demonstrated in 12- and 24-week double-blind, placebo-controlled trials. There was significantly more patients that achieved a 50% BASDAI score in the infliximab group compared to the placebo group at 12 weeks (P<0.0001)(Braun et al, 2002), At 24 weeks, significantly more patients in the infliximab group achieved ASAS 20 compared to the placebo group (P<0.001)(van der Heijde et al, 2005).
- INFLECTRA (infliximab-dyyb) was evaluated alongside REMICADE (infliximab; European Union formulation) for the treatment of AS in PLANETAS (N=250), a double-blind, multicenter, randomized trial (*Park et al 2013, Park et al 2016, Park et al 2017*). The primary endpoints related to pharmacokinetic equivalence. Secondary efficacy endpoints supported similar clinical activity between INFLECTRA and REMICADE. An ASAS 20 response was achieved by 72.4% and 70.5% of patients in the REMICADE and INFLECTRA groups, respectively, at 30 weeks, and by 69.4% and 67.0% of patients at 54 weeks. Other disease activity endpoints and a quality-of-life scale were also similar between groups.
    - In the extension study (N=174) through 102 weeks, all patients received INFLECTRA. From weeks 54 to 102, the proportion of patients achieving a clinical response was maintained at a similar level to that of the main study in both the maintenance and switch groups and was comparable between groups.
- The efficacy of CIMZIA (certolizumab) for the treatment of AS was established in one randomized, double-blind, placebo-controlled study (N=325) in which a significantly greater proportion of patients achieved ASAS 20 response with certolizumab 200 mg every two weeks and certolizumab 400 mg every four weeks compared to placebo at 12

weeks (Landewe et at, 2014). Patient-reported outcomes measured by the SF-36, health-related quality of life (HRQoL), and reports of pain, fatigue and sleep were significantly improved with certolizumab in both dose groups (Sieper et al, 2015a). A Phase 3, randomized, placebo-controlled trial found that 62.5% of patients on certolizumab maintained ASAS 20 response to week 96 in a population of patients with axial spondyloarthritis which includes AS (Sieper et al, 2015b).

- The efficacy and safety of COSENTYX (secukinumab) were evaluated in the double-blind, placebo-controlled, randomized MEASURE 1 and 2 studies (Baeten et al, 2015). MEASURE 1 enrolled 371 patients and MEASURE 2 enrolled 219 patients with active AS with radiologic evidence treated with NSAIDs. Patients were treated with secukinumab 75 or 150 mg SQ every 4 weeks (following IV loading doses) or placebo. The primary outcome, ASAS 20 response at week 16, was significantly higher in the secukinumab 75 mg (60%) and 150 mg (61%) groups compared to placebo (29%, P<0.001 for each dose) for MEASURE 1. For MEASURE 2 at week 16, ASAS 20 responses were seen in 61% of the secukinumab 150 mg group, 41% of the 75 mg group, and 28% of the placebo group (P<0.001 for secukinumab 150 mg vs placebo; P=0.10 for secukinumab 75 mg vs placebo). Common AEs reported included nasopharyngitis, headache, diarrhea, and upper respiratory tract infections. Improvements were observed from week 1 and sustained through week 52.
- In two systematic reviews of TNF blockers for the treatment of AS, patients taking SIMPONI (golimumab), ENBREL (etanercept), REMICADE (infliximab), and HUMIRA (adalimumab) were more likely to achieve ASAS 20 or ASAS 40 responses compared with patients from control groups. The RR of reaching ASAS 20 after 12 or 14 weeks was 2.21 (95% CI, 1.91 to 2.56) (Machado et al, 2013). After 24 weeks, golimumab, etanercept, infliximab, and adalimumab were more likely to achieve ASAS 40 compared to placebo (Maxwell et al, 2015). A systematic review and network meta-analysis evaluated biologic agents for the treatment of AS, including adalimumab, etanercept, golimumab, infliximab, COSENTYX (secukinumab), and ACTEMRA (tocilizumab; not FDA approved for AS) (Chen et al, 2016). A total of 14 studies were included. Infliximab was ranked best and secukinumab second best for achievement of ASAS 20 response; however, differences among agents were not statistically significant with the exception of infliximab 5 mg compared to tocilizumab (OR, 4.81; 95% credible interval [CrI], 1.43 to 17.04). Safety endpoints were not included in this analysis.

Crohn's disease (CD)

- In a trial evaluating REMICADE (infliximab) for induction of remission, significantly more patients achieved remission at four weeks with infliximab compared to placebo (P<0.005)(Targan et al, 1997). In a placebo-controlled trial, significantly more patients treated with infliximab 5 and 10 mg/kg had a reduction greater than or equal to 50% in the number of fistulas compared to patients treated with placebo (P=0.002 and P=0.02, respectively)(Present et al, 1999). In an open-label trial evaluating the use of infliximab in pediatric CD patients, 88.4% responded to the initial induction regimen, and 58.6% were in clinical remission at week 10 (Hyams et al, 2007).
- The safety and efficacy of ENTYVIO (vedolizumab) was demonstrated in two trials for CD in patients who responded inadequately to immunomodulator therapy, TNF blockers, and/or corticosteroids. In one trial, a higher percentage of ENTYVIO-treated patients achieved clinical response and remission at week 52 compared to placebo. However, in the second trial, ENTYVIO did not achieve a statistically significant clinical response or clinical remission over placebo at week six (Sandborn et al, 2013; Sands et al, 2014).
- A meta-analysis evaluating CIMZIA (certolizumab) use over 12 to 26 weeks for the treatment of CD demonstrated that the agent was associated with an increased rate of induction of clinical response (RR, 1.36; P=0.004) and remission (RR, 1.95; P<0.0001) over placebo. However, risk of infection was higher with certolizumab use (Shao et al, 2009).
- Additionally, HUMIRA (adalimumab), CIMZIA (certolizumab) and REMICADE (infliximab) demonstrated the ability to achieve clinical response (RR, 2.69; P<0.00001; RR, 1.74; P<0.0001 and RR, 1.66; P=0.0046, respectively) and maintain clinical remission (RR, 1.68; P=0.000072 with certolizumab and RR, 2.5; P=0.000019 with infliximab; adalimumab, data not reported) over placebo in patients with CD. Adalimumab and infliximab also had a steroid-sparing effect (Behm et al, 2008). Other systematic reviews have further demonstrated the efficacy of these agents in CD (Singh et al, 2014).
- In a systematic review of patients with CD who had failed a trial with REMICADE (infliximab), the administration of HUMIRA (adalimumab) was associated with remission rates of 19 to 68% at one year. Serious cases of sepsis, cellulitis, and fungal pneumonia occurred in zero to 19% of patients in up to four years of treatment (Ma et al, 2009).
- A systematic review of 8 randomized clinical trials with TYSABRI (natalizumab) or ENTYVIO (vedolizumab) for the management of CD evaluated the rates of failure of remission induction (Chandar et al, 2015). Fewer failures of remission induction were reported with natalizumab and vedolizumab compared to placebo (RR 0.87; 95% CI, 0.84 to 0.91; I^2=0%). The summary effect sizes were similar for both natalizumab (RR 0.86; 95% CI, 0.80 to 0.93) and vedolizumab (RR 0.87; 95% CI, 0.79 to 0.95). No significant difference was detected between the two active treatments (P=0.95). No significant differences between natalizumab and vedolizumab were observed for rates of

serious AEs, infections (including serious infections), and treatment discontinuation. Rates of infusion reactions in induction trials were more common with natalizumab over vedolizumab (P=0.007). Progressive multifocal leukoencephalopathy (PML) has been reported with natalizumab but has not been reported with vedolizumab.

- The use of STELARA (ustekinumab) for the treatment of CD was evaluated in the UNITI-1, UNITI-2, and IM-UNITI studies (Feagan et al, 2016). All were Phase 3, double-blind, placebo-controlled trials.
    - UNITI-1 (N=741) was an 8-week induction trial that compared single IV doses of ustekinumab 130 mg IV, weight-based ustekinumab (~6 mg/kg), and placebo in patients with nonresponse or intolerance to one or more TNF inhibitors. The primary endpoint was clinical response at week 6, which was defined as a decrease from baseline in the CDAI of ≥100 points or a CDAI score of <150. A clinical response was achieved by 34.4%, 33.7%, and 21.5% of patients in the ustekinumab 130 mg, weight-based ustekinumab, and placebo groups, respectively (P=0.002 for 130 mg dose vs placebo; P=0.003 for weight-based dose vs placebo). Benefits were also demonstrated on all major secondary endpoints, which included clinical response at week 8, clinical remission (CDAI <150) at week 8, and CDAI decrease of ≥70 points at weeks 3 and 6.
    - UNITI-2 (N=628) had a similar design to UNITI-1, but was conducted in patients with treatment failure or intolerance to immunosuppressants or glucocorticoids (with no requirement for prior TNF inhibitor use). In this trial, a clinical response was achieved by 51.7%, 55.5%, and 28.7% of patients in the ustekinumab 130 mg, weight-based ustekinumab, and placebo groups, respectively (P<0.001 for both doses vs placebo). Benefits were also demonstrated on all major secondary endpoints.
    - IM-UNITI was a 44-week maintenance trial that enrolled patients completing UNITI-1 and UNITI-2. Of 1,281 enrolled patients, there were 397 randomized patients (primary population); these were patients who had had a clinical response to ustekinumab induction therapy and were subsequently randomized to ustekinumab 90 mg SC every 8 or 12 weeks or placebo. The primary endpoint, clinical remission at week 44, was achieved by 53.1%, 48.8%, and 35.9% of patients in the ustekinumab every 8 week, ustekinumab every 12 week, and placebo groups, respectively (P=0.005 for every 8 week regimen vs placebo; P=0.04 for every 12 week regimen vs placebo). Numerical and/or statistically significant differences for ustekinumab vs placebo were observed on key secondary endpoints including clinical response, maintenance of remission, and glucocorticoid-free remission.

Hidradenitis suppurativa (HS)

- Two 36-week, Phase 3, double-blind, multicenter, placebo-controlled, randomized trials, PIONEER I and II, evaluated HUMIRA (adalimumab) for the treatment of HS (Kimball et al, 2016). A total of 633 adults (307 in PIONEER I and 326 in PIONEER II) with moderate to severe HS were enrolled. The study consisted of two treatment periods; in the first period, patients were randomized to placebo or weekly adalimumab for 12 weeks; in the second period, patients initially assigned to placebo received weekly adalimumab (PIONEER I) or placebo (PIONEER II) for 24 weeks and patients initially assigned to adalimumab were re-randomized to placebo, weekly adalimumab, or every-other-week adalimumab. The adalimumab dosage regimen was 160 mg at week zero, followed by 80 mg at week 2, followed by 40 mg doses starting at week 4.
    - The primary endpoint was HS clinical response (HiSCR) at week 12, defined as at least 50% reduction in total abscess and inflammatory nodule count with no increase in abscess count and no increase in draining fistula count compared to baseline. HiSCR rates at week 12 were significantly higher for the groups receiving adalimumab than for the placebo groups: 41.8% vs 26.0% in PIONEER I (P=0.003) and 58.9% vs 27.6% in PIONEER II (P<0.001).
    - Among patients with a clinical response at week 12, response rates in all treatment groups subsequently declined over time. During period 2, there were no significant differences in clinical response rates in either trial between patients randomly assigned to adalimumab at either a weekly dose or an every-other-week dose and those assigned to placebo, regardless of whether the patients had a response at week 12. For patients who received placebo in period 1, 41.4% of those assigned to adalimumab weekly in period 2 (PIONEER I) and 15.9% of those reassigned to placebo in period 2 (PIONEER II) had a clinical response at week 36.
    - The authors noted that the magnitude of improvement with adalimumab treatment was modest compared with adalimumab treatment in other disease states, and patients were unlikely to achieve complete symptom resolution.

Juvenile idiopathic arthritis (JIA)

- In a trial of pediatric patients (six to 17 years of age) with JIA (extended oligoarticular, polyarticular, or systemic without systemic manifestations), the patients treated with placebo had significantly more flares than the patients treated with ORENCIA (abatacept) (P=0.0003). The time to flare was significantly different favoring abatacept (P=0.0002) (Ruperto et al, 2008).

- HUMIRA (adalimumab) was studied in a group of patients (four to 17 years of age) with active polyarticular JIA who had previously received treatment with NSAIDs. Patients were stratified according to MTX use and received 24 mg/m^2 (maximum of 40 mg) of adalimumab every other week for 16 weeks. The patients with an American College of Rheumatology Pediatric 30 (ACR Pedi 30) response at week 16 were randomly assigned to receive adalimumab or placebo in a double-blind method every other week for up to 32 weeks. The authors found that 74% of patients not receiving MTX and 94% of those receiving MTX had an ACR Pedi 30 at week 16. Among those not receiving MTX, flares occurred in 43% receiving adalimumab and 71% receiving placebo (P=0.03). In the patients receiving MTX, flares occurred in 37 and 65% in the adalimumab and placebo groups, respectively (P=0.02). ACR Pedi scores were significantly greater with adalimumab than placebo and were sustained after 104 weeks of treatment (Lovell et al, 2008).
- A double-blind, multicenter, randomized controlled trial compared HUMIRA (adalimumab) and placebo in 46 children ages six to 18 years with enthesitis-related arthritis (Burgos-Vargas et al, 2015). Patients were TNF inhibitor naïve. At week 12, the percentage change from baseline in the number of active joints with arthritis was significantly reduced with adalimumab compared to placebo (-62.6% vs -11.6%, P=0.039). A total of seven patients (three placebo; four adalimumab) escaped the study early during the double-blind phase and moved to open-label adalimumab therapy. Analysis excluding these patients produced similar results (adalimumab, -83.3 vs placebo -32.1; P=0.018). At week 52, adalimumab-treated patients had a mean reduction in active joint count from baseline of 88.7%. A total of 93.5% of patients achieved complete resolution of their swollen joints with a mean of 41 days of adalimumab therapy.
- In a trial involving 69 pediatric patients with active polyarticular JIA despite treatment with NSAIDs and MTX, ENBREL (etanercept) was associated with a significant reduction in flares compared to placebo (28% vs 81%; P=0.003) (Lovell et al, 2000). Ninety-four percent of patients who remained in an open-label four year extension trial met ACR Pedi 30; C-reactive protein (CRP) levels, articular severity scores, and patient pain assessment scores all decreased. There were five cases of serious AEs related to etanercept therapy after four years (Lovell et al, 2006).
- The approval of ACTEMRA (tocilizumab) for the indication of SJIA was based on a randomized, placebo-controlled trial (N=112). Children age two to 17 years of age with active SJIA and inadequate response to NSAIDs and corticosteroids were included in the study. The primary endpoint was ACR 30 and absence of fever at week 12. At week 12, the proportion of patients achieving ACR 30 and absence of fever was significantly greater in the tocilizumab-treated patients compared to the placebo treated patients (85% vs 24%; P<0.0001)(De Benedetti et al, 2012). The double-blind, randomized CHERISH study evaluated tocilizumab for JIA flares in patients ages 2 to 17 years with JIA with an inadequate response or intolerance to MTX (Brunner et al, 2015). Tocilizumab-treated patients experienced significantly fewer JIA flares at week 40 compared to patients treated with placebo (25.6% vs 48.1%; P<0.0024).
- In two trials in patients with SJIA, ILARIS (canakinumab) was more effective at reducing flares than placebo. It also allowed for glucocorticoid dose tapering or discontinuation. More patients treated with canakinumab experienced infections than patients treated with placebo (Ruperto et al, 2012).
- A meta-analysis of trials evaluating biologics for the treatment of SJIA included 5 trials; one each for KINERET (anakinra), ILARIS (canakinumab), and ACTEMRA (tocilizumab), and 2 for rilonacept (not FDA approved for JIA and not included in this review) (Tarp et al, 2016). The primary endpoint, the proportion of patients achieving a modified ACR Pedi 30 response, was superior to placebo for all agents, but did not differ significantly among anakinra, canakinumab, and tocilizumab. However, comparisons were based on low-quality, indirect evidence and no firm conclusions can be drawn on their relative efficacy. No differences among drugs for serious AEs were demonstrated.

Plaque psoriasis (PsO)

- In a randomized, double-blind, double-dummy trial, HUMIRA (adalimumab) was compared to MTX and placebo in patients with moderate to severe PsO despite treatment with topical agents. The primary outcome was the proportion of patients that achieved Psoriasis Area and Severity Index (PASI) 75 at 16 weeks. Significantly more patients in the adalimumab group achieved the primary endpoint compared to patients in the MTX (P<0.001) and placebo (P<0.001) groups, respectively (Saurat et al, 2008).
- More than 2,200 patients were enrolled in two published, pivotal, phase III trials that served as the primary basis for the FDA approval of STELARA (ustekinumab) in PsO. PHOENIX 1 and PHOENIX 2 enrolled patients with moderate to severe PsO to randomly receive ustekinumab 45 mg, 90 mg or placebo at weeks zero, four and every 12 weeks thereafter (Leonardi et al, 2008; Papp et al, 2008; Langley et al, 2015). In PHOENIX 1, patients who were initially randomized to ustekinumab at week zero and achieved long-term response (at least PASI 75 at weeks 28 and 40) were re-randomized at week 40 to maintenance ustekinumab or withdrawal from treatment. Patients in the 45 mg ustekinumab and 90 mg ustekinumab groups had higher proportion of patients achieving PASI 75 compared to patients in the placebo group at week 12 (P<0.0001 for both). PASI 75 response was better maintained to at least one year in those receiving maintenance ustekinumab than in those withdrawn from treatment at week 40 (P<0.0001)

(Leonardi et al, 2008). In PHOENIX 2, the primary endpoint (the proportion of patients achieving a PASI 75 response at week 12) was achieved in significantly more patients receiving ustekinumab 45 and 90 mg compared to patients receiving placebo (P<0.0001). Partial responders were re-randomized at week 28 to continue dosing every 12 weeks or escalate to dosing every eight weeks. More partial responders at week 28 who received 90 mg every eight weeks achieved PASI 75 at week 52 than did those who continued to receive the same dose every 12 weeks. There was no such response to changes in dosing intensity in partial responders treated with 45 mg. AEs were similar between groups (Papp et al, 2008). A total of 70% (849 of 1,212) of ustekinumab-treated patients completed therapy through week 244. At week 244, the proportions of patients initially randomized to ustekinumab 45 mg and 90 mg who achieved PASI 75 were 76.5% and 78.6%, respectively. A total of 50.0% and 55.5% of patients, respectively, achieved PASI 90 (Langley et al, 2015).

- In a study comparing ENBREL (etanercept) and STELARA (ustekinumab), a greater proportion of PsO patients achieved the primary outcome (PASI 75 at week 12) with ustekinumab 45 (67.5%) and 90 mg (73.8%) compared to etanercept 50 mg (56.8%; P=0.01 vs ustekinumab 45 mg; P<0.001 vs ustekinumab 90 mg). In this trial, etanercept therapy was associated with a greater risk of injection site erythema (14.7% vs 0.7% of all ustekinumab patients) (Griffiths et al, 2010).
- Approval of OTEZLA (apremilast) for moderate to severe PsO was based on results from the ESTEEM trials. In the trials, 1,257 patients with moderate to severe PsO were randomized 2:1 to apremilast 30 mg twice daily (with a titration period) or placebo. The primary endpoint was the number of patients with a 75% improvement on the PASI 75. In ESTEEM 1, significantly more patients receiving apremilast achieved PASI 75 compared to placebo (33.1% vs 5.3%; P<0.0001) at 16 weeks. In ESTEEM 2, significantly more patients receiving apremilast also achieved PASI 75 compared to placebo (28.8% vs 5.8%; P<0.0001) at 16 weeks (Papp et al, 2015; Paul et al, 2015a).
    - Additional analyses of the ESTEEM trials have been published. In one (Thaçi et al, 2016), the impact of apremilast on health-related quality of life, general function, and mental health was evaluated using patient-reported outcome assessments. The study demonstrated improvement with apremilast vs placebo, including improvements on the dermatology life quality index (DLQI) and SF-36 mental component summary (MCS) that exceeded minimal clinically important differences. In another analysis (Rich et al, 2016), effects of apremilast on difficult-to-treat nail and scalp psoriasis were evaluated. At baseline in ESTEEM 1 and ESTEEM 2, respectively, 66.1% and 64.7% of patients had nail psoriasis and 66.7% and 65.5% had moderate to very severe scalp psoriasis. At week 16, apremilast produced greater improvements in Nail Psoriasis Severity Index (NAPSI) score vs placebo; greater NAPSI-50 response (50% reduction from baseline in target nail NAPSI score) vs placebo; and greater response on the Scalp Physician Global Assessment (ScPGA) vs placebo. Improvements were generally maintained over 52 weeks in patients with a PASI response at week 32.
- COSENTYX (secukinumab) was evaluated in two large, phase 3, double-blind trials in patients with moderate to severe PsO. The co-primary endpoints were the proportions of patients achieving PASI 75 and the proportions of patients with clear or almost clear skin (score 0 or 1) on the modified investigator's global assessment (IGA) at 12 weeks.
    - In ERASURE (N=738), 81.6%, 71.6%, and 4.5% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, and placebo, respectively, and 65.3%, 51.2%, and 2.4% achieved a score of 0 or 1 on the IGA (Langley et al, 2014).
    - In FIXTURE (N=1,306), 77.1%, 67%, 44%, and 4.9% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, ENBREL (etanercept) at FDA-recommended dosing, and placebo, respectively, and 62.5%, 51.1%, 27.2%, and 2.8% achieved a score of 0 or 1 on the IGA (Langley et al, 2014).
- Two smaller, phase 3, double-blind, placebo-controlled trials evaluated COSENTYX (secukinumab) given by prefilled syringe (FEATURE) or auto-injector/pen (JUNCTURE). Again, co-primary endpoints were the proportions of patients achieving PASI 75 and obtaining a score of 0 or 1 on the modified IGA at 12 weeks.
    - In FEATURE (N=177), 75.9%, 69.5%, and 0% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, and placebo, respectively, and 69%, 52.5%, and 0% achieved a score of 0 or 1 on the IGA (Blauvelt et al, 2015).
    - In JUNCTURE (N=182), 86.7%, 71.7%, and 3.3% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, and placebo, respectively, and 73.3%, 53.3%, and 0% achieved a score of 0 or 1 on the IGA (Paul et al, 2015b).
- Secondary endpoints, including the proportions of patients demonstrating a reduction of 90% or more on the PASI (PASI 90), a reduction of 100% (PASI 100), and change in the DLQI further support the efficacy of COSENTYX (secukinumab) (Blauvelt et al, 2015; Langley et al, 2014; Paul et al, 2015b).
- In the CLEAR study, COSENTYX (secukinumab) 300 mg SQ every four weeks and STELARA (ustekinumab) 45 mg or 90 mg SQ (based on body weight) every 12 weeks were compared for safety and efficacy in a double-blind,

randomized controlled trial in 676 patients with moderate to severe PsO (Thaçi et al, 2015). The primary endpoint, proportion of patients achieving PASI 90 at week 16, was significantly higher with secukinumab compared to ustekinumab (79% vs 57.6%; P<0.0001). Achievement of PASI 100 response at week 16 was also significantly higher with secukinumab over ustekinumab (44.3% vs 28.4%; P<0.0001). Infections and infestations were reported in 29.3% of secukinumab- and 25.3% of ustekinumab-treated patients. Most infections were not serious and were managed without discontinuation. The most commonly reported AEs included headache and nasopharyngitis. Serious AEs were reported in 3% of each group.

- A meta-analysis of seven Phase 3 clinical trials demonstrated the efficacy of COSENTYX (secukinumab) vs placebo and vs ENBREL (etanercept) in patients with PsO (Ryoo et al, 2016). The ORs for achieving PASI 75 and for achieving IGA 0 or 1 were both 3.7 for secukinumab vs etanercept. Secukinumab 300 mg was significantly more effective than 150 mg. Secukinumab was well-tolerated throughout the one-year trials.
- The use of TALTZ (ixekizumab) for the treatment of PsO was evaluated in the UNCOVER-1, UNCOVER-2, and UNCOVER-3 trials. All were Phase 3, double-blind, randomized trials.
    - UNCOVER-1 (N=1,296) compared ixekizumab 160 mg loading dose then 80 mg every 2 weeks, ixekizumab 160 mg loading dose then 80 mg every 4 weeks, and placebo (Gordon et al, 2016; Taltz product dossier, 2016). Co-primary endpoints were the proportion of patients achieving PASI 75 and the proportion of patients achieving a physician's global assessment (PGA) score of 0 or 1 (clear or almost clear) at week 12. In the ixekizumab every 2 week, ixekizumab every 4 week, and placebo groups, PASI 75 was achieved by 89.1%, 82.6%, and 3.9% of patients, respectively (P<0.001 for both doses vs placebo), and PGA 0 or 1 was achieved by 81.8%, 76.4%, and 3.2% of patients, respectively (P<0.001 for both doses vs placebo). Improvements for ixekizumab vs placebo were also seen in secondary endpoints including PASI 90, PASI 100, PGA 0, and change in DLQI.
    - UNCOVER-2 (N=1,224) compared ixekizumab 160 mg loading dose then 80 mg every 2 weeks, ixekizumab 160 mg then 80 mg every 4 weeks, etanercept 50 mg twice weekly, and placebo (Griffiths et al, 2015). Co-primary endpoints were the proportion of patients achieving PASI 75 and the proportion of patients achieving a PGA 0 or 1 at week 12. The proportions of patients achieving PASI 75 were 89.7%, 77.5%, 41.6%, and 2.4% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively (P<0.0001 for all active treatments vs placebo and for both ixekizumab arms vs etanercept). The proportions of patients achieving PGA 0 or 1 were 83.2%, 72.9%, 36%, and 2.4% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively (P<0.0001 for all active treatments vs placebo and for both ixekizumab arms vs etanercept). Improvements were also greater for ixekizumab vs placebo, etanercept vs placebo, and ixekizumab vs etanercept for all secondary endpoints including PGA 0, PASI 90, PASI 100, and DLQI.
    - UNCOVER-3 (N=1,346) had the same treatment groups and primary and secondary endpoints as UNCOVER-2 (Griffiths et al, 2015). The proportions of patients achieving PASI 75 were 87.3%, 84.2%, 53.4%, and 7.3% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively (P<0.0001 for all active treatments vs placebo and for both ixekizumab arms vs etanercept). The proportions of patients achieving PGA 0 or 1 were 80.5%, 75.4%, 41.6%, and 6.7% in the ixekizumab every 2 week, ixekizumab every 4 week, etanercept, and placebo groups, respectively (P<0.0001 for all active treatments vs placebo and for both ixekizumab arms vs etanercept). Improvements were also greater for ixekizumab vs placebo, etanercept vs placebo, and ixekizumab vs etanercept for all secondary endpoints including PGA 0, PASI 90, PASI 100, and DLQI.
    - Results through week 60 for UNCOVER-1, UNCOVER-2, and UNCOVER-3 have been reported (Gordon et al, 2016). At week 12 in UNCOVER-1 and UNCOVER-2, patients responding to ixekizumab (PGA 0 or 1) were re-randomized to receive ixekizumab 80 mg every 4 weeks, ixekizumab 80 mg every 12 weeks, or placebo through week 60. Among the patients who were randomly reassigned at week 12 to receive 80 mg of ixekizumab every 4 weeks (the approved maintenance dosing), 80 mg of ixekizumab every 12 weeks, or placebo, a PGA score of 0 or 1 was maintained by 73.8%, 39.0%, and 7.0% of the patients, respectively, and high rates were maintained or attained for additional measures such as PASI 75, PASI 90, and PASI 100 (pooled data for UNCOVER-1 and UNCOVER-2). At week 12 in UNCOVER-3, patients entered a long-term extension period in which they received ixekizumab 80 mg every 4 weeks through week 60. At week 60, at least 73% had a PGA score of 0 or 1 and at least 80% had a PASI 75 response. In addition, most patients had maintained or attained PASI 90 or PASI 100 at week 60.
- The use of SILIQ (brodalumab) for the treatment of PsO was evaluated in the AMAGINE-1, AMAGINE-2, and AMAGINE-3 trials. All were Phase 3, double-blind, randomized trials.
    - AMAGINE-1 (N=661) compared brodalumab 210 mg, brodalumab 140 mg, and placebo; each treatment was given at weeks zero, one, and two, followed by every two weeks to week 12 (Papp et al, 2016). This 12-week

induction phase was followed by a withdrawal/retreatment phase through week 52: patients receiving brodalumab who achieved PGA 0 or 1 (PGA success) were re-randomized to the placebo or induction dose, and patients randomized to brodalumab with PGA ≥2 and those initially receiving placebo received brodalumab 210 mg every two weeks. Patients in the withdrawal phase who had disease recurrence (PGA ≥3) between weeks 16 and 52 were retreated with their induction doses of brodalumab. Co-primary endpoints were the proportion of patients achieving PASI 75 and the proportion of patients achieving PGA success at week 12. PASI 75 was achieved by 83% (95% CI, 78 to 88), 60% (95% CI, 54 to 67), and 3% (95% CI, 1 to 6) of patients in the brodalumab 210 mg, brodalumab 140 mg, and placebo groups, respectively; PGA success was achieved by 76% (95% CI, 70 to 81), 54% (95% CI, 47 to 61), and 1% (95% CI, 0 to 4), respectively (P<0.001 for all comparisons of brodalumab vs placebo). Differences in key secondary endpoints at week 12 also favored brodalumab vs placebo, including PASI 90, PASI 100, and PGA 0. In the randomized withdrawal phase, high response rates were maintained in those who continued brodalumab, while most patients re-randomized to placebo experienced return of disease (but were able to recapture disease control with retreatment).

- AMAGINE-2 (N=1,831) and AMAGINE-3 (N=1,881) were identical in design and compared brodalumab 210 mg, brodalumab 140 mg, STELARA (ustekinumab), and placebo (Lebwohl et al, 2015). Brodalumab was given at weeks zero, one, and two, followed by every two weeks to week 12. Ustekinumab was given in weight-based doses per its FDA-approved labeling. At week 12, patients receiving brodalumab were re-randomized to receive brodalumab at a dose of 210 mg every two weeks or 140 mg every two, four, or eight weeks; patients receiving ustekinumab continued ustekinumab; and patients receiving placebo were switched to brodalumab 210 mg every two weeks; maintenance continued though week 52. The primary endpoints included a comparison of both brodalumab doses vs placebo with regard to the proportion of patients achieving PASI 75 and the proportion of patients achieving PGA success (PGA 0 or 1) at week 12, as well as a comparison of brodalumab 210 mg vs ustekinumab with regard to the proportion of patients achieving PASI 100 at week 12.
  - In AMAGINE-2, the proportion of patients achieving PASI 75 was 86% (95% CI, 83 to 89), 67% (95% CI, 63 to 70), 70% (95% CI, 65 to 75), and 8% (95% CI, 5 to 12) in the brodalumab 210 mg, brodalumab 140 mg, ustekinumab, and placebo groups, respectively, and the proportion of patients achieving PGA success was 79% (95% CI, 75 to 82), 58% (95% CI, 54 to 62), 61% (95% CI, 55 to 67), and 4% (95% CI, 2 to 7), respectively (P<0.001 for all comparisons of brodalumab vs placebo). The proportion of patients achieving PASI 100 was 44% (95% CI, 41 to 49), 26% (95% CI, 22 to 29), 22% (95% CI, 17 to 27), and 1% (95% CI, 0 to 2), respectively (P<0.001 for both brodalumab doses vs placebo and for brodalumab 210 mg vs ustekinumab; P=0.08 for brodalumab 140 mg vs ustekinumab).
  - In AMAGINE-3, the proportion of patients achieving PASI 75 was 85% (95% CI, 82 to 88), 69% (95% CI, 65 to 73), 69% (95% CI, 64 to 74), and 6% (95% CI, 4 to 9) in the brodalumab 210 mg, brodalumab 140 mg, ustekinumab, and placebo groups, respectively, and the proportion of patients achieving PGA success was 80% (95% CI, 76 to 83), 60% (95% CI, 56 to 64), 57% (95% CI, 52 to 63), and 4% (95% CI, 2 to 7), respectively (P<0.001 for all comparisons of brodalumab vs placebo). The proportion of patients achieving PASI 100 was 37% (95% CI, 33 to 41), 27% (95% CI, 24 to 31), 19% (95% CI, 14 to 23), and 0.3% (95% CI, 0 to 2), respectively (P<0.001 for both brodalumab doses vs placebo and for brodalumab 210 mg vs ustekinumab; P=0.007 for brodalumab 140 mg vs ustekinumab).
  - In both studies, the two brodalumab doses were superior to placebo with regard to all key secondary endpoints. Patients receiving brodalumab 210 mg throughout the induction and maintenance phases demonstrated an increase in PASI response rates through week 12 and a stabilization during weeks 16 to 52. Based on PGA success rates, maintenance with brodalumab 210 mg or 140 mg every two weeks was superior to the use of the less frequent maintenance regimens, and the 210 mg regimen was superior to the 140 mg regimen.

- For most immunomodulators that are FDA approved for the treatment of PsO, the indication is limited to adults. In 2016, ENBREL (etanercept) received FDA approval for treatment of PsO in pediatric patients aged four years and older. Limited information from published trials is also available on the use of STELARA (ustekinumab) in adolescent patients (age 12 to 17 years).
  - A 48-week, double-blind, placebo-controlled trial (N=211) evaluated the use of etanercept in patients 4 to 17 years of age with moderate-to-severe PsO (Paller et al, 2008). Patients received etanercept 0.8 mg SQ once weekly or placebo for 12 weeks, followed by 24 weeks of open-label etanercept; 138 patients underwent a second randomization to placebo or etanercept at week 36 to investigate effects of withdrawal and

retreatment. The primary endpoint, PASI 75 at week 12, was achieved by 57% and 11% of patients receiving etanercept and placebo, respectively. A significantly higher proportion of patients in the etanercept group than in the placebo group achieved PASI 90 (27% vs 7%) and a PGA of 0 or 1 (53% vs 13%) at week 12 (P<0.001). During the withdrawal period from week 36 to week 48, response was lost by 29 of 69 patients (42%) assigned to placebo at the second randomization. Four serious AEs (including three infections) occurred in three patients during treatment with open-label etanercept; all resolved without sequelae. The authors concluded that etanercept significantly reduced disease severity in this population. Results of a 5-year, open-label extension study (N=182) demonstrated that etanercept was generally well tolerated and efficacy was maintained in those who remained in the study for up to 264 weeks (69 of 181 patients) (Paller et al, 2016).

  - A 52-week, double-blind, placebo-controlled trial (N=110) evaluated the use of ustekinumab in patients 12 to 17 years of age with moderate-to-severe PsO (Landells et al, 2015). Patients received a weight-based standard dose (SD), a half-strength dose (HSD), or placebo. The primary endpoint, the proportion of patients achieving a PGA 0 or 1 at week 12, was significantly greater in the SD (69.4%) and HSD (67.6%) groups vs placebo (5.4%) (P<0.001 for both doses vs placebo). The proportions of patients achieving PASI 75 at this time point were 80.6%, 78.4%, and 10.8% in the SD, HSD, and placebo groups, respectively (P<0.001 for both doses vs placebo), and the proportions of patients achieving PASI 90 were 61.1%, 54.1%, and 5.4% in the SD, HSD, and placebo groups, respectively (P<0.001 for both doses vs placebo). In both groups, the proportions of patients achieving these endpoints were maintained from week 12 through week 52. The authors concluded that ustekinumab appears to be a viable treatment option for moderate-to-severe PsO in the adolescent population. The standard dose provided a response comparable to that in adults with no unexpected AEs through 1 year of treatment.

- Combination therapy is commonly utilized, such as with different topical therapies, systemic plus topical therapies, and combinations of certain systemic therapies with phototherapy (Feldman, 2015). Combinations of different systemic therapies have not been adequately studied; however, there are some data to show that combined therapy with ENBREL (etanercept) plus MTX may be beneficial for therapy-resistant patients (Busard et al, 2014; Gottlieb et al, 2012).
- In a meta-analysis evaluating the efficacy and tolerability of biologic and nonbiologic systemic treatments for moderate to severe PsO, HUMIRA (adalimumab) use was associated with a risk difference of 64% compared to placebo in achieving a PASI 75 response (P<0.00001) while ENBREL (etanercept) 25 and 50 mg twice weekly were associated with a risk difference of 30 and 44% compared to placebo (P<0.00001 for both strengths vs placebo). The REMICADE (infliximab) group had the greatest response with a risk difference of 77% compared to the placebo group (P<0.0001). The withdrawal rate was 0.5% with adalimumab, 0.4 to 0.5% with etanercept and 1.3% with infliximab (Schmitt et al, 2008).
- Another meta-analysis evaluated the efficacy and safety of long-term treatments (≥24 weeks) for moderate-to-severe PsO (Nast et al, 2015a). A total of 25 randomized trials (N=11,279) were included. Compared to placebo, RRs for achievement of PASI 75 were 13.07 (95% CI, 8.60 to 19.87) for REMICADE (infliximab), 11.97 (95% CI, 8.83 to 16.23) for COSENTYX (secukinumab), 11.39 (95% CI, 8.94 to 14.51) for STELARA (ustekinumab), 8.92 (95% CI, 6.33 to 12.57) for HUMIRA (adalimumab), 8.39 (95% CI, 6.74 to 10.45) for ENBREL (etanercept), and 5.83 (95% CI, 2.58 to 13.17) for OTEZLA (apremilast). Head-to-head studies demonstrated better efficacy for secukinumab and infliximab vs etanercept, and for infliximab vs MTX. The biologics and apremilast also had superior efficacy vs placebo for endpoints of PASI 90 and PGA 0 or 1. The investigators stated that based on available evidence, infliximab, secukinumab, and ustekinumab are the most efficacious long-term treatments, but noted that additional head-to-head comparisons and studies on safety and patient-related outcomes are desirable.

Psoriatic arthritis (PsA)

- In two trials, PsA patients receiving HUMIRA (adalimumab) 40 mg every other week achieved an ACR 20 at a higher rate than with placebo. Thirty-nine percent in the active treatment group vs 16% in the placebo group achieved this endpoint by week 12 (P=0.012) in a trial (N=100); while 58 and 14% of patients, respectively, achieved this endpoint in a second trial (P<0.001) (Genovese et al, 2007; Mease et al, 2005). Adalimumab use was also associated with an improvement in structural damage, as measured by the mTSS, compared to those receiving placebo (-0.2 vs 1; P<0.001) (Mease et al, 2005).
- In a 12-week trial in adult patients with PsA despite NSAID therapy, 87% of ENBREL (etanercept) treated patients met PsA response criteria, compared to 23% of those on placebo (P<0.0001). A PASI 75 improvement and ACR 20 response were detected in 26 and 73% of etanercept-treated patients vs 0 (P=0.0154) and 13% (P<0.0001) of placebo-treated patients (Mease et al, 2000). In a second trial, the mean annualized rate of change in the mTSS with ENBREL (etanercept) was -0.03 unit, compared to one unit with placebo (P<0.0001). At 24 weeks, 23% of etanercept

patients eligible for PsO evaluation achieved at least a PASI 75, compared to 3% of placebo patients (P=0.001). Additionally, HAQ scores were significantly improved with etanercept (54%) over placebo (6%; P<0.0001). Injection site reaction occurred at a greater rate with etanercept than placebo (36% vs 9%; P<0.001) (Mease et al, 2004).

- The FDA approval of SIMPONI (golimumab) for PsA was based on the GO-REVEAL study, a multicenter, randomized, double-blind, placebo-controlled trial in adult patients with moderate to severely active PsA despite NSAID or DMARD therapy (N=405). Golimumab with or without MTX compared to placebo with or without MTX, resulted in significant improvement in signs and symptoms as demonstrated by the percentage of patients achieving a ACR 20 response at week 14. The ACR responses observed in the golimumab-treated groups were similar in patients receiving and not receiving concomitant MTX therapy (Kavanaugh et al, 2009).
    - Subcutaneous golimumab for patients with active PsA demonstrated safety and efficacy over five years in the long-term extension of the GO-REVEAL study. Approximately one-half of patients took MTX concurrently. ACR 20 response rates at year five were 62.8 to 69.9% for golimumab SQ 50 or 100 mg every four weeks (Kavanaugh et al, 2014b).
    - Post-hoc analyses of the 5-year GO-REVEAL results evaluated the relationship between achieving minimal disease activity (MDA; defined as the presence of ≥5 of 7 PsA outcomes measures [(≤1 swollen joint, ≤1 tender joint, PASI ≤1, patient pain score ≤15, patient global disease activity score ≤20, HAQ disability index [HAQ DI] ≤0.5, and ≤1 tender enthesis point]) and long-term radiographic outcomes including radiographic progression. Among golimumab-treated patients, achieving long-term MDA was associated with better long-term functional improvement, patient global assessment, and radiographic outcomes. Radiographic benefit was more pronounced in patients using MTX at baseline. The authors conclude that in patients with active PsA, aiming for MDA as part of a treat-to-target strategy may provide long-term functional and radiographic benefits (Kavanaugh et al, 2016).
- In another trial, more REMICADE (infliximab) treated patients achieved ACR 20 at weeks 12 and 24 compared to placebo treated patients (P<0.001) (Antoni et al, 2005).
- The efficacy of CIMZIA (certolizumab) in the treatment of PsA was established in one multicenter, double-blind, placebo controlled trial (N=409). Patients were randomized to receive placebo, CIMZIA 200 mg every two weeks, or CIMZIA 400 mg every four weeks. At week 12, ACR 20 response was significantly greater in both active treatment groups compared to placebo (Mease et al, 2014).
- The FDA-approval of STELARA (ustekinumab) for PsA was based on the results of two randomized, double-blind, placebo-controlled trials in adult patients with active PsA despite NSAID or DMARD therapy (PSUMMIT 1 and PSUMMIT 2). In PSUMMIT 1 (N=615), a greater proportion of patients treated with ustekinumab 45 mg or 90 mg alone or in combination with MTX achieved ACR 20 response at week 24 compared to placebo (42.4% and 49.5% vs 22.8%; P<0.0001 for both comparisons); responses were maintained at week 52 (McInnes et al, 2013). Similar results were observed in the PSUMMIT 2 trial (N=312) with 43.8% of ustekinumab-treated patients and 20.2% of placebo-treated patients achieving an ACR 20 response (P<0.001) (Ritchlin et al, 2014).
    - In PSUMMIT-1, patients taking placebo or ustekinumab 45 mg could adjust therapy at week 16 if they had an inadequate response, and all remaining patients in the placebo group at week 24 were crossed over to receive treatment with ustekinumab 45 mg (McInnes et al, 2013). At week 100 (Kavanaugh et al, 2015a), the ACR 20 responses were 63.6%, 56.7%, and 62.7% in the 90 mg, 45 mg, and placebo crossover groups, respectively. ACR 50 and ACR 70 responses followed a similar pattern and ranged from 37.3% to 46% and 18.6% to 24.7%, respectively. At week 100, the proportions of patients achieving PASI 75 were 71.3%, 72.5%, and 63.9% in the 90 mg, 45 mg, and placebo crossover groups, respectively. Improvements in physical function and health-related quality of life (HRQoL) were sustained over time, with median decreases in HAQ-DI scores from baseline to week 100 of 0.38, 0.25, and 0.38 in the 90 mg, 45 mg, and placebo crossover groups, respectively.
- Cosentyx (secukinumab) gained FDA approval for the treatment of PsA based on two multicenter, double-blind, placebo-controlled randomized controlled trials – FUTURE 1 and FUTURE 2 (Mease et al, 2015; McInnes et al, 2015). The FUTURE 1 study randomized patients to secukinumab 75 mg or 150 mg every 4 weeks (following IV loading doses) or placebo and evaluated ACR 20 at week 24. In the FUTURE 2 study, patients were randomized to secukinumab 75 mg, 150 mg, or 300 mg SQ every 4 weeks (following SQ loading doses given at weeks 0, 1, 2, 3, and 4) or placebo and evaluated at week 24 for ACR 20 response.
    - In FUTURE 1 at week 24, both the secukinumab 75 mg and 150 mg doses demonstrated significantly higher ACR 20 responses vs placebo (50.5% and 50.0% vs 17.3%, respectively; P<0.0001 vs placebo).
    - All pre-specified endpoints including dactylitis, enthesitis, SF-36 PCS, HAQ-DI, DAS28-CRP, ACR 50, PASI 75, PASI 90, and mTSS score were achieved by week 24 and reached statistical significance.

  - In FUTURE 2 at week 24, ACR 20 response rates were significantly greater with secukinumab than with placebo: 54.0%, 51.0%, and 29.3% vs 15.3% with secukinumab 300 mg, 150 mg, and 75 mg vs placebo, respectively (P<0.0001 for secukinumab 300 mg and 150 mg; P<0.05 for 75 mg vs placebo).
  - Improvements were seen with secukinumab 300 mg and 150 mg with regard to PASI 75/90 scores, DAS28-CRP, SF-36 PCS, HAQ-DI, dactylitis, and enthesitis. Efficacy was observed in both TNF-naïve patients and in patients with prior TNF inadequate response or intolerance.
- The efficacy of OTEZLA (apremilast) was demonstrated in three placebo-controlled trials in patients with PsA. At week 16, significantly more patients in the OTEZLA groups had ≥20% improvement in symptoms, as defined by ACR response criteria (Cutolo et al, 2013; Edwards et al, 2016; Kavanaugh et al, 2014a). Clinical improvements observed at 16 weeks were sustained at 52 weeks (Edwards et al, 2016; Kavanaugh et al, 2015b).
- A small, single-center randomized trial (N=100) compared REMICADE (infliximab), ENBREL (etanercept), and HUMIRA (adalimumab) in patients with PsA who had had an inadequate response to DMARDs (Atteno et al, 2010). The investigators found that each of the agents effectively controlled the signs and symptoms of PsA, and ACR response rates were similar among agents. Patients receiving infliximab and adalimumab showed the greatest improvement in PASI scores, whereas patients receiving etanercept showed the greatest improvement on the tender joint count and HAQ. Limitations of this trial were lack of blinding and lack of a placebo group.
- A meta-analysis based on both direct and indirect comparisons evaluated the efficacy and safety of HUMIRA (adalimumab), ENBREL (etanercept), REMICADE (infliximab), and SIMPONI (golimumab) over 24 weeks for the treatment of PsA (Fénix et al, 2013). The investigators found no differences among products for the primary endpoint of ACR 50 or secondary endpoints of ACR 20 and ACR 70, except that etanercept was associated with a lower ACR 70 response. However, low sample sizes limited the power of the analysis.
- A meta-analysis of nine randomized controlled trials and six observational studies evaluated HUMIRA (adalimumab), ENBREL (etanercept), SIMPONI (golimumab), or placebo in the achievement of ACR 20, ACR 50, and ACR 70 endpoints in patients with moderate to severe PsA (Lemos et al, 2014). Patients who used adalimumab, etanercept and golimumab were more likely to achieve ACR 20 and ACR 50 after 12 or 24 weeks of treatment. In long-term analysis (after all participants used anti-TNF for at least 24 weeks), there was no difference in ACR 20 and ACR 50 between the anti-TNF and control groups, but patients originally randomized to anti-TNF were more likely to achieve ACR 70.
- Two indirect comparison meta-analyses sought to compare the efficacy of biologics for the treatment of PsA in patients with an inadequate response to prior therapies.
  - An analysis of 12 randomized trials compared various biologics in patients having an inadequate response to NSAIDs or traditional DMARDs (Ungprasert et al, 2016a). The investigators determined that patients receiving older TNF inhibitors (evaluated as a group: ENBREL [etanercept], REMICADE [infliximab], HUMIRA [adalimumab], and SIMPONI [golimumab]) had a statistically significantly higher chance of achieving ACR 20 compared to patients receiving CIMZIA (certolizumab), OTEZLA (apremilast), or STELARA (ustekinumab). Patients receiving COSENTYX (secukinumab) also had a higher chance of achieving ACR 20 compared to certolizumab, ustekinumab, and apremilast, but the relative risk did not always reach statistical significance. There was no statistically significant difference in this endpoint between secukinumab and the older TNF inhibitors, or between apremilast, ustekinumab, and certolizumab.
  - An analysis of 5 randomized trials compared various non-TNF inhibitor biologics (ORENCIA [abatacept], secukinumab, ustekinumab, and apremilast) in patients having an inadequate response or intolerance to TNF inhibitors (Ungprasert et al, 2016b). The investigators found no difference for any between-agent comparison in the likelihood of achieving an ACR 20 response.
  - These meta-analyses had limitations, notably being based on a small number of trials, and should be interpreted with caution.

Ulcerative colitis (UC)

- Two trials (ACT 1 and ACT 2) evaluated REMICADE (infliximab) compared to placebo for the treatment of UC. In both trials, clinical response at week eight was significantly higher in infliximab 5 and 10 mg/kg treated patients compared to placebo treated patients (all P<0.001). A significantly higher clinical response rate in both infliximab groups was maintained throughout the duration of the studies (Rutgeerts et al, 2005). A randomized open-label trial evaluated infliximab at different dosing intervals for the treatment of pediatric UC. At week eight, 73.3% of patients met the primary endpoint of clinical response (95% CI, 62.1 to 84.5%) (Hyams et al, 2012).
- In the ULTRA 2 study, significantly more patients taking HUMIRA (adalimumab) 160 mg at week zero, 80 mg at week two, and then 40 mg every other week for 52 weeks achieved clinical remission and clinical response vs patients taking placebo (Sandborn et al, 2012). These long term results confirm the findings of ULTRA 1. This eight-week induction trial demonstrated that adalimumab in same dosage as ULTRA 2 was effective for inducing clinical

remission (Reinisch et al, 2011). In ULTRA 1, significant differences between the adalimumab and placebo groups were only achieved for two of the secondary end points at week eight, i.e., rectal bleeding and PGA subscores. Conversely, in ULTRA 2, significantly greater proportions of adalimumab-treated patients achieved almost all secondary end points at week eight. This may have been because of the high placebo response rates in ULTRA 1. A meta-analysis of three randomized trials comparing adalimumab to placebo demonstrated that adalimumab increased the proportion of patients with clinical responses, clinical remission, mucosal healing, and inflammatory bowel disease questionnaire responses in the induction and maintenance phases. It also increased the proportion of patients with steroid-free remission in the maintenance phase (Zhang et al, 2016).

- SIMPONI (golimumab) was studied in 1,064 patients with moderate to severe UC. Patients receiving golimumab 200 mg then 100 mg or golimumab 400 mg then 200 mg at weeks zero and two were compared to patients receiving placebo. At week six, significantly greater proportions of patients in the golimumab 200/100 mg and golimumab 400/200 mg groups (51.8%, and 55%, respectively) were in clinical response than patients assigned to placebo (29.7%; P<0.0001 for both comparisons) (Sandborn et al, 2014b). In a study enrolling patients who responded in a prior study with golimumab, the proportion of patients who maintained a clinical response through week 54 was greater for patients treated with golimumab 100 mg and 50 mg compared to placebo (49.7 and 47 vs 31.2%; P<0.001 and P=0.01, respectively) (Sandborn et al, 2014a).
- The safety and efficacy of ENTYVIO (vedolizumab) was evaluated in a trial for UC in patients who responded inadequately to previous therapy. A higher percentage of ENTYVIO-treated patients achieved or maintained clinical response and remission over placebo at weeks six and 52, as measured by stool frequency, rectal bleeding, endoscopic findings, and PGA (Feagan et al, 2013). A systematic review and meta-analysis (N=606; 4 trials) demonstrated that vedolizumab was superior to placebo for clinical response (RR, 0.82; 95% CI, 0.75 to 0.91), induction of remission (RR, 0.86; 95% CI, 0.80 to 0.91), and endoscopic remission (RR, 0.82; 95% CI, 0.75 to 0.91) (Bickston et al, 2014; Mosli et al, 2015).

Uveitis (UV)

- The safety and efficacy of HUMIRA (adalimumab) were assessed in adult patients with non-infectious intermediate, posterior, and panuveitis in two randomized, double-masked, placebo-controlled studies, VISUAL I and VISUAL II.
    - VISUAL I (N=217) enrolled adults with active noninfectious intermediate UV, posterior UV, or panuveitis despite having received prednisone treatment for ≥2 weeks (Jaffe et al, 2016). Patients were randomized to adalimumab (80 mg loading dose then 40 mg every two weeks) or placebo; all patients also received a prednisone burst followed by tapering of prednisone over 15 weeks. The primary endpoint was the time to treatment failure (TTF) at or after week 6. TTF was a multicomponent outcome that was based on assessment of new inflammatory lesions, visual acuity, anterior chamber cell grade, and vitreous haze grade. The median TTF was 24 weeks in the adalimumab group and 13 weeks in the placebo group. Patients receiving adalimumab were less likely than those in the placebo group to have treatment failure (hazard ratio, 0.50; 95% CI, 0.36 to 0.70; P<0.001).
    - VISUAL II (N=226) had a similar design to VISUAL I; however, VISUAL II enrolled patients with inactive UV on corticosteroids rather than active disease (Nguyen et al, 2016a). Patients were randomized to adalimumab (80 mg loading dose then 40 mg every two weeks) or placebo; all patients tapered prednisone by week 19. TTF was significantly improved in the adalimumab group compared with the placebo group (median not estimable [>18 months] vs 8.3 months; hazard ratio, 0.57, 95% CI, 0.39 to 0.84; P=0.004). Treatment failure occurred in 61 (55%) of 111 patients in the placebo group compared with 45 (39%) of 115 patients in the adalimumab group.

CAPS, FMF, HIDS/MKD, and TRAPs

- The efficacy of KINERET (anakinra) for NOMID was evaluated in a prospective, open-label, uncontrolled study in 43 patients treated for up to 60 months. The study demonstrated improvements in all disease symptoms comprising the disease-specific Diary Symptom Sum Score (DSSS), as well as in serum markers of inflammation. A subset of patients (n=11) who went through a withdrawal phase experienced worsening of disease symptoms and inflammatory markers, which promptly responded to reinstitution of treatment (KINERET prescribing information, 2016). A cohort study of 26 patients followed for three to five years demonstrated sustained improvement in disease activity and inflammatory markers (Sibley et al, 2012).
- The efficacy and safety of ILARIS (canakinumab) has been evaluated for the treatment of CAPS, TRAPS, HIDS/MKD, and FMF.
    - Efficacy and safety in CAPS were evaluated in a trial in patients aged 9 to 74 years with the MWS phenotype and in a trial in patients aged 4 to 74 years with both MWS and FCAS phenotypes. Most of the trial periods were open-label. Trials demonstrated improvements based on physician's assessments of disease activity and assessments of skin disease, CRP, and serum amyloid A (ILARIS prescribing information, 2016).

Published data supports the use of canakinumab for these various CAPS phenotypes (Koné-Paut et al, 2011; Kuemmerle-Deschner et al, 2011; Lachmann et al, 2009).

- Efficacy and safety in TRAPS, HIDS/MKD, and FMF were evaluated in a study in which patients having a disease flare during a screening period were randomized into a 16-week double-blind, placebo-controlled period. For the primary efficacy endpoint, canakinumab was superior to placebo in the proportion of TRAPS, HIDS/MKD, and FMF patients who resolved their index disease flare at day 15 and had no new flare for the duration of the double-blind period. Resolution of the flare was defined as a PGA score <2 (minimal or no disease) and CRP within normal range (or reduction ≥70% from baseline) (ILARIS prescribing information, 2016).

Treatment Guidelines

- RA:
  - In patients with moderate or high disease activity despite DMARD monotherapy, the ACR recommends the use of combination DMARDs, a TNF inhibitor, or a non-TNF inhibitor biologic (tocilizumab, abatacept, or rituximab); tofacitinib is another option in patients with established RA. If disease activity remains moderate or high despite use of a TNF inhibitor, a non-TNF biologic is recommended over another TNF inhibitor or tofacitinib (Singh et al, 2016c).
  - EULAR guidelines are similar to ACR guidelines. These guidelines state that if the treatment target is not reached with a conventional DMARD strategy in a patient with poor prognostic factors, addition of a biologic DMARD or a targeted synthetic DMARD (eg, tofacitinib) should be considered, with current practice being a biologic DMARD. Biologic and targeted synthetic DMARDs should be combined with a conventional DMARD, but in patients who cannot use a conventional DMARD concomitantly, a targeted synthetic DMARD or an IL-6 inhibitor (eg, tocilizumab) may have some advantages compared with other biologic DMARDs. The guideline notes that if a TNF inhibitor has failed, patients may receive another TNF inhibitor or an agent with another mode of action. An effective biologic should not be switched to another biologic for non-medical reasons (Smolen et al, 2017).
  - The ACR released a position statement on biosimilars, which stated that the decision to substitute a biosimilar product for a reference drug should only be made by the prescriber. The ACR does not endorse switching stable patients to a different medication (including a biosimilar) of the same class for cost saving reasons without advance consent from the prescriber and knowledge of the patient (ACR, 2016).
  - EULAR has released guidelines for use of antirheumatic drugs in pregnancy, which state that etanercept and certolizumab are among possible treatment options for patients requiring therapy (Götestam Skorpen et al, 2016).
- JIA:
  - The American College of Rheumatology (ACR) published recommendations for the treatment of JIA in 2011, followed by an update in 2013 focusing on the management of SJIA (and tuberculosis screening) (Beukelman et al, 2011; Ringold et al, 2013).
    - According to the 2011 guideline, recommendations for JIA treatment vary based on factors such as disease characteristics and activity, current medication, and prognostic features. For patients with a history of arthritis in ≥5 joints (which includes extended oligoarthritis, polyarthritis, and some related subtypes), a TNF inhibitor is generally recommended in patients with continued disease activity after receiving an adequate trial of a conventional DMARD. In patients with a history of ≥5 affected joints failing a TNF inhibitor, treatment approaches may include switching to a different TNF inhibitor or abatacept (Beukelman et al, 2011).
    - According to the 2013 update, the inflammatory process in SJIA is likely different from that of other JIA categories, with IL-1 and IL-6 playing a central role. In patients with SJIA and active systemic features, recommendations vary based on the active joint count and the physician global assessment. Anakinra is one of the recommended first-line therapies; canakinumab, tocilizumab, and TNF-inhibitors are among the second-line therapies. In patients with SJIA and no active systemic features, treatments vary based on the active joint count. Abatacept, anakinra, tocilizumab, and TNF inhibitors are among the second-line treatments for these patients (Ringold et al, 2013).
- UC:
  - For the treatment of UC, sulfasalazine is recommended by the American College of Gastroenterology (ACG) as first-line treatment of active disease. Balsalazide, mesalamine, olsalazine and sulfasalazine are recommended for maintenance of remission and reduction of relapses. If these therapies fail, infliximab should be considered (Kornbluth et al, 2010). Note that other immunomodulators were not indicated for UC when these guidelines were written; an update is currently in process.

- CD:
  - The ACG states that the anti-TNF monoclonal antibodies adalimumab, certolizumab, and infliximab are effective in the treatment of moderate to severely active CD in patients who have not responded despite complete and adequate therapy with a corticosteroid or an immunosuppressive agent. These TNF inhibitors may also be used as alternatives to steroid therapy in selected patients in whom corticosteroids are contraindicated or not desired. Maintenance therapy with TNF inhibitors is effective. An update to these guidelines is currently in process (Lichtenstein et al, 2009).
  - The American Gastroenterological Association (AGA) recommends using anti-TNF drugs to induce remission in patients with moderately severe CD (Terdiman et al, 2013). The AGA supports the use of TNF inhibitors and/or thiopurines as pharmacologic prophylaxis in patients with surgically-induced CD remission (Nguyen et al, 2017).
  - An AGA Institute clinical decision tool for CD notes the importance of controlling both symptoms and the underlying inflammation, and makes recommendations for treatments (budesonide, azathioprine, 6-mercaptopurine, prednisone, MTX, a TNF inhibitor, or certain combinations) based on the patient's risk level (Sandborn, 2014).
  - The European Crohn's and Colitis Organisation (ECCO) recommends TNF inhibitors for patients with CD who have relapsed or are refractory to corticosteroids, depending on disease location and severity, and states that early TNF inhibitor therapy should be initiated in patients with high disease activity and features indicating a poor prognosis. Furthermore, the ECCO guideline states that all currently available TNF inhibitors seem to have similar efficacy in luminal CD and similar AE profiles; therefore the choice depends on availability, route of administration, patient preference, and cost. Vedolizumab is noted to be an appropriate alternative to TNF inhibitors for some patients (Gomollón et al, 2017).
- Pregnancy in inflammatory bowel disease:
  - Consensus statements for the management of inflammatory bowel disease in pregnancy, coordinated by the Canadian Association of Gastroenterology, state that TNF inhibitor treatment does not appear to be associated with unfavorable pregnancy outcomes and should generally be continued during pregnancy. Because of the low risk of transfer across the placenta, certolizumab may be preferred in women who initiate TNF inhibitor therapy during pregnancy (Nguyen et al, 2016b).
- PsO and PsA:
  - Consensus guidelines from the National Psoriasis Foundation Medical Board state that treatment of PsO includes topical agents; oral therapies such as acitretin, cyclosporine, and MTX; and biologic therapies (Hsu et al, 2012).
  - Guidelines from the American Academy of Dermatology state that for the management of PsO, topical agents including corticosteroids are used adjunctively to either ultraviolet light or systemic medications for resistant lesions in patients with more severe disease (Gottleib et al, 2008; Menter et al, 2008; Menter et al, 2009a; Menter et al, 2009b; Menter et al, 2010; Menter et al, 2011). Biologic agents are routinely used when one or more traditional systemic agents are not tolerated, fail to produce an adequate response, or are unable to be used due to patient comorbidities. First-line agents for PsO (>5% BSA) with concurrent PsA include adalimumab, etanercept, golimumab, infliximab, MTX, or a combination of a TNF blocker and MTX.
  - Guidelines for PsO from the European Dermatology Forum, European Association for Dermatology and Venereology, and International Psoriasis Council (European S3 guidelines) state that adalimumab, etanercept, infliximab, and ustekinumab are recommended as second-line medications for induction and long-term treatment if phototherapy and conventional systemic agents were inadequate, contraindicated, or not tolerated (Nast et al, 2015b). In patients with PsA and active joint involvement despite use of NSAIDs and a potential poor prognosis due to polyarthritis, increased inflammatory markers and erosive changes, it is recommended to start synthetic DMARDs early to prevent progression of disease and erosive joint destruction. For inadequately responding patients with PsA after at least one synthetic DMARD, biologic DMARDS are recommended in combination with synthetic DMARDs or as monotherapy.
  - The American Academy of Dermatology recommends that moderate to severe PsA that is more extensive or aggressive in nature or that significantly impacts quality of life should be treated with MTX, TNF-blockers, or both (Gottleib et al, 2008; Menter et al, 2009b; Menter et al, 2011).
  - EULAR 2015 PsA guidelines recommend TNF inhibitors in patients with peripheral arthritis and an inadequate response to at least one synthetic DMARD, such as MTX. For patients with peripheral arthritis and an inadequate response to at least one synthetic DMARD, in whom a TNF inhibitor is not appropriate, biologics targeting IL-12/23 or IL-17 pathways may be considered. Apremilast is considered a treatment option in patients with peripheral arthritis and an inadequate response to at least one synthetic DMARD, in whom biologics are not appropriate (Gossec et al, 2016; Ramiro et al, 2016).

  - The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommendations for PsA vary based on whether the arthritis is peripheral or axial and based on prior therapies, and may include DMARDS, NSAIDs, simple analgesics, a TNF inhibitor, an IL-12/23 inhibitor, or a PDE-4 inhibitor (Coates et al, 2016).
- AS:
  - Joint recommendations for the management of axial spondyloarthritis are available from ASAS and EULAR. (Ankylosing spondylitis [AS] is synonymous with radiographic axial spondyloarthritis; these guidelines also include non-radiographic axial spondyloarthritis). The guidelines state that NSAIDs should be used first-line in patients with pain and stiffness; other analgesics might be considered if NSAIDs have failed or are contraindicated or poorly tolerated. Glucocorticoid injections may be considered but patients with axial disease should not receive long-term systemic glucocorticoids. Sulfasalazine may be considered in patients with peripheral arthritis, but patients with purely axial disease should normally not be treated with conventional DMARDs. Biologic DMARDs should be considered in patients with persistently high disease activity despite conventional treatments, and current practice is to start with a TNF inhibitor. If a TNF inhibitor fails, switching to another TNF inhibitor or to an IL-17 inhibitor should be considered (van der Heijde et al, 2017).
  - The 2015 ACR, Spondylitis Association of America, and Spondyloarthritis Research and Treatment Network guidelines strongly recommend TNF inhibitors for patients who have active disease despite NSAIDs. No particular TNF inhibitor is preferred over another, except in patients with concomitant inflammatory bowel disease or recurrent iritis, in whom infliximab or adalimumab would be preferred over etanercept (Ward et al, 2016).
- Ocular inflammatory disorders:
  - Expert panel recommendations for the use of TNF inhibitors in patients with ocular inflammatory disorders are available from the American Uveitis Society (Levy-Clarke et al, 2014). Infliximab and adalimumab can be considered as first-line immunomodulatory agents for the treatment of ocular manifestations of Behçet's disease and as second-line immunomodulatory agents for the treatment of UV associated with juvenile arthritis. They also can be considered as potential second-line immunomodulatory agents for the treatment of severe ocular inflammatory conditions including posterior UV, panuveitis, severe UV associated with seronegative spondyloarthropathy, and selected patients with scleritis. Etanercept seems to be associated with lower rates of treatment success in these conditions.
- Additional indications:
  - Based upon guidelines from the European Dermatology Forum, adalimumab is recommended among first-line therapies for HS, and infliximab may be considered a second-line option (Gulliver et al, 2016; Zouboulis et al, 2015).
  - For the treatment of FMF, EULAR recommendations state that treatment with colchicine should begin as soon as FMF is diagnosed. Biologic treatment, such as anti-IL-1 therapy, is indicated in patients not responding to the maximum tolerated dose of colchicine. TNF inhibitors have also been used in colchicine-resistant patients, with good responses seen in observational studies (Ozen et al, 2016).
  - No recent guidelines were identified for CAPS, HIDS/MKD, or TRAPS.

SAFETY SUMMARY

- Contraindications:
  - ACTEMRA (tocilizumab), COSENTYX (secukinumab), ENTYVIO (vedolizumab), ILARIS (canakinumab), INFLECTRA (infliximab-dyyb), KINERET (anakinra), OTEZLA (apremilast), REMICADE (infliximab), STELARA (ustekinumab), and TALTZ (ixekixumab) use in patients with hypersensitivity to any component of the product.
  - SILIQ is contraindicated in patients with Crohn's disease because SILIQ may cause worsening of disease.
  - ENBREL (etanercept) in patients with sepsis.
  - KINERET (anakinra) in patients with hypersensitivity to *E coli*-derived proteins.
  - REMICADE (infliximab) and INFLECTRA (infliximab-dyyb) in patients with hypersensitivity to murine proteins; and doses >5 mg/kg in patients with moderate to severe heart failure.
- Boxed Warnings:
  - ACTEMRA (tocilizumab), CIMZIA (certolizumab), ENBREL (etanercept), HUMIRA (adalimumab), INFLECTRA (infliximab-dyyb), REMICADE (infliximab), SIMPONI / SIMPONI ARIA (golimumab), and XELJANZ / XELJANZ XR (tofacitinib) all have warnings for serious infections such as active tuberculosis, which may present with pulmonary or extrapulmonary disease; invasive fungal infections; and bacterial, viral, and other infections due to opportunistic pathogens.

  - In addition, CIMZIA (certolizumab), ENBREL (etanercept), HUMIRA (adalimumab), INFLECTRA (infliximab-dyyb), REMICADE (infliximab), SIMPONI / SIMPONI ARIA (golimumab), and XELJANZ (tofacitinib) all have warnings for increased risk of malignancies.
  - RITUXAN (rituximab) can cause fatal infusion reactions, hepatitis B activation, severe mucocutaneous reactions, and progressive multifocal leukoencephalopathy (PML).
  - SILIQ has a boxed warning that suicidal ideation and behavior, including completed suicides, have occurred in patients treated with SILIQ. The prescriber should weigh potential risks and benefits in patients with a history of depression and/or suicidal ideation or behavior, and patients should seek medical attention if these conditions arise or worsen during treatment.
- Warnings/Precautions (applying to some or all of the agents in the class):
  - Reactivation of HBV or other viral infections
  - Serious infections including tuberculosis
  - New onset or exacerbation of central nervous system demyelinating disease and peripheral demyelinating disease
  - Pancytopenia
  - Worsening and new onset congestive heart failure
  - Hypersensitivity reactions
  - Lupus-like syndrome
  - Increased lipid parameters and liver function tests with XELJANZ / XELJANZ XR (tofacitinib)
  - Increased incidence of CD and UC with COSENTYX (secukinumab) and TALTZ (ixekixumab); risk of new-onset CD or exacerbation of CD with SILIQ (brodalumab)
  - Consult prescribing information for other drug-specific warnings/precautions
- Adverse Reactions:
  - Infusion site reactions, diarrhea, nausea/vomiting, abdominal pain, infections, hypertension and headache.
  - Consult prescribing information for other drug-specific AEs
- Risks of Long-Term Treatment: As it becomes accepted practice to treat patients with these conditions for long-term, it is imperative to assess the long-term safety of these products. Because these agents suppress the immune system, serious infections and malignancies are a concern. Several long-term efficacy and safety studies support several agents in this class. The extension studies were performed in an open-label manner and were subject to attrition bias.
  - Rheumatoid Arthritis
    - Safety of adalimumab for RA has been supported in a five-year study in RA and a 10-year study in patients with early RA (Keystone et al, 2014a; Burmester et al, 2014b). In the five-year extension study, overall rates of serious AEs and serious infections were 13.8 events per 100 patient-years and 2.8 events per 100 patient-years, respectively. The rate of serious events was highest in the first six months and then declined. No new safety signals were reported in the 10-year study.
    - Certolizumab plus MTX had a consistent safety profile over five years in patients with RA (Keystone et al, 2014b). The most frequently reported AEs included urinary tract infections (rate of 7.9 per 100 patient-years), nasopharyngitis (rate of 7.3 per 100 patient-years), and upper respiratory infections (rate of 7.3 per 100 patient-years). Serious AE rates were 5.9 events per 100 patient-years for serious infections and 1.2 events per 100 patient-years for malignancies.
    - Abatacept has been evaluated in two long-term extension studies. Abatacept IV plus MTX demonstrated a similar safety profile between the seven year follow-up and a 52-week double-blind study (Westhovens et al, 2014). Serious AEs reported in both the double-blind and long-term follow-up studies were the following: serious infections (17.6 events per 100 patient-years), malignancies (3.2 events per100 patient-years), and autoimmune events (1.2 events per 100 patient-years). In a five-year extension trial, rates of serious infections, malignancies, and autoimmune events were 2.8, 1.5, and 0.99 events per 100 patient-years exposure, respectively. Efficacy was demonstrated by ACR 20 with response rates of 82.3% and 83.6% of patients at year one and year five, respectively.
    - Data from five RCTs of ACTEMRA (tocilizumab), their open-label extension trials, and a drug interaction study were analyzed for measures of safety. A total of 4,009 patients with moderate to severe RA received at least one dose of tocilizumab. Mean duration of tocilizumab treatment was 3.07 years (up to 4.6 years); total duration of observation was 12,293 patient-years (PY). The most common AEs and serious AEs were infections. A longer-term safety profile from this analysis matches previous observations. No new safety signals were identified (Genovese et al, 2013).
    - A Cochrane review showed no evidence of a statistically significant difference in the rate of withdrawal because of AEs in the ENBREL (etanercept) plus DMARD group and the DMARD alone group at six months, 12 months, and two years. At three years, withdrawals were significantly reduced in the

etanercept 25 mg plus DMARD group compared with the DMARD alone group (RR, 0.7; 95% CI, 0.5 to 1). There was no evidence of statistically significant differences in the rates of breast cancer at 12 months, fever at six months, flu-like syndrome at six months and two years, infection at six months and two years, malignancy at 12 months and two years, pneumonia at 12 months, and serious infection at 12 months and two years between the etanercept plus DMARD group and the DMARD group (Lethaby et al, 2013).

- A systematic review analyzed 66 randomized controlled trials and 22 long-term extension studies evaluating biologics and tofacitinib for the rate of serious infections in patients with moderate to severe active RA (Strand et al, 2015b). The estimated incidence rates (unique patients with events/100 patient-years) of serious infections were 3.04 (95% CI, 2.49 to 3.72) for abatacept, 3.72 (95% CI, 2.99 to 4.62) for rituximab, 5.45 (95% CI, 4.26 to 6.96) for tocilizumab, 4.90 (95% CI, 4.41 to 5.44) for TNF inhibitors, and 3.02 (95% CI, 2.25 to 4.05) for tofacitinib 5 mg and 3.00 (95% CI, 2.24 to 4.02) for tofacitinib 10 mg. Authors concluded that the rates of serious infections with tofacitinib in RA patients are within the range of those reported for biologic DMARDs.

o PsO
  - A total of 3,117 patients treated with at least one dose of STELARA (ustekinumab) for moderate to severe PsO were evaluated for long-term safety. At least four years of ustekinumab exposure was seen in 1,482 patients (including 838 patients with greater than or equal to five years of exposure). The most commonly reported AEs were nasopharyngitis, upper respiratory tract infection, headache and arthralgia. Infections, malignancies and cardiac disorders were the most commonly reported serious AEs. Twenty deaths were reported through year five. The causes of death were considered related to cardiovascular events (n=5), malignancy (n=5), infection (n=3) and other causes (n=7). The observed mortality rate among ustekinumab-treated patients was consistent with that expected in the general U.S. population (SMR = 0.36; 95% CI, 0.22 to 0.55). From year one to year five, rates of overall AEs, and AEs leading to discontinuation generally decreased. Serious AE rates demonstrated year-to-year variability with no increasing trend. The results of this long-term study of AEs are similar to reports of shorter-term studies (Papp et al, 2013).
  - In a five-year extension study, a total of 2,510 patients on etanercept for the treatment of PsO were evaluated for long-term safety and efficacy (Kimball et al, 2015). Serious AEs were reported as a cumulative incidence of the entire five-year observation period. The following incidences were reported: serious infections (6.5%, 95% CI, 5.4 to 7.7%); malignancies excluding nonmelanoma skin cancer (3.2%, 95% CI, 2.3 to 4.1%); nonmelanoma skin cancer (3.6%, 95% CI, 2.7 to 4.1%); coronary artery disease (2.8%, 95% CI, 2 to 3.6%); PsO worsening (0.7%, 95% CI, 0.3 to 1.2%); CNS demyelinating disorder (0.2%, 95%CI, 0 to 0.4%); lymphoma and tuberculosis each (0.1%, 95% CI, 0 to 0.3%); and opportunistic infection and lupus each (0.1%, 95%CI, 0 to 0.2%). A total of 51% of patients reported clear/almost clear rating at month six and remained stable through five years.
  - A multicenter registry called Psoriasis Longitudinal Assessment and Registry (PSOLAR) evaluated the risk of serious infections in patients with PsO (Kalb et al, 2015). Patients were followed for up to eight years with a total of 11,466 patients with PsO enrolled, 74.3% of whom were from the U.S. A total of 22,311 patient-years of data were collected. Ustekinumab, infliximab, adalimumab, and etanercept as well as traditional DMARDs were included in the data analysis. During the follow-up period, 323 serious infections were reported. The rates of serious infections per 100 patient-years were 0.83 (secukinumab), 1.47 (etanercept), 1.97 (adalimumab), and 2.49 (infliximab). The most commonly reported serious infection was cellulitis. Risk factors for serious infections were increasing age, diabetes mellitus, smoking, and history of significant infections prior to registry entry. Exposure to infliximab (hazard ratio, 2.51; 95% CI, 1.45 to 4.33; P<0.001) and adalimumab (hazard ratio, 2.13; 95% CI, 1.33 to 3.41; P=0.002) during the registry were independently associated with the risk of serious infections whereas use of ustekinumab or etanercept were not.

o PsA
  - Subcutaneous golimumab for patients with active PsA demonstrated safety and efficacy over five years in the long-term extension of the randomized, placebo-controlled GO-REVEAL study (Kavanaugh et al, 2014b). Approximately one-half of patients also took MTX concurrently. No new safety signals were observed.

o Multiple indications
  - One study looked at 23,458 patients who were treated with HUMIRA (adalimumab) for RA, JIA, AS, PsA, PsO and CD. Patients received adalimumab for up to 12 years. No new safety signals were observed from this analysis. Rates of malignancies and infections were similar to the general

population and also similar to rates reported in other shorter-term trials for anti-TNF therapies (Burmester et al, 2013b).

- Pooled data from five Phase 3 trials of SQ golimumab over at least three years demonstrated a safety profile consistent with other TNF inhibitors (Kay et al, 2015). A total of 1,179 patients with RA, PsA or AS were treated for at least 156 weeks. Rates of AEs up to week 160 for placebo, golimumab 50 mg and golimumab 100 mg, respectively, were as follows: 0.28, 0.30, 0.41 for death; 5.31, 3.03, 5.09 for serious infection; 0, 0.17, 0.35 for tuberculosis; 0, 0.13, 0.24 for opportunistic infection; 0, 0, 0.12 for demyelination; and 0, 0.04, 0.18 for lymphoma.
- A total of 18 multicenter, placebo-controlled, randomized controlled trials evaluated the safety profile of certolizumab pegol monotherapy or in combination with DMARDs in RA, CD, AS, PsA and PsO (Capogrosso Sansone et al, 2015). All but one trial was conducted in a double-blind manner. The overall pooled risk ratios for all doses of certolizumab pegol were reported as follows: AEs (defined as AE reported but not evaluated for causality) 1.09 (95% CI, 1.04 to 1.14), serious AEs 1.50 (95% CI, 1.21 to 1.86), ADRs (defined as an AE possibly related to drug treatment by investigators) 1.20 (95% CI, 1.13 to 1.45), infectious AEs 1.28 (95% CI, 1.13 to 1.45), infectious serious AEs 2.17 (95% CI, 1.36 to 3.47), upper respiratory tract infections 1.34 (95% CI, 1.15 to 1.57), neoplasms 1.04 (95% CI, 0.49 to 2.22), and tuberculosis 2.47 (95% CI, 0.64 to 9.56). Rare AEs may not have been captured by the studies due to limiting the reporting of most AEs to those occurring in > 3 to 5%.
- Several recent meta-analyses evaluated the safety of TNF inhibitors.
  - An analysis of TNF inhibitors in RA, PsA, and AS included data from 71 randomized trials (follow-up one to 36 months) and seven open-label extension studies (follow-up six to 48 months) (Minozzi et al, 2016). The data demonstrated that use of TNF inhibitors increases the risk of infectious AEs. Overall, there was a 20% increase of any infections, a 40% increase of serious infections, and a 250% increase of tuberculosis. The tuberculosis incidence rate was higher with infliximab and adalimumab compared to etanercept. There was little data on the incidence of opportunistic infections.
  - An analysis of TNF inhibitors in RA, PsA, and AS included data from 32 randomized trials (follow-up two to 36 months) and six open-label extension trials (follow-up six to 48 months) (Bonovas et al, 2016). Synthesis of the data did not demonstrate that the use of TNF inhibitors significantly affects cancer risk during this length of treatment. However, few malignancy events were observed and evidence may be insufficient to make definitive conclusions, particularly regarding longer-term risks.

- Drug interactions
  - Do not give with live (including attenuated) vaccines; additionally, non-live vaccines may not elicit a sufficient immune response.
  - Do not give two immunomodulators together.
  - For XELJANZ / XELJANZ XR (tofacitinib), do not give with potent inhibitors of cytochrome P450 (CYP) 3A4; medications that result in both moderate inhibition of CYP3A4 and potent inhibition of CYP2C19; potent CYP3A4 inducers; and potent immunosuppressive drugs.
- Risk Evaluation and Mitigation Strategy (REMS)
  - STELARA (ustekinumab) has a REMS program in place, which consists of a communication plan regarding potential risk of serious infections, malignancy, and reversible posterior leukoencephalopathy syndrome (RPLS).
  - SILIQ (brodalumab) is available only through the SILIQ REMS program. The goal of the program is to mitigate the risk of suicidal ideation and behavior, including completed suicides, which occurred in clinical trials. Key requirements of the REMS program include:
    - Prescribers must be certified with the program.
    - Patients must sign a patient-prescriber agreement form.
    - Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive the product.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
ACTEMRA (tocilizumab)	Vials: 80 mg/4 mL; 200 mg/10 mL; 400 mg/20 mL Prefilled syringe: 162 mg/0.9 mL	**RA:** 4 mg/kg IV every 4 weeks. May increase to 8 mg/kg IV every 4 weeks. Maximum dose=800 mg. SQ: <100 kg, administer 162 mg SQ every other week, followed by an increase to every week based on clinical response. >100 kg, 162 mg administered SQ every week. **PJIA:** <30 kg, 10 mg/kg IV every 4 weeks; ≥30 kg, 8 mg/kg IV every 4 weeks. **SJIA:** <30 kg, 12 mg/kg IV every 2 weeks; ≥30 kg, 8 mg/kg IV every 2 weeks.	**RA:** Can give with MTX or other DMARDs. **PJIA and SJIA:** Can give with MTX. Adjust dose for liver enzyme abnormalities, low platelet count and low ANC.	Give as a single 60-minute intravenous infusion. <30 kg, use a 50 mL infusion bag. ≥30 kg, use a 100 mL infusion bag. Before infusion, allow bag to come to room temperature. Do not administer with other drugs. Patients can self-inject with the prefilled syringe.
CIMZIA (certolizumab)	Powder for reconstitution: 200 mg Prefilled syringe: 200 mg/mL	**CD:** 400 mg SQ initially and at weeks 2 and 4. Maintenance dose is 400 mg every 4 weeks. **RA, PsO:** 400 mg SQ initially and at weeks 2 and 4. Then 200 mg every 2 weeks. Can consider a maintenance dose of 400 mg every 4 weeks. **AS:** 400 mg SQ initially and at weeks 2 and 4. Maintenance dose is 200 mg every 2 weeks or 400 mg every 4 weeks.	Patients can self-inject with the prefilled syringe.	When a 400 mg dose is required, give as two 200 mg SQ injections in separate sites in the thigh or abdomen.
COSENTYX (secukinumab)	Sensoready pen: 150 mg/1 mL Prefilled syringe: 150 mg/1 mL Vial: 150 mg lyophilized powder	**PsO:** 300 mg by SQ injection at weeks 0, 1, 2, 3 and 4, followed by 300 mg every 4 weeks **PsA, AS:** With a loading dose (not required): 150 mg at weeks 0, 1, 2, 3, and 4, followed by 150 mg every 4 weeks; without loading dose: 150 mg	**PsO:** For some patients, a dose of 150 mg may be acceptable. **PsA:** For PsA patients with coexistent moderate to severe PsO, dosing for PsO	Each 300 mg dose is given as two subcutaneous injections of 150 mg. Patients may self-administer with the pen or prefilled syringe. The vial is for healthcare professional use only.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		every 4 weeks	should be followed. If active PsA continues, consider 300 mg dose.	
ENBREL (etanercept)	Prefilled syringe: 25 mg and 50 mg Prefilled SureClick autoinjector: 50 mg Multiple-use vial: 25 mg	**RA, AS, PsA:** 50 mg SQ weekly **PsO (adults):** 50 mg SQ twice weekly for three months, then 50 mg weekly **PJIA and PsO (pediatrics):** ≥63 kg, 50 mg SQ weekly; <63 kg, 0.8 mg/kg SQ weekly	**RA, AS, PsA:** MTX, NSAIDs, glucocorticoids, salicylates, or analgesics may be continued **JIA:** NSAIDs glucocorticoids, or analgesics may be continued	Patients may be taught to self-inject. May bring to room temperature prior to injecting.
ENTYVIO (vedolizumab)	Lyophilized cake for injection in single dose 20 mL vials: 300 mg	**CD and UC:** 300 mg administered by intravenous infusion at time zero, two and six weeks, and then every eight weeks thereafter. Discontinue therapy if there is no evidence of therapeutic benefit by week 14.	All immunizations should be to date according to current guidelines prior to initial dose.	ENTYVIO should be reconstituted at room temperature and prepared by a trained medical professional. It should be used as soon as possible after reconstitution and dilution.
HUMIRA (adalimumab)	Prefilled syringe: 10 mg/0.2 mL 20 mg/0.4 mL 40 mg/0.4 mL 40 mg/0.8 mL Single-use pen: 40 mg/0.8 mL Single-use vial: 40 mg/0.8 mL	**RA, AS, PsA**: 40 mg SQ every other week. For RA, may increase to 40 mg every week if not on MTX. **PJIA:** 10 kg to <15 kg: 10 mg SQ every other week; 15 kg to <30 kg: 20 mg SQ every other week; ≥30 kg, 40 mg SQ every other week **CD, HS and UC:** 160 mg SQ on Day 1 (given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days), followed by 80 mg SQ two weeks later (Day 15). Two weeks later (Day 29) begin a maintenance dose of 40 mg SQ every other week. **PsO and UV:** initial	**RA, AS, PsA:** MTX, other non-biologic DMARDS, glucocorticoids, NSAIDs, and/or analgesics may be continued. **JIA:** NSAIDs, MTX, analgesics, and/or glucocorticoids, may be continued. **CD and UC:** aminosalicylates and/or corticosteroids may be continued. Azathioprine, 6-MP or MTX may be continued if necessary. Needle cover of the syringe contains dry rubber (latex).	Patients may be taught to self-inject. Injections should occur at separate sites in the thigh or abdomen. Rotate injection sites.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		dose of 80 mg SQ, followed by 40 mg SQ every other week starting one week after the initial dose. **CD in pediatric patients ≥6 years and older:** 17 kg to <40 kg: 80 mg on day 1 (given as two 40 mg injections) and 40 mg two weeks later (on day 15); maintenance dose is 20 mg every other week starting at week 4. ≥40 kg: 160 mg on day (given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days) and 80 mg two weeks later (on day 150); maintenance dose is 40 mg every other week starting at week 4.		
ILARIS (canakinumab)	Vial: 150 mg (lyophilized powder and injection solution formulations)	**SJIA:** ≥7.5 kg, 4 mg/kg SQ every 4 weeks (maximum dose of 300 mg). **CAPS**: ≥15 to ≤40 kg, 2 mg/kg SQ; >40 kg, 150 mg SQ; frequency every 8 weeks **TRAPS, HIDS/MKD, and FMF**: ≤40 kg, 2 mg/kg SQ; >40 kg, 150 mg SQ; frequency every 4 weeks	For CAPS: children 15 to 40 kg with an inadequate response can be increased to 3 mg/kg For TRAPS, HIDS/MKD, and FMF: If the clinical response is inadequate, the dose may be increased to 4 mg/kg (weight ≤40 kg) or 300 mg (weight >40 kg)	Do not inject into scar tissue.
INFLECTRA (infliximab-dyyb)	Vial: 100 mg	**CD (≥6 years old), PsA, PsO and UC**: 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks. In adults with CD who lose response, can increase dose to 10	**RA:** give with MTX **CD:** If no response by week 14, consider discontinuation.	Premedication to help stop infusion reactions can include antihistamines (anti-H1 ± anti-H2), acetaminophen and/or corticosteroids. Use 250 mL 0.9% sodium chloride for infusion.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		mg/kg. **RA:** 3 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks. Can increase to 10 mg/kg or give every 4 weeks. **AS:** 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 weeks.		Infuse over 2 hours. Do not administer with other drugs.
KINERET (anakinra)	Prefilled syringe: 100 mg/0.67 mL	**RA:** 100 mg SQ once daily. **CAPS (NOMID):** 1 to 2 mg/kg SQ once daily. Maximum dose is 8 mg/kg/day.	**NOMID**: dose can be given once or twice daily.	Patients may be taught to self-inject. A new syringe must be used for each dose.
ORENCIA (abatacept)	Vial: 250 mg Prefilled syringe: 125 mg/1 mL ClickJect autoinjector: 125 mg/mL	**RA:** <60kg, 500 mg IV; 60 to 100 kg, 750 mg IV; >100 kg, 1,000 mg IV initially, then 2 and 4 weeks after the first infusion and every 4 weeks thereafter SQ: 125 mg SQ once weekly initiated with or without an IV loading dose. With IV loading dose, use single IV infusion as per body weight listed above, followed by the first 125 mg SQ injection within a day of the IV infusion and then once weekly. **PJIA:** 6 to 17 years and <75 kg: 10 mg/kg IV initially, then 2 and 4 weeks after the first infusion and every 4 weeks thereafter. >75 kg, follow adult RA IV schedule; maximum dose = 1,000 kg.		IV infusion should be over 30 minutes. Use 100 mL bag for IV infusion. Do not administer with other drugs. Patients may be taught to self-inject the SQ dose. For SQ, injection sites should be rotated.
OTEZLA (apremilast)	Tablet: 10 mg, 20 mg, and 30 mg	**PsA, PsO:** Day 1: 10 mg in the morning Day 2: 10 mg in the morning and in the evening Day 3: 10 mg in the	Titrate according to the labeling when initiating therapy to reduce gastrointestinal symptoms.	May be taken with or without food. Do not crush, split, or chew the tablets.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		morning and 20 mg in evening Day 4: 20 mg in the morning and evening Day 5: 20 mg in the morning and 30 mg in the evening Day 6 and thereafter: 30 mg twice daily	Dosage should be reduced to 30 mg once daily in patients with severe renal impairment (CrCl <30 mL/min as estimated by the Cockcroft-Gault equation). For initial dosing in these patients, use only the morning titration schedule listed above (evening doses should be excluded).	
REMICADE (infliximab)	Vial: 100 mg	**CD (≥6 years old), PsA, PsO and UC (≥6 years old)**: 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks. In adults with CD who lose response, can increase dose to 10 mg/kg. **RA:** 3 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks. Can increase to 10 mg/kg or give every 4 weeks. **AS:** 5 mg/kg IV at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 weeks.	**RA:** give with MTX **CD:** If no response by week 14, consider discontinuation.	Premedication to help stop infusion reactions can include antihistamines (anti-H1 ± anti-H2), acetaminophen and/or corticosteroids. Use 250 mL 0.9% sodium chloride for infusion. Infuse over 2 hours. Do not administer with other drugs.
RITUXAN (rituximab)	Vial: 100 mg 500 mg	**RA:** 1,000 mg IV every 2 weeks times two doses. Additional doses should be given every 24 weeks or based on clinical evaluation but no sooner than 16 weeks.	Give with MTX.	Give methyl-prednisolone 100 mg IV 30 minutes prior to each infusion to reduce the incidence and severity of infusion reactions.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
SILIQ (brodalumab)	Prefilled syringe: 210 mg/1.5 mL	**PsO:** 210 mg SQ at weeks 0, 1, and 2 followed by every 2 weeks	**PsO**: If an adequate response has not been achieved after 12 to 16 weeks, consider discontinuation	Patients may self-inject when appropriate and after proper training. The syringe should be allowed to reach room temperature before injecting.
SIMPONI/ SIMPONI ARIA (golimumab)	SmartJect® autoinjector: 50 mg and 100 mg Prefilled syringe: 50 mg and 100 mg ARIA, Vial: 50 mg/4 mL	**RA, PsA, and AS**: 50 mg SQ once monthly **UC:** 200 mg SQ at week 0; then 100 mg at week 2; then 100 mg every 4 weeks. **ARIA**: 2 mg/kg IV at weeks 0 and 4, then every 8 weeks.	**RA:** give with MTX **PsA and AS**: may give with or without MTX or other DMARDs. Needle cover of the syringe contains dry rubber (latex). **ARIA**: give with MTX Efficacy and safety of switching between IV and SQ formulations have not been established.	Patients may be taught to self-inject the SQ dose. For SQ, injection sites should be rotated. For SQ, bring to room temperature for 30 minutes prior to injecting. **ARIA**: IV infusion should be over 30 minutes. Dilute with 0.9% sodium chloride or 0.45% sodium chloride for a final volume of 100 mL. Do not administer with other drugs.
STELARA (ustekinumab)	Prefilled syringe: 45 mg and 90 mg Vial: 130 mg	**PsO, PsA**: ≤100 kg, 45 mg SQ initially and 4 weeks later, followed by 45 mg every 12 weeks. >100 kg, 90 mg SQ initially and 4 weeks later, followed by 90 mg every 12 weeks. **CD**: Initial single IV dose: ≤55 kg, 260 mg; >55 kg to ≤85 kg, 390 mg; >85 kg, 520 mg; followed by 90 mg SQ every 8 weeks (irrespective of body weight)	Needle cover of the syringe contains dry rubber (latex).	Patients may be taught to self-inject using the prefilled syringes. STELARA for IV infusion must be diluted, prepared and infused by a healthcare professional; it is diluted in 0.9% sodium chloride and infused over at least one hour. Rotate injection sites.
TALTZ (ixekizumab)	Prefilled syringe: 80 mg Autoinjector: 80 mg	**PsO:** 160 mg by SQ injection at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks		Patients may be taught to self-inject with either the prefilled syringe or the autoinjector. Bring to room temperature prior to injecting. Rotate injection sites.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
XELJANZ / XELJANZ XR (tofacitinib)	Tablet: 5 mg Extended release Tablet: 11 mg	**RA:** 5 mg PO twice daily or 11 mg PO once daily	Patients may switch from XELJANZ 5 mg twice daily to XELJANZ XR 11 mg once daily the day following the last dose of XELJANZ 5 mg. Use as monotherapy or in combination with MTX or other nonbiologic DMARDs. Use of XELJANZ in combination DMARDs or with potent immunosuppres-sants such as azathioprine and cyclosporine is not recommended. Dose interruption is recommended for management of lymphopenia (< 500 cells/mm^3), neutropenia (absolute neutrophil count [ANC] < 500 cells/mm^3) and anemia. Dose adjustment needed for hepatic and renal impairment and patients taking CYP450 inhibitors.	May take with or without food. Swallow XELJANZ XR tablets whole; do not crush, split, or chew.

ANC=absolute neutrophil count; AS=ankylosing spondylitis; DMARD=disease-modifying anti-rheumatic drug; HS=hidradenitis suppurativa; IV=intravenous infusion; JIA=juvenile idiopathic arthritis; MTX=methotrexate; NOMID= neonatal-onset multisystem inflammatory disease; NSAID=non-steroidal anti-inflammatory drug; PJIA=polyarticular juvenile idiopathic arthritis; PO=orally; PsA=psoriatic arthritis; PsO= plaque psoriasis; RA=rheumatoid arthritis; SJIA=systemic juvenile idiopathic arthritis; SQ=subcutaneously; UC=ulcerative colitis

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
ACTEMRA (tocilizumab)	Frequency of serious infection greater in ≥65 years. Use caution.	Not studied in children <2 years. Safety and efficacy only established in SJIA and PJIA.	No dose adjustment in mild impairment. Not studied in moderate to severe impair-ment.	Not studied in patients with impairment.	Uncategorized† Limited data in pregnant women not sufficient to determine risks. Unknown whether excreted in breast milk; risks and benefits should be considered.
CIMZIA (certolizumab)	The number of subjects ≥65 years in clinical trials was not sufficient to determine whether they responded differently from younger subjects. Use caution.	Safety and effectiveness have not been established.	No data	No data	Uncategorized† Limited data from ongoing pregnancy registry not sufficient to inform risks. Unknown whether excreted in breast milk, but data suggest systemic exposure to a breastfed infant is expected to be low; risks and benefits should be considered.
COSENTYX (secukinumab)	The number of subjects ≥65 years in clinical trials was not sufficient to determine whether they responded differently from younger subjects.	Safety and efficacy have not been established.	No data	No data	Pregnancy category B* Unknown whether excreted in breast milk; use with caution.
ENTYVIO (vedolizumab)	The number of patients ≥65 years in clinical trials was insufficient to determine differences.	Safety and efficacy have not been established.	Safety and efficacy have not been established.	Safety and efficacy have not been established.	Pregnancy category B* Unknown whether excreted in breast milk; use with caution.
ENBREL (etanercept)	Use caution.	Not studied in children <2 years with PJIA or <4 years with PsO.	No data	No data	Pregnancy category B* Present in low levels in breast milk; use caution.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
HUMIRA (adalimumab)	Frequency of serious infection and malignancies is greater in ≥65 years. Use caution.	Only studied in PJIA (ages 2 years and older) and CD (6 years and older).	No data	No data	Uncategorized† Present in low levels in breast milk; use caution.
ILARIS (canakinumab)	The number of patients ≥65 years in clinical trials was insufficient to determine differences.	Not studied in children <2 years (SJIA, TRAPS, HIDS/ MKD, and FMF) or <4 years (CAPS).	No data	No data	Uncategorized † Limited data from postmarketing reports not sufficient to inform risks. Unknown whether excreted in breast milk; use caution.
INFLECTRA (infliximab-dyyb)	Frequency of serious infection is greater in ≥65 years. Use caution.	Not recom-mended in <6 years in children with CD.	No data	No data	Pregnancy category B* Unknown whether excreted in breast milk; discontinue nursing or discontinue the drug.
KINERET (anakinra)	Use caution.	For NOMID, has been used in all ages. Not possible to give a dose <20 mg.	CrCl<30 mL/min: give dose every other day	No data	Pregnancy category B* Unknown whether excreted in breast milk; use caution.
ORENCIA (abatacept)	Frequency of serious infection and malignancies is greater in ≥65 years. Use caution.	Not recom-mended in <6 years. SQ formulation has not been studied in patients <18 years.	No data	No data	Uncategorized † Data on use in pregnant women insufficient to inform risks. Unknown whether excreted in breast milk.
OTEZLA (apremilast)	No overall differences were observed in the safety profile of elderly patients.	Safety and efficacy have not been established.	The dose of OTEZLA should be reduced to 30 mg once daily in patients with severe renal impairment (CrCl<30 mL/min).	No dosage adjustment necessary.	Pregnancy category C* Unknown whether excreted in breast milk; use caution.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
REMICADE (infliximab)	Frequency of serious infection is greater in ≥65 years. Use caution.	Not recommended in <6 years in children with CD or UC.	No data	No data	Pregnancy category B* Unknown whether excreted in breast milk; discontinue nursing or discontinue the drug.
RITUXAN (rituximab)	Rates of serious infections, malignancies, and cardiovascular events were higher in older patients.	Safety and effectiveness have not been established.	No data	No data	Pregnancy category C* Unknown whether excreted in breast milk; risks and benefits should be weighed before use.
SILIQ (brodalumab)	No differences in safety or efficacy were observed between older and younger patients, but the number of patients ≥65 years was insufficient to determine any differences in response.	Safety and effectiveness in <18 years have not been established.	No data	No data	Uncategorized † There are no human data in pregnant women to inform risks. Unknown whether excreted in breast milk; risks and benefits should be weighed before use.
SIMPONI/ SIMPONI ARIA (golimumab)	SQ: No differences in AEs observed between older and younger patients. Use caution. IV ARIA: Use caution.	Safety and effectiveness in <18 years have not been established.	No data	No data	Pregnancy category B* Unknown whether excreted in breast milk; discontinue nursing or discontinue the drug.
STELARA (ustekinumab)	No differences observed between older and younger patients. Use caution.	Safety and effectiveness have not been established.	No data	No data	Uncategorized † Limited data in pregnant women are insufficient to inform risks. Unknown whether excreted in breast milk; systemic exposure to breasted infant expected to be low; consider risks and benefits.

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
TALTZ (ixekizumab)	No differences observed between older and younger patients; however, the number of patients ≥65 years was not sufficient to determine differences.	Safety and effectiveness have not been established.	No data	No data	Uncategorized † There are no available data in pregnant women to inform risks. Unknown whether excreted in breast milk; consider risks and benefits.
XELJANZ / XELJANZ XR (tofacitinib)	Frequency of serious infection is greater in ≥65 years. Use caution.	Safety and effectiveness have not been established.	Reduce dose to 5 mg daily in moderate to severe impairment.	Reduce dose to 5 mg daily in moderate hepatic impairment. Not recom-mended in severe hepatic impairment.	Pregnancy category C* Unknown whether excreted in breast milk; discontinue nursing or discontinue the drug.

CrCl=creatinine clearance; NOMID= Neonatal-Onset Multisystem Inflammatory Disease; PJIA=polyarticular juvenile idiopathic arthritis; SJIA=systemic juvenile idiopathic arthritis
*Pregnancy Category B = No evidence of risk in humans, but there remains a remote possibility. Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women.
Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
†In accordance with the FDA's Pregnancy and Lactation Labeling Rule (PLLR), this product is not currently assigned a Pregnancy Category. Consult product prescribing information for details.

CONCLUSION

- Immunomodulators for a variety of conditions associated with inflammation are available. Mechanisms of action and indications vary among the products. Products in this class have clinical trial data supporting efficacy for their FDA-approved indications.
- Limited head-to-head clinical trials between the agents have been completed.
    - In patients with RA, abatacept and infliximab showed comparable efficacy at six months, but abatacept demonstrated greater efficacy after one year on some endpoints such as DAS28-ESR, EULAR response, LDAS, and ACR 20 responses (Schiff et al, 2008).
    - In patients with RA, abatacept and adalimumab were comparable for ACR 20 and ACR 50 responses over two years in a single-blind study (Schiff et al, 2014).
    - Patients with severe arthritis who could not take MTX were randomized to monotherapy with tocilizumab or adalimumab for 24 weeks in a randomized, double-blind study (Gabay et al, 2013). The patients in the tocilizumab group had a significantly greater improvement in DAS28 at week 24 than patients in the adalimumab group.
    - In biologic-naïve patients with RA and an inadequate response to DMARDs, initial treatment with rituximab was demonstrated to have non-inferior efficacy to initial TNF inhibitor treatment (Porter et al, 2016).
    - A randomized, open-label trial evaluated biologic treatments in patients with RA who had had an inadequate response to a TNF inhibitor. In this population, a non-TNF biologic (tocilizumab, rituximab, or abatacept) was more effective in achieving a good or moderate disease activity response at 24 weeks than use of a second TNF inhibitor. However, a second TNF inhibitor was also often effective in producing clinical improvement (Gottenberg et al, 2016). Another recent randomized trial did not demonstrate clinical efficacy differences between abatacept, rituximab, and use of a second TNF inhibitor in this patient population (Manders et al, 2015).
    - Secukinumab and ustekinumab were compared for safety and efficacy in the CLEAR study, a double-blind, randomized controlled trial in 676 patients with moderate to severe PsO (Thaçi et al, 2015). The proportion of

patients achieving PASI 90 at week 16 was significantly higher with secukinumab compared to ustekinumab (79% vs 57.6%; P<0.0001).
    - A greater proportion of PsO patients achieved the primary outcome, PASI 75 at week 12, with ustekinumab 45 mg (67.5%) and 90 mg (73.8%) compared to etanercept 50 mg (56.8%; P=0.01 vs ustekinumab 45 mg; P<0.001 vs ustekinumab 90 mg). In this trial, etanercept therapy was associated with a greater risk of injection site erythema than ustekinumab (14.7% vs 0.7%) (Griffiths et al, 2010).
    - In the FIXTURE study in patient with moderate to severe PsO, 77.1%, 67%, 44%, and 4.9% of patients achieved PASI 75 with secukinumab 300 mg, secukinumab 150 mg, etanercept at FDA-recommended dosing, and placebo, respectively (Langley et al, 2014).
    - In the UNCOVER-2 and UNCOVER-3 studies, the proportions of patients achieving PASI 75 and achieving PGA 0 or 1 were higher in patients treated with ixekizumab compared to those treated with etanercept.
    - In the AMAGINE-2 and AMAGINE-3 studies, the proportions of patients achieving PASI 100 were higher in patients treated with brodalumab compared to those treated with ustekinumab (Lebwohl et al, 2015).
    - No meaningful differences were shown in the treatment of RA and PsA in comparisons of infliximab and infliximab-dyyb conducted to establish biosimilarity between these agents (Park et al, 2013; Park et al, 2016; Park et al, 2017; Yoo et al, 2013; Yoo et al, 2016; Yoo et al, 2017).
    - More comparative studies are needed.
- For RA, patients not responding to initial DMARD treatment may be treated with combination DMARDs, TNF inhibitors, non-TNF inhibitor biologics, and/or tofacitinib (Singh et al, 2016c; Smolen et al, 2017). EULAR has released guidelines for use of antirheumatic drugs in pregnancy, which state that the TNF inhibitors etanercept and certolizumab are among possible treatment options for patients requiring therapy (Götestam Skorpen et al, 2016).
- For the management of PsO, biologic agents are routinely used when one or more traditional systemic agents are not tolerated, fail to product an adequate response, or are unable to be used due to patient comorbidities (Gottleib et al, 2008; Menter et al, 2008; Menter et al, 2009a; Menter et al, 2009b; Menter et al, 2010; Menter et al, 2011; Nast et al, 2015b). EULAR 2015 PsA guidelines recommend TNF inhibitors in patients with peripheral arthritis and an inadequate response to at least one synthetic DMARD, such as MTX (Gossec et al, 2016; Ramiro et al, 2016). For patients with peripheral arthritis and an inadequate response to at least one synthetic DMARD, in whom a TNF inhibitor is not appropriate, biologics targeting IL-12/23 or IL-17 pathways may be considered. Apremilast is considered a treatment option in patients with peripheral arthritis and an inadequate response to at least one synthetic DMARD, in whom biologics are not appropriate. Guidelines from GRAPPA recommend various biologics for the treatment of PsO and PsA based on patient-specific factors, including TNF inhibitors, IL-17 and IL-12/23 inhibitors, and PDE-4 inhibitors (Coates et al, 2016).
- In patients with JIA and involvement of ≥5 joints, the ACR recommends the use of a TNF inhibitor after an adequate trial of a conventional DMARD (Beukelman et al, 2011). The ACR updated guideline for SJIA notes that IL-1 and IL-6 play a central role in the inflammatory process for this condition, and recommend agents such as anakinra, canakinumab, tocilizumab, abatacept, and TNF inhibitors among either first- or second-line treatments (Ringold et al, 2013).
- According to the ACG, for the treatment of UC, infliximab should be considered after failure of first-line non-biologic agents (Kornbluth et al, 2010). Other immunomodulators were not indicated for UC when these guidelines were written.
- Based on ACG guidelines, the anti-TNF monoclonal antibodies adalimumab, certolizumab, and infliximab are effective in the treatment of moderate to severely active CD in patients who have not responded despite complete and adequate therapy with a corticosteroid or an immunosuppressive agent. These TNF inhibitors may also be used as alternatives to steroid therapy in selected patients in whom corticosteroids are contraindicated or not desired (Lichtenstein et al, 2009). The AGA recommends using anti-TNF drugs to induce remission in patients with moderately severe CD (Terdiman et al, 2013). ECCO recommends TNF inhibitors for patients with CD who have relapsed or are refractory to corticosteroids, depending on disease location and severity, and states that early TNF inhibitor therapy should be initiated in patients with high disease activity and features indicating a poor prognosis; vedolizumab is an alternative for some patients (Gomollón et al, 2017).
- Consensus statements for the management of inflammatory bowel disease in pregnancy, coordinated by the Canadian Association of Gastroenterology, state that TNF inhibitor treatment does not appear to be associated with unfavorable pregnancy outcomes and should generally be continued during pregnancy (Nguyen et al, 2016b).
- Based upon guidelines from the European Dermatology Forum, adalimumab is recommended among first-line therapies for HS, with infliximab a potential second-line option (Gulliver et al, 2016; Zouboulis et al, 2015).
- Joint guidelines from ASAS and EULAR state that biologic DMARDs should be considered in patients with AS and persistently high disease activity despite conventional treatments (van der Heijde et al, 2017). The 2015 ACR, Spondylitis Association of America, and Spondyloarthritis Research and Treatment Network guidelines strongly

recommend TNF inhibitors for patients who have active disease despite NSAIDs; no TNF inhibitor is preferred over another for AS for most patients (Ward et al, 2016).

- Infliximab and adalimumab are recommended over etanercept for various ocular inflammatory disorders (Levy-Clarke et al, 2016).
- Caution is warranted with these biologic agents due to severe infections and malignancies that can occur with their use. Tocilizumab, TNF inhibitors, and tofacitinib have boxed warnings regarding a risk of serious infections. TNF inhibitors and tofacitinib also have boxed warnings regarding an increased risk of malignancies. Brodalumab has a boxed warning regarding the risk of suicidal ideation and behavior.
- Warnings, precautions, and AE profiles vary in this class.
- All of the biologic agents with the exception of apremilast and tofacitinib are given by subcutaneous injection and/or intravenous infusion. Administration schedule varies among the injectable agents in the class. Apremilast and tofacitinib are given orally.
- Selection of an agent for a patient is determined by approved indications, response, administration method, tolerability, AE profile, and cost of the agent.

REFERENCES

- ACTEMRA prescribing information. Genentech, Inc. South San Francisco, CA. September 2016.
- American College of Rheumatology. Position statement on biosimilars. April 2016. http://www.rheumatology.org/Portals/0/Files/Biosimilars-Position-Statement.pdf. Accessed March 14, 2017.
- Antoni C, Krueger GG, de Vam K, et al. IMPACT 2 Trial Investigators. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis. 2005;64(8):1150-7.
- ARCALYST prescribing information. Regeneron Pharmaceuticals, Inc. Tarrytown, NY. September 2016.
- Atsumi T, Yamamoto K, Takeuchi T, et al. The first double-blind, randomised, parallel-group certolizumab pegol study in methotrexate-naïve early rheumatoid arthritis patients with poor prognostic factors, C-OPERA, shows inhibition of radiographic progression. Ann Rheum Dis. 2016;75:75-83.
- Atteno M, Peluso R, Costa L, et al. Comparison of effectiveness and safety of infliximab, etanercept, and adalimumab in psoriatic arthritis patients who experienced an inadequate response to previous disease-modifying antirheumatic drugs. Clin Rheumatol. 2010;29:399-403.
- Baeten D, Sieper J, Braun J, et al for the MEASURE 1 Study Group and MEASURE 2 Study Group. Secukinumab, an interleukin-17A inhibitor, in ankylosing spondylitis. N Engl J Med. 2015; 373(26):2534-48.
- Behm BW, Bickston SJ. Tumor necrosis factor-alpha antibody for maintenance of remission in Crohn's disease. Cochrane Database of Systematic Reviews. 2008, Issue 1. Art. No.: CD006893. doi: 10.1002/14651858. CD006893.
- Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011;63(4):465-482.
- Bickston SJ, Behm BW, Tsoulis DJ, et al. Vedolizumab for induction and maintenance of remission in ulcerative colitis (review). Cochrane Database Syst Rev. 2014;8:CD007571. doi: 10.1002/14651858.
- Bijlsma JW, Welsing PM, Woodworth TG, et al. Early rheumatoid arthritis treated with tocilizumab, methotrexate, or their combination (U-Act-Early): a multicentre, randomised, double-blind, double-dummy, strategy trial. Lancet. 2016;388:343-55.
- Bingham CO, Mendelsohn AM, Kim L, et al. Maintenance of clinical and radiographic benefit with intravenous golimumab therapy in patients with active rheumatoid arthritis despite methotrexate therapy: week-112 efficacy and safety results of the open-label long-term extension of a phase III, double-blind, randomized, placebo-controlled trial. Arthritis Care Res. 2015;67:1627-1636.
- Blauvelt A, Prinz JC, Gottlieb AB, et al. Secukinumab administration by pre-filled syringe: efficacy, safety and usability results from a randomized controlled trial in psoriasis (FEATURE). Br J Dermatol. 2015;172(2):484-93.
- Bonovas S, Minozzi S, Lytras T, et al. Risk of malignancies using anti-TNF agents in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a systematic review and meta-analysis. Expert Opin Drug Saf. 2016;15(sup1):35-54.
- Braun J, Brandt J, Listing J, et al. Treatment of active ankylosing spondylitis with infliximab: a randomized controlled multicentre trial. Lancet. 2002;359(9313):1187-93.
- Braun J, van der Horst-Bruinsma IE, Huang F, et al. Clinical efficacy and safety of etanercept vs sulfasalazine in patients with ankylosing spondylitis: a randomized, double-blind trial. Arthritis Rheum. 2011;63(6):1543-51.
- Brunner H, Ruperto N, Zuber Z, et al. Efficacy and safety of tocilizumab in patients with polyarticular-course juvenile idiopathic arthritis: results from a phase 3, randomized, double-blind withdrawal trial. Ann Rheum Dis. 2015;74:1110-117. doi:10.1136/annrheumdis-2014-205351.
- Burmester GR, Blanco R, Charles-Schoeman C, et al for the ORAL Step Investigators. Tofacitinib (CP-690,550) in combination with methotrexate in patients with active rheumatoid arthritis with an inadequate response to tumour necrosis factor inhibitors: a randomized phase 3 trial. Lancet. 2013[a];381:451-60.
- Burmester GR, Matucci-Cerinic M, Mariette X, et al. Safety and effectiveness of adalimumab in patients with rheumatoid arthritis over 5 years of therapy in a phase 3b and subsequent postmarketing observational study. Arthritis Res Ther. 2014b;16(1):R24. doi: 10.1186/ar4452.
- Burmester GR, Panaccione R, Gordon KB, et al. Adalimumab: long-term safety in 23,458 patients from global clinical trials in rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis and Crohn's disease. Ann Rheum Dis. 2013[b];72: 517–24.
- Burmester GR, Rubbert-Roth A, Cantagrel A, et al. A randomised, double-blind, parallel-group study of the safety and efficacy of subcutaneous tocilizumab vs intravenous tocilizumab in combination with traditional disease-modifying antirheumatic drugs in patients with moderate to severe rheumatoid arthritis (SUMMACTA study). Ann Rheum Dis. 2014a;73:69-74.
- Burmester GR, Rubbert-Roth A, Cantagrel A, et al. Efficacy and safety of subcutaneous tocilizumab versus intravenous tocilizumab in combination with traditional DMARDs in patients with RA at week 97 (SUMMACTA). Ann Rheum Dis. 2016;75:68-74.
- Busard C, Zweegers J, Limpens J, et al. Combined use of systemic agents for psoriasis: a systematic review. JAMA Dermatol. 2014;150(11):1213-1220.
- Calin A, Dijkmans BAC, Emery P, et al. Outcomes of a multicentre randomized clinical trial of etanercept to treat ankylosing spondylitis. Ann Rheum Dis. 2004; 63:1594-600.

- Capogrosso Sansone A, Mantarro S, Tuccori M, et al. Safety profile of certolizumab pegol in patients with immune-mediated inflammatory diseases: a systematic review and meta-analysis. Drug Saf. 2015;38:869-888.
- Chandar AK, Singh S, Murad MH, et al. Efficacy and safety of natalizumab and vedolizumab for the management of Crohn's Disease: A systematic review and meta-analysis. Inflamm Bowel Dis. 2015;21:1695-1708.
- Chen C, Zhang X, Xiao L, et al. Comparative effectiveness of biologic therapy regimens for ankylosing spondylitis: a systematic review and a network meta-analysis. Medicine (Baltimore). 2016;95(11):e3060. doi: 10.1097/MD.0000000000003060.
- Choy EH, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. N Engl J Med. 2001;344(12):907-16.
- CIMZIA prescribing information. UCB, Inc. Smyrna, GA. January 2017.
- Coates LC, Kavanaugh A, Mease PJ, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis. Arthritis Rheumatol. 2016;68(5):1060-71.
- Cohen SB, Emery P, Greenwald MW, et al. Rituximab for rheumatoid arthritis refractory to anti–tumor necrosis factor therapy results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial evaluating primary efficacy and safety at twenty-four weeks. Arthritis Rheum. 2006;54: 2793-806.
- Combe B, Dasgupta B, Louw I, et al. Efficacy and safety of golimumab as add-on therapy to disease-modifying antirheumatic drugs: results of the GO-MORE study. Ann Rheum Dis. 2014;73:1477-1486.
- COSENTYX prescribing information. Novartis Pharmaceuticals Corporation. East Hanover, NJ. January 2016.
- Cutolo M, Myerson GE, Fleischmann RM, et al. Long-term (52-week) results of a Phase 3, randomized, controlled trial of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with psoriatic arthritis (PALACE 2). Abstract session presented at: The American College of Rheumatology and Association of Rheumatology Health Professionals Annual Meeting; 2013 October 25-30; San Diego, CA.
- Davis JC, van der Heijde DM, Braun J, et al. Efficacy and safety of up to 192 weeks of etanercept therapy in patients with ankylosing spondylitis. Ann Rheum Dis. 2008;67:346-52.
- De Benedetti, Brunner H, Ruperto N, et al. Randomized trial of tocilizumab in systemic juvenile idiopathic arthritis. N Engl J Med. 2012;367:2385-95.
- Deodhar A, Braun J, Inman RD, et al. Golimumab administered subcutaneously every 4 weeks in ankylosing spondylitis: 5-year results of the GO-RAISE study. Ann Rheum Dis. 2015;74:757-61.
- Donahue KE, Jonas DE, Hansen RA, et al. Drug therapy for rheumatoid arthritis in adults: an update [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 Apr. (Comparative Effectiveness Reviews, No. 55.) Available from: http://www.ncbi.nlm.nih.gov/books/NBK97388/. Accessed March 17, 2017.
- Drugs@FDA. Food and Drug Administration. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed March 17, 2017.
- Edwards CJ, Blanco FJ, Crowley J, et al. Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with psoriatic arthritis and current skin involvement: a phase III, randomized, controlled trial (PALACE 3). Ann Rheum Dis. 2016;75(6):1065-73.
- Emery P, Fleischmann RM, Moreland LW, et al. Golimumab, a human anti-tumor necrosis factor alpha monoclonal antibody, injected subcutaneously every four weeks in methotrexate-naive patients with active rheumatoid arthritis: twenty-four-week results of a phase III, multicenter, randomized, double-blind, placebo-controlled study of golimumab before methotrexate as first-line therapy for early-onset rheumatoid arthritis. Arthritis Rheum. 2009;60(8):2272-83.
- Emery P, Keystone E, Tony H, et al. IL-6 receptor inhibition with tocilizumab improves treatment outcomes in patients with rheumatoid arthritis refractory to anti-tumor necrosis factor biological: results from a 24-week multicenter randomized placebo-controlled trial. Ann Rheum Dis. 2008;67:1516-23.
- ENBREL prescribing information. Amgen. Thousand Oaks, CA. November 2016.
- ENTYVIO prescribing information. Takeda Pharmaceuticals America, Inc. Deerfield, IL. May 2014.
- Feagan BG, Rutgeerts P, Sands B, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2013;369(8):699-710.
- Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2016;375:1946-60.
- Fénix-Caballero S, Alegre-del Rey EJ, Castano-Lara R, et al. Direct and indirect comparison of the efficacy and safety of adalimumab, etanercept, infliximab and golimumab in psoriatic arthritis. J Clin Pharm Ther. 2013;38(4):286-93.
- Fleischmann RM, Halland AM, Brzosko M, et al. Tocilizumab inhibits structural joint damage and improves physical function in patients with rheumatoid arthritis and inadequate responses to methotrexate: LITHE study 2-year results. J Rheumatol. 2013;40(2):113-26.
- Fleischmann R, Kremer J, Cush J, et al. Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. N Engl J Med. 2012;367(6): 495-507.
- Fleischmann R, Vencovsky J, van Vollenhoven RF, et al. Efficacy and safety of certolizumab pegol monotherapy every four weeks in patients with rheumatoid arthritis failing previous disease-modifying antirheumatic therapy: the FAST4WARD study. Ann Rheum Dis. 2009; 68:805-11.
- Furst DE, Kavanaugh A, Florentinus S, et al. Final 10-year effectiveness and safety results from study DE020: adalimumab treatment in patients with rheumatoid arthritis and an inadequate response to standard therapy. Rheumatology. 2015;54:2188-2197.
- Gabay C, Emery P, van Vollenhoven R, et al. ADACTA Study Investigators. Tocilizumab monotherapy vs adalimumab monotherapy for treatment of rheumatoid arthritis (ADACTA): a randomised, double-blind, controlled phase 4 trial. Lancet. 2013; 381(9877):1541-50.
- Galvao TF, Zimmermann IR, da Mota LM, et al. Withdrawal of biologic agents in rheumatoid arthritis: a systematic review and meta-analysis. Clin Rheumatol. 2016;35(7):1659-68.
- Genovese M, McKay J, Nasonov E, et al. Interleukin-6 receptor inhibition with tocilizumab reduces disease activity in rheumatoid arthritis with inadequate response to disease-modifying antirheumatic drugs. Arthritis Rheum. 2008;58(10):2968-80.
- Genovese MC, Covarrubias A, Leon G, et al. Subcutaneous abatacept vs intravenous abatacept: A phase IIIb noninferiority study in patients with an inadequate response to methotrexate. Arthritis Rheum. 2011;63(10):2854-64.
- Genovese MC, Mease PJ, Thomson GTD, et al. Safety and efficacy of adalimumab in treatment of patients with psoriatic arthritis who had failed disease modifying antirheumatic drug therapy. J Rheum. 2007;34:1040-50.
- Genovese MC, Rubbert-Roth A, Smolen JS, et al. Long-term safety and efficacy of tocilizumab in patients with rheumatoid arthritis: a cumulative analysis of up to 4.6 years of exposure. J Rheumatol. 2013;40: 768–80. doi:10.3899/jrheum.120687.
- Gomollón F, Dignass A, Annese V, et al. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 1: diagnosis and medical management. J Crohns Colitis. 2017;11(1):3-25.
- Gordon KB, Blauvelt A, Papp KA, et al. Phase 3 trials of ixekizumab in moderate-to-severe plaque psoriasis. N Engl J Med. 2016;375:345-56.

- Gorman JD, Sack KE, Davis JC. Treatment of ankylosing spondylitis by inhibition of tumor necrosis factor α. N Engl J Med. 2002;346(18):1349-56.
- Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies. Ann Rheum Dis. 2016;75(3):499-510.
- Götestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016;75(5):795-810.
- Gottenberg JE, Brocq O, Perdriger A, et al. Non-TNF-targeted biologic vs a second anti-TNF drug to treat rheumatoid arthritis in patients with insufficient response to a first anti-TNF drug: a randomized clinical trial. JAMA. 2016;316(11):1172-1180.
- Gottlieb AB, Langley RG, Strober BE, et al. A randomized, double-blind, placebo-controlled study to evaluate the addition of methotrexate to etanercept in patients with moderate to severe plaque psoriasis. Br J Dermatol. 2012;167:649-657.
- Griffiths CE, Reich K, Lebwohl M, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. Lancet. 2015;386:541-51.
- Griffiths CE, Strober BE, van de Kerkhof P, et al; ACCEPT Study Group. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. N Engl J Med. 2010;362(2):118-28.
- Gulliver W, Zouboulis CC, Prens E, et al. Evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa, based on the European guidelines for hidradenitis suppurativa. Rev Endocr Metab Disord. 2016;17(3):343-51.
- Haraoui B, Bokarewa M, Kallmeyer I, et al. Safety and effectiveness of rituximab in patients with rheumatoid arthritis following an inadequate response to 1 prior tumor necrosis factor inhibitor: the RESET trial. J Rheumatol. 2011;38; 2548-56.
- Hazlewood GS, Barnabe C, Tomlinson G, et al. Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying anti-rheumatic drugs for rheumatoid arthritis: a network meta-analysis. Cochrane Database of Systematic Reviews. 2016, Issue 8. Art. No.: CD010227. doi: 10.1002/14651858.CD010227.pub2.
- Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. Arch Dermatol. 2012;148(1):95-102.
- HUMIRA prescribing information. AbbVie Inc. North Chicago, IL. June 2016.
- Hyams J, Crandall W, Kugathasan S, et al; REACH Study Group. Induction and maintenance infliximab therapy for the treatment of moderate-to-severe Crohn's disease in children. Gastroenterology. 2007;132(3):863-73; quiz 1165-6.
- Hyams JS, Damaraju L, Blank M, et al. Induction and maintenance therapy with infliximab for children with moderate to severe ulcerative colitis. Clin Gastroenterol Hepatol. 2012;10(4):391-399.
- ILARIS prescribing information. Novartis Pharmaceuticals Corporation. East Hanover, NJ. December 2016.
- INFLECTRA prescribing information. Hospira. Lake Forest, IL. April 2016.
- Jaffe GJ, Dick AD, Brézin AP, et al. Adalimumab in patients with active noninfectious uveitis. N Engl J Med. 2016;375:932-43.
- Jones G, Sebba A, Gu J, et al. Comparison of tocilizumab monotherapy vs methotrexate monotherapy in patients with moderate to severe rheumatoid arthritis: The AMBITION study. Ann Rheum Dis. 2010;69(1):88-96.
- Kalb RE, Fiorentino DF, Lebwohl MG, et al. Risk of serious infection with biologic and systemic treatment of psoriasis: Results from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). JAMA Dermatol. 2015;151(9):961-9.
- Kavanaugh A, McInnes I, Mease P, et al. Golimumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four week efficacy and safety results of a randomized, placebo-controlled study. Arthritis Rheum. 2009;60(4):976-86.
- Kavanaugh A, McInnes IB, Mease P, et al. Clinical efficacy, radiographic and safety findings through 5 years of subcutaneous golimumab treatment in patients with active psoriatic arthritis: results from a long-term extension of a randomized, placebo-controlled trial (the GO-REVEAL study). Ann Rheum Dis. 2014[b];73(9):1689-94. doi: 10.1136/annrheumdis-2013-204902
- Kavanaugh A, Mease PJ, Gomez-Reino JJ, et al. Long-term (52-week) results of a phase III randomized, controlled trial of apremilast in patients with psoriatic arthritis. J Rheumatol. 2015[b];42:479-88.
- Kavanaugh A, Mease PJ, Gomez-Reino JJ, et al. Treatment of psoriatic arthritis in a phase 3, randomized, placebo-controlled trial with apremilast, an oral phosphodiesterase 4 inhibitor. Ann Rheum Dis. 2014[a];73(6):1020-6. doi: 10.1136/annrheumdis-2013-205056.
- Kavanaugh A, Puig L, Gottlieb AB, et al; PSUMMIT 1 Study Group. Maintenance of clinical efficacy and radiographic benefit through two years of ustekinumab therapy in patients with active psoriatic arthritis: results from a randomized, placebo-controlled phase III trial. Arthritis Care Res. 2015[a];67(12):1739-1749.
- Kavanaugh A, van der Heijde D, Beutler A, et al. Radiographic progression of patients with psoriatic arthritis who achieve minimal disease activity in response to golimumab therapy: results through 5 years of a randomized, placebo-controlled study. Arthritis Care Res (Hoboken). 2016;68(2):267-74.
- Kay J, Fleischmann R, Keystone E, et al. Golimumab 3-year safety update: an analysis of pooled data from the long-term extensions of randomized, double-blind, placebo-controlled trials conducted in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis. Ann Rheum Dis. 2015;74(3):538-46. doi: 10.1136/annrheumdis-2013-204195.
- Keystone E, Landewe R, van Vollenhoven R, et al. Long-term safety and efficacy of certolizumab pegol in combination with methotrexate in the treatment of rheumatoid arthritis: 5-year results from the RAPID 1 trial and open-label extension. Ann Rheum Dis. 2014[a];73(12):2094-100. doi: 10.1136/annrheumdis-2013-203695.
- Keystone E, van der Heijde D, Mason D, et al. Certolizumab pegol plus methotrexate is significantly more effective than placebo plus methotrexate in active rheumatoid arthritis. Arthritis Rheum. 2008;58(11):3319-29.
- Keystone EC, Breedveld FC, van der Heijde D, et al. Long-term effect of delaying combination therapy with tumor necrosis factor inhibitor in patients with aggressive early rheumatoid arthritis: 10-year efficacy and safety of adalimumab from the randomized controlled PREMIER trial with open-label extension. J Rheumatol. 2014[b];41(1):5-14. doi: 10.3899/jrheum.130543.
- Keystone EC, Genovese MC, Hall S, et al. Golimumab in patients with active rheumatoid arthritis despite methotrexate therapy: results through 2 years of the GO-FORWARD study extension. J Rheumatol. 2013[a];40; 1097-1103.
- Keystone EC, Genovese MC, Klareskog L, et al. Golimumab, a human antibody to tumor necrosis factor alpha given by monthly subcutaneous injections, in active rheumatoid arthritis despite methotrexate therapy: the GO-FORWARD Study. Ann Rheum Dis. 2009;68(6):789-96.
- Keystone ED, van der Heijde D, Kavanaugh A, et al. Clinical, functional, and radiographic benefits of long-term adalimumab plus methotrexate: final 10-year data in longstanding rheumatoid arthritis. J Rheum. 2013[b];40(9): 2-11.
- Kimball AB, Okun MM, Williams DA, et al. Two phase 3 trials of adalimumab for hidradenitis suppurativa. N Engl J Med. 2016;375:422-34.
- Kimball AB, Rothman KJ, Kricorian G, et al. OBSERVE-5: Observational postmarketing safety surveillance registry of etanercept for the treatment of psoriasis final 5-year results. J Am Acad Dermatol. 2015;72(1):115-22. doi: 10.1016/j.jaad.2014.08.050

- KINERET prescribing information. Swedish Orphan Biovitrum (SOBI, INC). Stockholm, Sweden. May 2016.
- Kivitz A, Olech E, Borofsky M, et al. Subcutaneous tocilizumab versus placebo in combination with disease-modifying antirheumatic drugs in patients with rheumatoid arthritis. Arthritis Care Res. 2014;66:1653-61.
- Koné-Paut I, Lachmann HJ, Kuemmerle-Deschner JB, et al. Sustained remission of symptoms and improved health-related quality of life in patients with cryopyrin-associated periodic syndrome treated with canakinumab: results of a double-blind placebo-controlled randomized withdrawal study. Arthritis Res Ther. 2011;13(1):R34.
- Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010;105(3):501-23.
- Kremer J, Ritchlin C, Mendelsohn A, et al. Golimumab, a new human anti–tumor necrosis factor alpha antibody, administered intravenously in patients with active rheumatoid arthritis. Forty-eight–week efficacy and safety results of a phase III randomized, double-blind, placebo-controlled study. Arthritis Rheum. 2010;62(4): 917–28.
- Kremer JM, Blanco R, Brzosko M, et al. Tocilizumab inhibits structural joint damage in rheumatoid arthritis patients with inadequate responses to methotrexate: results from the double-blind treatment phase of a randomized placebo-controlled trial of tocilizumab safety and prevention of structural joint damage at one year. Arthritis Rheum. 2011;63:609-21.
- Kuemmerle-Deschner JB, Hachulla E, Cartwright R, et al. Two-year results from an open-label, multicentre, phase III study evaluating the safety and efficacy of canakinumab in patients with cryopyrin-associated periodic syndrome across different severity phenotypes. Ann Rheum Dis. 2011;70:2095-2102.
- Lachmann HJ, Koné-Paut I, Keummerle-Deschner JB, et al. Use of Canakinumab in the Cryopyrin Associated Periodic Syndrome. N Engl J Med. 2009;360:2416-25.
- Landells I, Marano C, Hsu MC, et al. Ustekinumab in adolescent patients age 12 to 17 years with moderate-to-severe plaque psoriasis: results of the randomized phase 3 CADMUS study. J Am Acad Dermatol. 2015;73:594-603.
- Landewe R, Braun J, Deodhar A, et al. Efficacy of certolizumab pegol on signs and symptoms of axial spondyloarthritis including ankylosing spondylitis: 24 week results of a double-blind randomized placebo-controlled Phase 3 study. Ann Rheum Dis. 2014;73:39-47.
- Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis – results of two phase 3 trials. N Engl J Med. 2014;371:326-38.
- Langley RG, Lebwohl M, Krueger GG, et al for the Phoenix 2 Investigators. Long-term efficacy and safety of ustekinumab, with and without dosing adjustment, in patients with moderate to severe psoriasis: results from the PHOENIX 2 study through 5 years of follow-up. Br J Dermatol. 2015;172(5):1371-1383.
- Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. N Engl J Med. 2015;373:1318-28.
- Lee EB, Fleischmann R, Hall S, et al for the Oral Start Investigators. Tofacitinib versus methotrexate in rheumatoid arthritis. N Engl J Med. 2014;370:2377-86.
- Lemos LLP, de Oliveira Costa J, Almeida AM, et al. Treatment of psoriatic arthritis with anti-TNF agents: a systematic review and meta-analysis of efficacy, effectiveness and safety. Rheumatol Int. 2014;34:3145-1360.
- Leonardi C, Kimball A, Papp K, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomized, double-blind, placebo-controlled trial (PHOENIX 1). Lancet. 2008;371:1665-74.
- Lethaby A, Lopez-Olivo MA, Maxwell L, et al. Etanercept for the treatment of rheumatoid arthritis (Review). The Cochrane Collaboration. Cochrane Library. 2013;5:1-452.
- Levy-Clarke G, Jabs DA, Read RW, et al. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. Ophthalmology. 2014;121(3):785-96.
- Lichtenstein GR, Hanauer SB, Sandborn WJ; Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol. 2009;104:465-83.
- Lopez-Olivio MA, Amezaga Urruela M, McGahan L, et al. Rituximab for rheumatoid arthritis. Cochrane Database Syst Reviews. 2015, Issue 1. Art. No.: CD007356. doi: 10.1002/14651858.CD007356.pub2.
- Lovell D, Ruperto N, Goodman S, et al. Adalimumab with or without methotrexate in juvenile rheumatoid arthritis. N Engl J Med. 2008; 359(8):810-20.
- Lovell DJ, Giannini EH, Reiff A, et al. Etanercept in children with polyarticular juvenile rheumatoid arthritis. N Engl J Med. 2000;342:763-9.
- Lovell DJ, Reiff A, Jones OY, et al. Long-term safety and efficacy of etanercept in children with polyarticular-course juvenile rheumatoid arthritis. Arthritis Rheum. 2006;54:1987-94.
- Ma C, Panaccione R, Heitman SJ, et al. Systematic review: the short-term and long-term efficacy of adalimumab following discontinuation of infliximab. Aliment Pharmacol Ther. 2009;30:977-86.
- Machado MA, Barbaos MM, Almeida AM, et al. Treatment of ankylosing spondylitis with TNF blockers: a meta-analysis. Rheumatol Int. 2013;33(9):2199-2213. doi: 10.1007/s00296-013-2772-6.
- Manders SH, Kievit W, Adang E, et al. Cost-effectiveness of abatacept, rituximab, and TNFi treatment after previous failure with TNFi treatment in rheumatoid arthritis: a pragmatic multi-centre randomised trial. Arthritis Research & Therapy. 2015;17:134.
- Maxwell L, Singh JA. Abatacept for rheumatoid arthritis. Cochrane Database Syst Rev. 2009;(4):CD007277.
- Maxwell LJ, Zochling J, Boonen A, et al. TNF-alpha inhibitors for ankylosing spondylitis. Cochrane Database Syst Rev. 2015, Issue 4. Art. No.: CD005468. doi: 10.1002/14651858.CD005468.pub2.
- McInnes IB, Kavanaugh A, Gottlieb AB, et al. Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial. Lancet. 2013;382:780-9.
- McInnes IB, Mease PJ, Kirkham B, et al for the FUTURE 2 Study Group. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomized, double-blind, placebo-controlled, phase 3 trial. Lancet. 2015;386(9999):1137-46.
- Mease PJ, Fleischmann R, Deodhar AA, et al. Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a Phase 3 double-blind randomised placebo-controlled study (RAPID-PsA). Ann Rheum Dis. 2014;73:48-55.
- Mease PJ, Gladman DD, Ritchlin CT, et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis. Arthritis Rheum. 2005; 52(10):3279-89.
- Mease PJ, Goffe BS, Metz J, et al. Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomized trial. Lancet. 2000;356;385-90.
- Mease PJ, Kivitz AJ, Burch FX, et al. Etanercept treatment of psoriatic arthritis: safety, efficacy and effect on disease progression. Arthritis Rheum. 2004;50:2264-72.
- Mease PJ, McInnes IB, Kirkham B, et al. Secukinumab inhibition of interleukin-17A in patients with psoriatic arthritis. N Engl J Med. 2015;373(14):1329-39.

- Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008;58:826-50.
- Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 5: Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. J Am Acad Dermatol. 2010;62:114-35.
- Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol. 2009[a];60:643-59.
- Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol. 2009[b]; 61(3):451-85.
- Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. J Am Acad Dermatol. 2011;(1):137-74.
- Mertens M, Singh JA. Anakinra for rheumatoid arthritis. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD005121. doi: 10.1002/14651858. CD005121.pub3.
- Minozzi S, Bonovas S, Lytras T, et al. Risk of infections using anti-TNF agents in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a systematic review and meta-analysis. Expert Opin Drug Saf. 2016;15(sup1):11-34.
- Mosli MH, MacDonald JK, Bickston SJ, et al. Vedolizumab for induction and maintenance of remission in ulcerative colitis: a Cochrane systemic review and meta-analysis. Inflamm Bowel Dis. 2015;21:1151-9.
- Nast A, Gisondi P, Ormerod AD, et al. European S3-guidelines on the systemic treatment of psoriasis vulgaris-update 2015-short version-EDF in cooperation with EADV and IPC. J Eur Acad Dermatol Venereol. 2015[b];29(12):2277-94.
- Nast A, Jacobs A, Rosumeck S, Werner RN. Efficacy and safety of systemic long-term treatments for moderate-to-severe psoriasis: a systematic review and meta-analysis. J Invest Dermatol. 2015[a];135(11):2641-8.
- Navarro-Sarabia F, Ariza-Ariza R, Hernandez-Cruz B, et al. Adalimumab for treating rheumatoid arthritis. Cochrane Database Syst Rev. 2005, Issue 3. Art. No.: CD005113. doi: 10.1002/14651858.CD005113.pub2.
- Nguyen GC, Loftus EV, Hirano I, et al. American Gastroenterological Institute guideline on the management of Crohn's disease after surgical resection. Gatroenterology. 2017;152(1):271-5.
- Nguyen GC, Seow CH, Maxwell C, et al. The Toronto Consensus Statements for the Management of Inflammatory Bowel Disease in Pregnancy. Gastroenterology. 2016[b];150:734-57.
- Nguyen QD, Merrill PT, Jaffe GJ, et al. Adalimumab for prevention of uveitic flare in patients with inactive non-infectious uveitis controlled by corticosteroids (VISUAL II): a multicentre, double-masked, randomised, placebo-controlled phase 3 trial. Lancet. 2016[a];388:1183-92.
- Nixon R, Bansback N, Brennan A. The efficacy of inhibiting tumor necrosis factor α and interleukin 1 in patients with rheumatoid arthritis: a meta-analysis and adjusted indirect comparisons. Rheumatology. 2007;46:1140-7.
- O'Dell JR, Mikuls TR, Taylor TH, et al. Therapies for active rheumatoid arthritis after methotrexate failure. N Engl J Med. 2013;369 (4):307-18.
- ORENCIA prescribing information. Bristol Myers Squibb. Princeton, NJ. June 2016.
- OTEZLA prescribing information. Celgene Corporation. Summit, NJ. December 2015.
- Ozen S, Demirkaya E, Erer B, et al. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis. 2016;75:644-51.
- Paller AS, Siegfried EC, Langley RG, et al. Etanercept treatment for children and adolescents with plaque psoriasis. N Engl J Med. 2008;358:241-51.
- Paller AS, Siegfried EC, Pariser DM, et al. Long-term safety and efficacy of etanercept in children and adolescents with plaque psoriasis. J Am Acad Dermatol. 2016;74:280-7.
- Papp K, Langley R, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomized, double-blind, placebo-controlled trial (PHOENIX 2). Lancet. 2008;371:1675-84.
- Papp K, Reich K, Leonardi CL, et al. Apremilast, an oral phosphodiesterase 4 (PDE 4) inhibitor, in patients with moderate to severe plaque psoriasis: Results of a phase III, randomized, controlled trial (Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis [ESTEEM] 1). J Am Acad Dermatol. 2015;73(1):37-49.
- Papp KA, Griffiths CEM, Gordon K, et al. Long-term safety of ustekinumab in patients with moderate-to-severe psoriasis: final results from 5 years of follow-up. Br J Derm. 2013;168: 844–54.
- Papp KA, Reich K, Paul C, et al. A prospective, phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2016;175:273-86.
- Park W, Hrycaj P, Jeka S, et al. A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. Ann Rheum Dis. 2013;72:1605-1612.
- Park W, Yoo DH, Jaworski J, et al. Comparable long-term efficacy, as assessed by patient-reported outcomes, safety and pharmacokinetics, of CT-P13 and reference infliximab in patients with ankylosing spondylitis: 54-week results from the randomized, parallel-group PLANETAS study. Arthritis Res Ther. 2016;18:25. doi: 10.1186/s13075-016-0930-4.
- Park W, Yoo DH, Miranda P, et al. Efficacy and safety of switching from reference infliximab to CT-P13 compared with maintenance of CT-P13 in ankylosing spondylitis: 102-week data from the PLANETAS extension study. Ann Rheum Dis. 2017;76(2):346-54.
- Paul C, Cather J, Gooderham M, et al. Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate to severe psoriasis over 52 weeks: a phase III randomized, controlled trial (ESTEEM 2). Br J Dermatol. 2015[a];173:1355-56.
- Paul C, Lacour JP, Tedremets L, et al. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). J Eur Acad Dermatol Venereol. 2015[b];29(6):1082-90. doi: 10.1111/jdv.12751.
- Porter D, van Melckebeke J, Dale J, et al. Tumor necrosis factor inhibition versus rituximab for patients with rheumatoid arthritis who require biological treatment (ORBIT): an open-label, randomised controlled, non-inferiority, trial. Lancet. 2016;388:239-47.
- Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999 May 6;340(18):1398-405.
- Ramiro S, Smolen JS, Landewe R, et al. Pharmacological treatment of psoriatic arthritis: a systematic literature review for the 2015 update of the EULAR recommendations for the management of psoriatic arthritis. Ann Rheum Dis. 2016;75(3):490-8.
- Reinisch W, Sandborn WJ, Hommes DW, et al. Adalimumab for induction of clinical remission in moderately to severely active ulcerative colitis: results of a randomised controlled trial. Gut. 2011;60: 780–7.
- REMICADE prescribing information. Janssen Biotech. Horsham, PA. October 2015.

- Rich P, Gooderham M, Bachelez H, et al. Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with difficult-to-treat nail and scalp psoriasis: results of 2 phase III randomized, controlled trials (ESTEEM 1 and ESTEEM 2). J Am Acad Dermatol. 2016;74(1):134-42.
- Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the treatment of juvenile idiopathic arthritis. Arthritis & Rheumatism. 2013;65(10):2499-2512.
- Ritchlin C, Rahman P, Kavanaugh A, et al. Efficacy and safety of the anti-IL-12/23 p40 monoclonal antibody, ustekinumab, in patients with active psoriatic arthritis despite conventional non-biological and biological anti-tumour necrosis factor therapy: 6-month and 1-year results of the phase 3, multicentre, double-blind, placebo controlled, randomised PSUMMIT 2 trial. Ann Rheum Dis. 2014;73:990-999.
- RITUXAN prescribing information. Genentech, Inc. South San Francisco, CA. August 2014.
- Ruperto N, Brunner HI, Quartier P, et al. Two randomized trials of canakinumab in systemic juvenile idiopathic arthritis. N Engl J Med. 2012;367: 2396-406. doi: 10.1056/NEJMoa1205099.
- Ruperto N, Lovell DJ, Quartier P, et al; Pediatric Rheumatology International Trials Organization; Pediatric Rheumatology Collaborative Study Group. Abatacept in children with juvenile idiopathic arthritis: a randomized, double-blind, placebo-controlled withdrawal trial. Lancet. 2008;372(9636):383-91.
- Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005 Dec 8;353(23):2462-76.
- Ryoo JY, Yang HJ, Ji E, Yoo BK. Meta-analysis of the efficacy and safety of secukinumab for the treatment of plaque psoriasis. Ann Pharmacother. 2016;50(5):341-51.
- Sandborn WJ. Crohn's Disease Evaluation and Treatment: Clinical Decision Tool. Gastroenterology. 2014;147:702-5.
- Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab induces clinical response and remission in patients with moderate to severe ulcerative colitis. Gastroenterology. 2014a;146(1):96-109. doi: 10.1053/j.gastro.2013.05.048.
- Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab maintains clinical response in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2014b;146:96-109.
- Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2013;369(8):711-721.
- Sandborn WJ, Van Assche G, Reinisch W, et al. Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2012;142: 257–65.
- Sands BE, Feagan BG, Rutgeerts P, et al. Effects of Vedolizumab Induction Therapy for Patients With Crohn's Disease in Whom Tumor Necrosis Factor Antagonist Treatment Failed. Gastr. 2014;147:618-627.
- Saurat JH, Stingl G, Dubertret L, et al; CHAMPION Study Investigators. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs methotrexate vs placebo in patients with psoriasis (CHAMPION). Br J Dermatol. 2008;158(3):558-66.
- Schiff M, Keiserman M, Codding C, et al. Efficacy and safety of abatacept or infliximab vs placebo in ATTEST: a phase III, multi-centre, randomised, double-blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate. Ann Rheum Dis. 2008;67:1096-1103.
- Schiff M, Weinblatt ME, Valente R, et al. Head-to-head comparison of subcutaneous abatacept vs adalimumab for rheumatoid arthritis: two-year efficacy and safety findings from AMPLE trial. Ann Rheum Dis. 2014;73:86-94.
- Schmitt J, Zhang Z, Wozel, G, et al. Efficacy and tolerability of biologic and nonbiologic systemic treatments for moderate-to-severe psoriasis: meta-analysis of randomized controlled trials. Br J Derm. 2008;159:513-26.
- Shao L-M, Chen M-Y, Chen Q-Y, et al. Meta-analysis: the efficacy and safety of certolizumab pegol in Crohn's disease. Aliment Pharmacol Ther. 2009;29(6):605-14.
- Sibley CH, Plass N, Snow J, et al. Sustained response and prevention of damage progression in patients with neonatal-onset multisystem inflammatory disease treated with anakinra. A cohort study to determine three- and five-year outcomes. Arthritis Rheum. 2012;64(7): 2375-86.
- Sieper J, Kivitz A, van Tubergen A, et al. Impact of certolizumab pegol on patient-reported outcomes in patients with axial spondyloarthritis. Arthritis Care Res. 2015[a];67(10):1475-1480.
- Sieper J, Landewe R, Rudwaleit M, et al. Effects of certolizumab pegol over ninety-six weeks in patients with axial spondyloarthritis. Arthritis & Rheumatology. 2015[b];67(3):668-677.
- SILIQ prescribing information. Valeant Pharmaceuticals. Bridgewater, NJ. February 2017.
- SIMPONI ARIA prescribing information. Janssen Biotech, Inc. Horsham, PA. January 2017.
- SIMPONI prescribing information. Janssen Biotech, Inc. Horsham, PA. January 2017.
- Singh JA, Hossain A, Tanjong Ghogomu E, et al. Biologic or tofacitinib monotherapy for rheumatoid arthritis in people with traditional disease-modifying anti-rheumatic drug failure: a Cochrane systematic review and network meta-analysis. Cochrane Database of Systematic Reviews. 2016[b], Issue 11. Art. No.: CD012437. doi: 10.1002/14651858.CD012437.
- Singh JA, Hossain A, Tanjong Ghogomu E, et al. Biologics or tofacitinib for people with rheumatoid arthritis unsuccessfully treated with biologics; a systematic review and network meta-analysis. Cochrane Database of Systematic Reviews. 2017, Issue 3. Art. No.: CD012591. doi: 10.1002/14651858.CD012591.
- Singh JA, Hossain A, Tanjong Ghogomu E, et al. Biologics or tofacitinib for rheumatoid arthritis in incomplete responders to methotrexate or other traditional disease-modifying anti-rheumatic drugs: a systematic review and network meta-analysis. Cochrane Database of Systematic Reviews. 2016[a], Issue 5. Art. No.: CD012183. doi: 10.1002/14651858.CD012183.
- Singh JA, Saag KG, Bridges L Jr, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Care Res. 2016[c];68(1):1-26.
- Singh S, Kumar S, Pardi D, et al. Comparative efficacy of biologic therapy in biologic naïve patients with Crohn's disease: a systematic review and network meta-analysis. Mayo Clin Proc. 2014;89:1621-35.
- Smolen J, Landewe R, Mease P, et al. Efficacy and safety of certolizumab pegol plus methotrexate in active rheumatoid arthritis: the RAPID 2 study. A randomized controlled trial. Ann Rheum Dis. 2009[a];68:797-804.
- Smolen JS, Beaulieu A, Rubbert-Roth A, et al. Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (OPTION study): a double-blind, placebo-controlled, randomized trial. Lancet. 2008;371(9617):987-97.
- Smolen JS, Emery P, Ferraccioli GF, et al. Certolizumab pegol in rheumatoid arthritis patients with low to moderate activity: the CERTAIN double-blind, randomized, placebo-controlled trial. Ann Rheum Dis. 2015[a];74:843-850. doi:10.1136/annrheumdis-2013-204632

- Smolen JS, Kay J, Doyle M, et al. Golimumab in patients with active rheumatoid arthritis after treatment with tumor necrosis factor inhibitors: findings with up to five years of treatment in the multicenter, randomized, double-blind, placebo-controlled, phase 3 GO-AFTER study. Arthritis Res Ther. 2015[b];17(1):14. doi: 10.1186/s13075-015-0516-6.
- Smolen JS, Kay J, Doyle MK, et al; GO-AFTER study investigators. Golimumab in patients with active rheumatoid arthritis after treatment with tumor necrosis factor alpha inhibitors (GO-AFTER study): a multicentre, randomized, double-blind, placebo-controlled, phase III trial. Lancet. 2009[b];374(9685):210-21.
- Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Mar 6 [Epub]. doi: 10.1136/annrheumdis-2016-210715.
- STELARA prescribing information. Janssen Biotech. Horsham, PA. September 2016.
- Strand V, Ahadieh S, French J, et al. Systematic review and meta-analysis of serious infections with tofacitinib and biologic disease-modifying antirheumatic drug treatment in rheumatoid arthritis clinical trials. Arthritis Res Ther. 2015[b];17:362. doi 10.1186/s13075-015-0880-2.
- Strand V, Burmester GR, Zerbini CAF, et al. Tofacitinib with methotrexate in third-line treatment of patients with active rheumatoid arthritis: patient-reported outcomes from a phase III trial. Arthritis Care Res. 2015[a];67(4):475-483.
- TALTZ AMCP dossier. Eli Lilly and Company, Indianapolis, IN. March 2016.
- TALTZ prescribing information. Eli Lilly and Company, Indianapolis, IN. March 2016.
- Targan SR, Hanauer SB, van Deventer SJ, et al. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. N Engl J Med. 1997;337(15):1029-35.
- Tarp S, Amarilyo G, Foeldvari I, et al. Efficacy and safety of biological agents for systemic juvenile idiopathic arthritis: a systematic review and meta-analysis of randomized trials. Rheumatology. 2016;55:669-79.
- Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti–TNF-a biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. Gastroenterology. 2013;145(6):1459-1463.
- Thaçi D, Blauvelt A, Reich K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. J Am Acad Dermatol. 2015;73(3):400-9.
- Thaçi D, Kimball A, Foley P, et al. Apremilast, an oral phosphodiesterase inhibitor, improves patient-reported outcomes in the treatment of moderate to severe psoriasis: results of two phase III randomized, controlled trials. J Eur Acad Dermatol Venereol. 2017;31(3):498-506.
- TYSABRI prescribing information. Biogen Idec Inc., Cambridge, MA. May 2016.
- Ungprasert P, Thongprayoon C, Davis JM. Indirect comparisons of the efficacy of biological agents in patients with psoriatic arthritis with an inadequate response to traditional disease-modifying anti-rheumatic drugs or to non-steroidal anti-inflammatory drugs: a meta-analysis. Semin Arthritis Rheum. 2016[a];45(4):428-38.
- Ungprasert P, Thongprayoon C, Davis JM. Indirect comparisons of the efficacy of subsequent biological agents in patients with psoriatic arthritis with an inadequate response to tumor necrosis factor inhibitors: a meta analysis. Clin Rheumatol. 2016;35:1795-1803.
- van der Heijde D, Dijkmans B, Geusens P, et al; Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy Study Group. Efficacy and safety of infliximab in patients with ankylosing spondylitis: results of a randomized, placebo-controlled trial (ASSERT). Arthritis Rheum. 2005;52(2):582-91.
- van der Heijde D, Kivitz A, Schiff MH, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis. Arthritis Rheum. 2006;54(7):2136-46.
- van der Heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017 Jan 13 [Epub]. doi: 10.1136/annrheumdis-2016-210770.
- van der Heijde D, Tanaka Y, Fleischmann R, et al. Tofacitinib (CP-690,550) in patients with rheumatoid arthritis receiving MTX. Twelve-month data from a twenty-four–month Phase III randomized radiographic study. Arthritis Rheum. 2013;65(3): 559-70.
- Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis & Rheumatology. 2016;68(2):282-98. doi 10.1002/ART.39298.
- Weinblatt ME, Bingham CO, Mendelsohn AM, et al. Intravenous golimumab is effective in patients with active rheumatoid arthritis despite methotrexate therapy with responses as early as week 2: results of the phase 3, randomised, multicentre, double-blind, placebo-controlled GO-FURTHER trial. Ann Rheum Dis. 2013;72: 381-89.
- Westhovens R, Kremer JM, Emery P, et al. Long-term safety and efficacy of abatacept in patients with rheumatoid arthritis and an inadequate response to methotrexate: a 7-year extended study. Clin Exp Rheumatol. 2014;32(4):553-62.
- Wiens A, Correr CJ, Venson R, et al. A meta-analysis of the efficacy and safety of using infliximab for the treatment of rheumatoid arthritis. Clin Rheumatol. 2009 Dec;28(12):1365-73.
- XELJANZ / XELJANZ XR prescribing information. Pfizer, Inc. New York, NY. February 2016.
- Yoo DH, Hrycaj P, Miranda P, et al. A randomised, double-blind, parallel-group study to demonstrate equivalence in efficacy and safety of CT-P13 compared with innovator infliximab when coadministered with methotrexate in patients with active rheumatoid arthritis: the PLANETRA study. Ann Rheum Dis. 2013;72:1613-1620.
- Yoo DH, Prodanovic N, Jaworski J, et al. Efficacy and safety of CT-P13 (biosimilar infliximab) in patients with rheumatoid arthritis: comparison between switching from reference infliximab to CT-P13 and continuing CT-P13 in the PLANETRA extension study. Ann Rheum Dis. 2017;76(2):355-63.
- Yoo DH, Racewicz A, Brzezicki J, et al. A phase III randomized study to evaluate the efficacy and safety of CT-P13 compared with reference infliximab in patients with active rheumatoid arthritis: 54-week results from the PLANETRA study. Arthritis Res Ther. 2016;18:82. doi: 10.1186/s13075-016-0981-6.
- Zhang ZM, Li W, Jiang XL. Efficacy and safety of adalimumab in moderately to severely active cases of ulcerative colitis: a meta-analysis of published placebo-controlled trials. Gut Liver. 2016;10(2):262-74.
- Zouboulis CC, Desai N, Emtestam L, et al. European S1 guideline for the treatment of hidradenitis suppurative/acne inversa. J Eur Acad Dermatol Venereol. 2015;29(4):619-44.

Publication Date: March 27, 2017

Codeine and Tramadol Utilization

August 2016 - July 2017

Age	Count of MemberID
0	**4**
APAP/CODEINE SOL 120-12/5	**4**
FAMILY PRACTICE	1
HEAD/NECK SURGERY	1
MAMMOGRAPHY	1
(blank)	1
1	**33**
APAP/CODEINE SOL 120-12/5	**33**
CARDIO-VASCULAR	1
DERMATOLOGY	2
EMERGENCY MEDICINE	2
FAMILY NURSE PRACTITIONER	1
GASTROENTEROLOGY	1
GENERAL SURGERY	1
HEAD/NECK SURGERY	5
MAMMOGRAPHY	2
PEDIATRICS	3
RADIOLOGY	2
UROLOGIC SURGERY	3
(blank)	10
2	**44**
APAP/CODEINE SOL 120-12/5	**44**
DERMATOLOGY	3
EMERGENCY MEDICINE	4
FAMILY NURSE PRACTITIONER	1
GASTROENTEROLOGY	1
GENERAL SURGERY	1
HEAD/NECK SURGERY	2
HEMATOLOGY/ONCOLOGY, PEDS	2
INTERNAL MEDICINE	5
MAMMOGRAPHY	1
PEDIATRIC DENTISTRY	3
PEDIATRICS	2
PHYSICAL THERAPY	4
RADIOLOGY	2
SPEECH PATHOLOGIST	1
UROLOGIC SURGERY	4
(blank)	8
3	**48**
APAP/CODEINE SOL 120-12/5	**48**
DERMATOLOGY	8
EMERGENCY MEDICINE	11
GENERAL DENTISTRY	2
HEAD/NECK SURGERY	4

Age		Count of MemberID
	HEMATOLOGY	1
	HEMATOLOGY/ONCOLOGY, PEDS	1
	INTERNAL MEDICINE	1
	MAMMOGRAPHY	2
	ORTHOPEDIC SURGERY	1
	PHYSICAL THERAPY	1
	RADIOLOGY	2
	UROLOGIC SURGERY	4
	(blank)	10
4		**59**
	APAP/CODEINE SOL 120-12/5	**59**
	DERMATOLOGY	1
	EMERGENCY MEDICINE	12
	FAMILY NURSE PRACTITIONER	1
	FAMILY PRACTICE	2
	GASTROENTEROLOGY	2
	GENERAL DENTISTRY	3
	GENERAL SURGERY	1
	HEAD/NECK SURGERY	3
	HEMATOLOGY	1
	HEMATOLOGY/ONCOLOGY, PEDS	1
	INTERNAL MEDICINE	1
	MAMMOGRAPHY	7
	ORTHOPEDIC SURGERY	2
	PEDIATRICS	1
	PHYSICAL THERAPY	4
	RADIOLOGY	2
	SPEECH PATHOLOGIST	2
	UROLOGIC SURGERY	5
	(blank)	8
5		**65**
	APAP/CODEINE SOL 120-12/5	**64**
	ATTENDANT SERVICES	1
	DERMATOLOGY	4
	EMERGENCY MEDICINE	7
	FAMILY NURSE PRACTITIONER	4
	FAMILY PRACTICE	1
	GASTROENTEROLOGY	1
	GENERAL DENTISTRY	3
	HEAD/NECK SURGERY	2
	HEMATOLOGY	2
	HEMATOLOGY/ONCOLOGY, PEDS	2
	MAMMOGRAPHY	4
	OPHTHALMOLOGY	1
	ORAL SURGERY	1
	ORTHOPEDIC SURGERY	1

Age		Count of MemberID
	OTOLARYNGOLOGY	1
	PEDIATRIC DENTISTRY	1
	PHYSICAL THERAPY	4
	SPEECH PATHOLOGIST	3
	UROLOGIC SURGERY	2
	(blank)	19
APAP/CODEINE TAB 300-30MG		**1**
	FAMILY NURSE PRACTITIONER	1
6		**72**
APAP/CODEINE SOL 120-12/5		**70**
	CARDIO-VASCULAR	1
	DERMATOLOGY	1
	EMERGENCY MEDICINE	5
	ENDOCRINOLOGY	3
	FAMILY NURSE PRACTITIONER	5
	FAMILY PRACTICE	1
	GASTROENTEROLOGY	1
	GENERAL DENTISTRY	6
	GENERAL SURGERY	1
	HEAD/NECK SURGERY	1
	HEMATOLOGY/ONCOLOGY, PEDS	2
	INTERNAL MEDICINE	1
	MAMMOGRAPHY	4
	OCCUPATIONAL THERAPY	1
	ONCOLOGY	1
	ORAL SURGERY	5
	ORTHOPEDIC SURGERY	2
	PEDIATRICS	3
	PHYSICAL THERAPY	9
	SPEECH PATHOLOGIST	1
	UROLOGIC SURGERY	2
	(blank)	14
APAP/CODEINE TAB 300-30MG		**1**
	(blank)	1
TRAMADOL HCL TAB 50MG		**1**
	EMERGENCY MEDICINE	1
7		**51**
APAP/CODEINE SOL 120-12/5		**49**
	DERMATOLOGY	1
	EMERGENCY MEDICINE	7
	ENDOCRINOLOGY	5
	FAMILY NURSE PRACTITIONER	2
	FAMILY PRACTICE	2
	GASTROENTEROLOGY	1
	GENERAL DENTISTRY	1
	HEAD/NECK SURGERY	1

Age	Count of MemberID
HEMATOLOGY/ONCOLOGY, PEDS	1
INTERNAL MEDICINE	2
MAMMOGRAPHY	3
OCCUPATIONAL THERAPY	1
ONCOLOGY	1
ORAL SURGERY	2
PEDIATRICS	3
PHYSICAL THERAPY	4
UROLOGIC SURGERY	1
(blank)	11
APAP/CODEINE TAB 300-30MG	**1**
(blank)	1
TRAMADOL HCL TAB 50MG	**1**
FAMILY NURSE PRACTITIONER	1
8	**63**
APAP/CODEINE SOL 120-12/5	**53**
EMERGENCY MEDICINE	3
FAMILY NURSE PRACTITIONER	1
FAMILY PRACTICE	3
GASTROENTEROLOGY	2
GENERAL DENTISTRY	5
GENERAL SURGERY	3
HEAD/NECK SURGERY	3
HEMATOLOGY/ONCOLOGY, PEDS	2
MAMMOGRAPHY	2
ORAL SURGERY	3
ORTHOPEDIC SURGERY	2
OTOLARYNGOLOGY	3
PHYSICAL THERAPY	2
SPEECH PATHOLOGIST	1
(blank)	18
APAP/CODEINE TAB 300-15MG	**1**
(blank)	1
APAP/CODEINE TAB 300-30MG	**8**
EMERGENCY MEDICINE	1
FAMILY NURSE PRACTITIONER	2
GASTROENTEROLOGY	2
GENERAL SURGERY	1
UROLOGIC SURGERY	1
(blank)	1
TRAMADOL HCL TAB 50MG	**1**
MAMMOGRAPHY	1
9	**70**
APAP/CODEINE SOL 120-12/5	**60**
ANESTHESIOLOGY	3
CASE MANAGEMENT	1

Age	Count of MemberID
DERMATOLOGY	2
EMERGENCY MEDICINE	3
FAMILY NURSE PRACTITIONER	1
FAMILY PRACTICE	4
GENERAL DENTISTRY	3
GENERAL SURGERY	3
HEAD/NECK SURGERY	1
INTERNAL MEDICINE	1
MAMMOGRAPHY	4
OPHTHALMOLOGY	1
ORAL SURGERY	5
ORTHOPEDIC SURGERY	3
OTOLARYNGOLOGY	1
PEDIATRIC DENTISTRY	1
PEDIATRICS	1
PHYSICAL THERAPY	1
RADIOLOGY	1
SPEECH PATHOLOGIST	1
(blank)	19
APAP/CODEINE TAB 300-15MG	**1**
NEUROLOGICAL SURGERY	1
APAP/CODEINE TAB 300-30MG	**8**
GASTROENTEROLOGY	1
GENERAL SURGERY	1
HEAD/NECK SURGERY	1
ORTHOPEDIC SURGERY	1
SPEECH PATHOLOGIST	1
(blank)	3
TRAMADOL HCL TAB 50MG	**1**
FAMILY NURSE PRACTITIONER	1
10	**62**
APAP/CODEINE SOL 120-12/5	**33**
DERMATOLOGY	1
EMERGENCY MEDICINE	3
GENERAL DENTISTRY	3
GENERAL PRACTICE	1
GENERAL SURGERY	4
HEAD/NECK SURGERY	1
HEMATOLOGY/ONCOLOGY, PEDS	1
MAMMOGRAPHY	1
ORAL SURGERY	1
PEDIATRICS	2
PHYSICAL THERAPY	2
RADIOLOGY	1
RESPITE	1
(blank)	11

Age	Count of MemberID
APAP/CODEINE TAB 300-15MG	**2**
PEDIATRICS-PULMONARY	2
APAP/CODEINE TAB 300-30MG	**25**
EMERGENCY MEDICINE	2
FAMILY NURSE PRACTITIONER	2
GENERAL DENTISTRY	1
GENERAL SURGERY	3
HEMATOLOGY/ONCOLOGY, PEDS	1
MAMMOGRAPHY	1
ORTHOPEDIC SURGERY	3
PEDIATRICS	2
PHYSICAL THERAPY	4
(blank)	6
TRAMADOL HCL TAB 50MG	**2**
FAMILY NURSE PRACTITIONER	1
NUCLEAR MEDICINE	1
11	**67**
APAP/CODEINE SOL 120-12/5	**37**
CASE MANAGEMENT	1
EMERGENCY MEDICINE	6
FAMILY NURSE PRACTITIONER	1
FAMILY PRACTICE	1
GENERAL DENTISTRY	4
GENERAL SURGERY	1
HEMATOLOGY/ONCOLOGY, PEDS	1
ORAL SURGERY	4
PEDIATRICS	6
PHYSICAL THERAPY	1
(blank)	11
APAP/CODEINE TAB 300-30MG	**22**
DERMATOLOGY	1
FAMILY NURSE PRACTITIONER	1
GASTROENTEROLOGY	1
GENERAL DENTISTRY	1
GENERAL SURGERY	1
MAMMOGRAPHY	1
NEUROLOGICAL SURGERY	1
OBSTETRICS AND GYNECOLOGY	1
ORAL SURGERY	3
ORTHOPEDIC SURGERY	2
RADIOLOGY	1
SPEECH PATHOLOGIST	1
(blank)	7
APAP/CODEINE TAB 300-60MG	**1**
(blank)	1
TRAMADOL HCL TAB 50MG	**7**

Age	Count of MemberID
OBSTETRICS AND GYNECOLOGY	1
PHYSICAL THERAPY	1
(blank)	5
12	**75**
APAP/CODEINE SOL 120-12/5	**19**
DERMATOLOGY	1
EMERGENCY MEDICINE	2
FAMILY NURSE PRACTITIONER	1
GENERAL DENTISTRY	1
GENERAL SURGERY	1
MAMMOGRAPHY	2
ORAL SURGERY	3
OTOLARYNGOLOGY	1
PHYSICAL THERAPY	1
(blank)	6
APAP/CODEINE TAB 300-30MG	**45**
ANESTHESIOLOGY	1
DERMATOLOGY	1
EMERGENCY MEDICINE	2
FAMILY NURSE PRACTITIONER	1
GASTROENTEROLOGY	2
GENERAL DENTISTRY	2
MAMMOGRAPHY	1
OBSTETRICS AND GYNECOLOGY	2
OCCUPATIONAL THERAPY	2
OPHTHALMOLOGY	1
ORAL SURGERY	3
ORTHOPEDIC SURGERY	1
PEDIATRICS	4
PHYSICAL THERAPY	8
RADIOLOGY	2
REHABILITATION	1
(blank)	11
TRAMADL/APAP TAB 37.5-325	**1**
GENERAL SURGERY	1
TRAMADOL HCL TAB 50MG	**10**
FAMILY PRACTICE	1
GENERAL DENTISTRY	1
OCCUPATIONAL THERAPY	1
(blank)	7
13	**88**
APAP/CODEINE SOL 120-12/5	**16**
CHORE	1
EMERGENCY MEDICINE	1
GASTROENTEROLOGY	4
GENERAL DENTISTRY	2

Age	Count of MemberID
INTERNAL MEDICINE	1
ORAL SURGERY	1
OTOLARYNGOLOGY	1
PHYSICAL THERAPY	2
(blank)	3
APAP/CODEINE TAB 300-15MG	**4**
PHYSICAL THERAPY	1
(blank)	3
APAP/CODEINE TAB 300-30MG	**57**
EMERGENCY MEDICINE	3
FAMILY PRACTICE	2
GASTROENTEROLOGY	1
GENERAL DENTISTRY	5
GENERAL PRACTICE	1
MAMMOGRAPHY	8
NEUROLOGICAL SURGERY	2
OCCUPATIONAL THERAPY	2
ORAL SURGERY	3
PEDIATRICS	1
PHYSICAL THERAPY	3
RADIOLOGY	1
REHABILITATION	2
SPEECH PATHOLOGIST	2
(blank)	21
APAP/CODEINE TAB 300-60MG	**2**
FAMILY PRACTICE	1
RESPITE	1
TRAMADL/APAP TAB 37.5-325	**1**
FAMILY NURSE PRACTITIONER	1
TRAMADOL HCL TAB 50MG	**8**
EMERGENCY MEDICINE	1
HEMATOLOGY/ONCOLOGY, PEDS	1
(blank)	6
14	**100**
APAP/CODEINE SOL 120-12/5	**12**
DERMATOLOGY	1
FAMILY NURSE PRACTITIONER	1
GASTROENTEROLOGY	5
HEMATOLOGY/ONCOLOGY, PEDS	2
MAMMOGRAPHY	1
ORTHOPEDIC SURGERY	1
(blank)	1
APAP/CODEINE TAB 300-30MG	**62**
EMERGENCY MEDICINE	2
ENDOCRINOLOGY	1
FAMILY PRACTICE	3

Age	Count of MemberID
GASTROENTEROLOGY	2
GENERAL DENTISTRY	10
GENERAL PRACTICE	2
GENERAL SURGERY	2
MAMMOGRAPHY	5
NEUROLOGICAL SURGERY	1
OCCUPATIONAL THERAPY	2
ORAL SURGERY	1
PEDIATRICS	2
PHYSICAL THERAPY	4
RESPITE	1
SPEECH PATHOLOGIST	2
(blank)	22
APAP/CODEINE TAB 300-60MG	**2**
FAMILY PRACTICE	2
TRAMADL/APAP TAB 37.5-325	**4**
EMERGENCY MEDICINE	1
FAMILY NURSE PRACTITIONER	2
(blank)	1
TRAMADOL HCL TAB 50MG	**20**
CHORE	1
EMERGENCY MEDICINE	3
FAMILY NURSE PRACTITIONER	2
GENERAL SURGERY	1
NEUROLOGICAL SURGERY	1
PHYSICAL THERAPY	1
QMHP	1
SPEECH PATHOLOGIST	1
(blank)	9
15	**127**
APAP/CODEINE SOL 120-12/5	**7**
EMERGENCY MEDICINE	1
FAMILY PRACTICE	1
MAMMOGRAPHY	1
OCCUPATIONAL THERAPY	1
PEDIATRIC SURGERY	1
SPEECH PATHOLOGIST	1
(blank)	1
APAP/CODEINE TAB 300-30MG	**71**
ANESTHESIOLOGY	1
CRITICAL CARE	1
DERMATOLOGY	1
EMERGENCY MEDICINE	1
FAMILY NURSE PRACTITIONER	3
FAMILY PRACTICE	5
GASTROENTEROLOGY	5

Age	Count of MemberID
GENERAL DENTISTRY	13
GENERAL SURGERY	3
HEMATOLOGY/ONCOLOGY, PEDS	1
INTERNAL MEDICINE	1
OPHTHALMOLOGY	1
ORAL SURGERY	1
OTOLARYNGOLOGY	1
PEDIATRIC DENTISTRY	1
PEDIATRICS	1
PHYSICAL THERAPY	4
RESPITE	1
SPEECH PATHOLOGIST	1
(blank)	25
APAP/CODEINE TAB 300-60MG	**6**
GASTROENTEROLOGY	1
(blank)	5
TRAMADL/APAP TAB 37.5-325	**3**
FAMILY NURSE PRACTITIONER	2
PHYSICAL THERAPY	1
TRAMADOL HCL TAB 50MG	**40**
EMERGENCY MEDICINE	2
FAMILY NURSE PRACTITIONER	8
FAMILY PRACTICE	4
HAND SURGERY	1
MAMMOGRAPHY	1
OBSTETRICS AND GYNECOLOGY	2
OCCUPATIONAL THERAPY	4
QMHP	1
(blank)	17
16	**98**
APAP/CODEINE SOL 120-12/5	**3**
EMERGENCY MEDICINE	1
OCCUPATIONAL THERAPY	1
PHYSICAL THERAPY	1
APAP/CODEINE TAB 300-30MG	**46**
CASE MANAGEMENT	1
DERMATOLOGY	1
EMERGENCY MEDICINE	4
FAMILY NURSE PRACTITIONER	2
GENERAL DENTISTRY	7
GENERAL PRACTICE	1
GENERAL SURGERY	3
HEMATOLOGY/ONCOLOGY, PEDS	2
MAMMOGRAPHY	1
OCCUPATIONAL THERAPY	2
ORAL SURGERY	2

Age	Count of MemberID
ORTHOPEDIC SURGERY	1
PHYSICAL THERAPY	5
SPEECH PATHOLOGIST	1
(blank)	13
APAP/CODEINE TAB 300-60MG	**4**
(blank)	4
TRAMADOL HCL TAB 50MG	**45**
ANESTHESIOLOGY	1
EMERGENCY MEDICINE	5
FAMILY NURSE PRACTITIONER	7
FAMILY PRACTICE	5
MAMMOGRAPHY	2
ORAL SURGERY	1
PEDIATRICS-PULMONARY	1
PHYSICAL MEDICINE/REHAB	1
PHYSICAL THERAPY	1
QMHP	1
SPEECH PATHOLOGIST	2
(blank)	18
17	**142**
APAP/CODEINE SOL 120-12/5	**5**
FAMILY NURSE PRACTITIONER	1
GASTROENTEROLOGY	1
GENERAL DENTISTRY	1
OTOLARYNGOLOGY	2
APAP/CODEINE TAB 300-30MG	**69**
CASE MANAGEMENT	1
DERMATOLOGY	1
FAMILY NURSE PRACTITIONER	2
FAMILY PRACTICE	6
GENERAL DENTISTRY	18
HEMATOLOGY/ONCOLOGY, PEDS	1
MAMMOGRAPHY	3
OBSTETRICS AND GYNECOLOGY	3
OCCUPATIONAL THERAPY	7
ORAL SURGERY	2
ORTHOPEDIC SURGERY	1
PEDIATRIC SURGERY	1
PHYSICAL THERAPY	9
REHABILITATION	1
UROLOGIC SURGERY	1
(blank)	12
APAP/CODEINE TAB 300-60MG	**4**
ANESTHESIOLOGY	1
FAMILY NURSE PRACTITIONER	1
(blank)	2

Age	Count of MemberID
BUT/APAP/CAF CAP CODEINE	**3**
(blank)	3
TRAMADL/APAP TAB 37.5-325	**7**
EMERGENCY MEDICINE	1
FAMILY NURSE PRACTITIONER	4
PHYSICAL THERAPY	1
(blank)	1
TRAMADOL HCL TAB 50MG	**54**
ATTENDANT SERVICES	1
EMERGENCY MEDICINE	5
FAMILY NURSE PRACTITIONER	2
FAMILY PRACTICE	4
GENERAL DENTISTRY	1
INTERNAL MEDICINE	1
MAMMOGRAPHY	4
NEUROLOGICAL SURGERY	1
OCCUPATIONAL THERAPY	5
ORTHOPEDIC SURGERY	1
PATHOLOGY	1
PHYSICAL THERAPY	4
QMHP	1
SPEECH PATHOLOGIST	2
(blank)	21
Grand Total	**1268**

Therapeutic Class Overview
Tramadol and Related Products

INTRODUCTION

- Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage (International Association for the Study of Pain [IASP], 2012). Pain is a subjective experience that is unique to the individual and is difficult to identify or quantify by any observer. The type of pain being experienced is often classified by its pathophysiologic etiology. Somatic pain results from the activation of pain receptors in cutaneous or deep tissues (skin, bone, joint, or connective tissues) and is generally localized and described as sharp in nature. Visceral pain involves internal areas of the body (organs) and may be poorly localized and described as an aching pain. Neuropathic pain is commonly described by patients as burning or electrical in nature and results from injury or damage to the nervous system (Baumann et al, 2014). An individual's reaction or response to treatment of pain can be highly variable. Pain thresholds are highly individualized among patients, and responses to therapy vary between patients and even within the same patient from day to day. Pain management is multifaceted and should incorporate both pharmacological and non-pharmacological measures.
- Tramadol (ULTRAM®) and tapentadol (NUCYNTA®) are both centrally-acting opioid analgesics that exert their analgesic effects through opioid agonist properties as well as by blocking the reuptake of norepinephrine and serotonin. Tramadol blocks norepinephrine and serotonin reuptake and has relatively weak μ-opioid receptor activity. Compared to tramadol, tapentadol has greater μ-opioid receptor activity, similar norepinephrine reuptake inhibitor activity, and weaker serotonin reuptake inhibitor activity (Tsutaoka et al, 2015).
- Tapentadol is a Schedule II controlled substance. In the past, tramadol was not classified as a controlled substance on the federal level; however, the Drug Enforcement Administration has moved tramadol-containing products into Schedule IV as of August 18, 2014 (Federal Register, 2014).
- Tapentadol may be associated with lower rates of gastrointestinal adverse events compared to other available opioid products. Tramadol is associated with reduced cardiovascular and respiratory side effects when compared to other opioids and appears to possess a low potential for abuse and psychological/physical dependence when used short term. However, cases of abuse and dependence have occurred, particularly in patients with a history of opioid abuse and those utilizing the tramadol-containing products long term (Leppert et al, 2005). Based on data reported to the National Poison Data System, tapentadol was associated with more toxic effects and severe outcomes than tramadol, consistent with an opioid agonist, whereas tramadol was associated with significantly higher rates of seizures and vomiting than tapentadol (Tsutaoka et al, 2015).
- This review includes all products that contain tramadol or tapentadol, including short-acting, long-acting, and combination products. Both tramadol and tapentadol are available in immediate-release and extended-release formulations. ULTRAM ER is an extended-release tablet formulation of tramadol, and CONZIP™ is a capsule formulation that contains tramadol in a combination of immediate-release and extended-release components. In addition to immediate-release tablets, tapentadol is available as extended-release tablets. Tapentadol oral solution has been approved by the FDA, but has not been made available. Tramadol is also available in combination with acetaminophen as ULTRACET® and generics. Another tramadol formulation, RYZOLT™, is a tablet formulation with both immediate-release and extended-release components. Please see Table 1 for information on product availability.
- One additional product in this class has been discontinued by its manufacturer and is not included within this review. RYBIX ODT™ (tramadol orally disintegrating tablet) was FDA approved in May 2005 and was discontinued by the manufacturer in May 2013.
- Medispan class: Tramadol and tapentadol are classified within the opioid agonist class.

Table 1. Medications Included Within Class Review

Drug	Manufacturer	FDA Approval Date	Generic Availability
NUCYNTA (tapentadol)	Depomed	Oral tablet: 11/20/2008 Oral solution: 10/15/2012*	-
NUCYNTA ER (tapentadol extended-release tablet)	Depomed	08/25/2011	-
ULTRAM (tramadol)	Various	03/03/1995	✔
ULTRAM ER† (tramadol extended-release tablet)	Various	09/08/2005	✔
RYZOLT† (tramadol extended-release tablet)	Various	12/30/2008	✔
CONZIP (tramadol extended-release capsule)	Vertical Pharmaceutical	05/07/2010	-‡
ULTRACET (tramadol/acetaminophen)	Various	08/15/2001	✔

* NUCYNTA oral solution has been approved by the FDA, but has not been launched.
† Brand-name RYZOLT and ULTRAM ER have been removed from the market, but generic versions remain available.
‡ Although no A-rated generics have been approved by the FDA, an authorized generic of CONZIP is marketed by Trigen Pharmaceuticals.

(Drugs@FDA, 2017; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2017)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	NUCYNTA (tapentadol)	NUCYNTA ER (tapentadol ER)	ULTRAM (tramadol)	ULTRAM ER, CONZIP, RYZOLT (tramadol ER)	ULTRACET (tramadol/ acetaminophen)
Management of moderate to moderately severe pain in adults for whom alternative treatments are inadequate			✔		
Management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time and for whom alternative treatments are inadequate				✔	
Management of neuropathic pain associated with diabetic peripheral neuropathy in adults severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate		✔			
Management of moderate to severe acute pain in adults for whom alternative treatments are inadequate	✔				
Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate		✔			

Indication	NUCYNTA (tapentadol)	NUCYNTA ER (tapentadol ER)	ULTRAM (tramadol)	ULTRAM ER, CONZIP, RYZOLT (tramadol ER)	ULTRACET (tramadol/ acetaminophen)
Management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate (indicated for short-term use of five days or less)					✔

(Prescribing information: CONZIP, 2016; NUCYNTA (oral solution), 2016; NUCYNTA (tablets), 2016; NUCYNTA ER, 2016; tramadol extended-release tablets, 2016; ULTRACET, 2016; ULTRAM, 2016; ULTRAM ER, 2016)

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

CLINICAL EFFICACY SUMMARY

Tramadol

- Tramadol has been evaluated in various settings for the management of moderate-to-moderately severe pain:
  - In patients with symptomatic osteoarthritis (OA), tramadol (up to 400 mg daily) did not significantly improve the mean final pain intensity score compared to placebo when administered over three months (P=0.082); however, mean final pain relief score was superior in the tramadol group (0.43 vs -0.57; P=0.004), and both patient and investigator assessment of treatment favored tramadol over placebo (P=0.038 and P=0.001, respectively) (Fleischmann et al, 2001).
  - In patients with post-tonsillectomy pain, there was no statistically significant difference in visual analog scale (VAS) pain scores between tramadol and diclofenac over two weeks of treatment (P=0.66) (Courtney et al, 2001).
  - However, in some studies, tramadol has been demonstrated to be less effective than nonsteroidal anti-inflammatory drugs (NSAIDs). In studies by O'Donnell et al, a significantly greater proportion of patients with low back pain receiving celecoxib 200 mg twice daily achieved a ≥30% improvement from baseline in numeric rating scale (NRS)-pain scale scores compared to tramadol 50 mg administered four times daily (63.2 vs 49.9%; P<0.001 in one study and 64.1 vs 55.1%; P=0.008 in another study) (O'Donnell et al, 2009).
- Tramadol ER has been compared in clinical studies to placebo, immediate-release tramadol, and buprenorphine:
  - Tramadol ER formulations have consistently demonstrated significant improvements in pain scores compared to placebo in patients with moderate-to-moderately severe chronic pain (Burch et al, 2007; Kean et al, 2009; Fishman et al, 2007).
  - In one study, tramadol ER 300 mg significantly improved patient global assessment scores compared to placebo (P≤0.05); however, no improvements in Western Ontario and McMaster Universities (WOMAC) pain subscale scores were reported for tramadol ER 100 mg, 200 mg or 300 mg after 12 weeks of treatment (DeLemos et al, 2011).
  - Compared to tramadol, tramadol ER was associated with a significant reduction in VAS scores in an eight-week crossover study of patients with chronic pain (29.9 vs 36.2 mm; P<0.001) (Beaulieu et al, 2007).
  - In a 12-week study comparing tramadol ER to the buprenorphine transdermal patch, the least squares mean (LSM) change from baseline in Box Scale-11 pain score between treatments was -0.17 (95% CI, -0.89 to 0.54; P value not reported), which was within the non-inferiority margin, demonstrating that buprenorphine was non-inferior to tramadol ER in patients with OA of the hip or knee (Karlsson et al, 2009).
- The combination tramadol/acetaminophen (APAP) has been compared to placebo, other combination opioid/APAP products, and NSAIDs:
  - In patients with low back pain (N=318), the combination of tramadol/APAP was significantly more effective compared to placebo with regard to changes in VAS pain scores over three months (44.4 vs 52.3 mm; P=0.015) (Ruoff et al, 2003).

- In a study by Fricke et al comparing tramadol/APAP to hydrocodone/APAP in patients undergoing molar removal, both treatments provided statistically significant pain relief compared to placebo (P<0.024); however, the differences were not significantly different from one another during the eight hour evaluation period (Fricke et al, 2002).
- In an eight-week study comparing tramadol/APAP to meloxicam or aceclofenac (not available in the U.S.) in patients with OA, there was a similar improvement in WOMAC pain scores between the treatment arms (6.75 vs 6.51, respectively; P value not reported). Similarly, there was no statistically significant difference in the percentage of patients who reported pain relief with tramadol/APAP compared to the NSAIDs (68.2 vs 78.7%; P>0.05) (Park et al, 2012).
- Alfano et al reported that tramadol/APAP was associated with significantly lower visual rating scale pain scores compared to codeine/APAP (1.4±0.76 vs 2.52±0.86; P<0.001) in patients undergoing surgical procedures; however, the trial was only two days in duration (Alfano et al, 2011).
- The results of a four-week trial in patients with low back pain demonstrated similar improvements in pain scores between tramadol/APAP and codeine/APAP (Mullican et al, 2001).

Tapentadol

- Several clinical studies have demonstrated the superior analgesic efficacy of tapentadol compared to placebo in the treatment of moderate to severe pain (Daniels et al, 2009; Hale et al, 2009; Hartrick et al, 2009; Kleinert et al, 2008; Lee et al, 2014; Stegman et al, 2008). In addition to reducing pain intensity and providing pain relief, therapy with tapentadol was associated with a shorter time to 50% pain relief, a longer time to first dose of rescue medication, a decrease in the use of rescue medications, and a greater number of treatment responders compared to placebo (Daniels et al, 2009; Kleinert et al, 2008; Lee et al, 2014; Stegman et al, 2008).
- Several trials compared the efficacy of tapentadol to oxycodone:
  - In one study of patients who were candidates for joint replacement surgery, tapentadol significantly reduced pain intensity scores compared to placebo and was noninferior to oxycodone for analgesia. In addition, the incidence of gastrointestinal-related adverse events was significantly lower with tapentadol compared to oxycodone (P<0.001) (Hartrick et al, 2009).
  - In a short-term (four day) study of postoperative pain in patients who had undergone bunionectomy, both tapentadol and oxycodone significantly lowered summed pain intensity scores after three days of treatment compared to placebo (P≤0.05 for all); however, only the tapentadol 100 mg doses demonstrated statistically significant differences compared to placebo on day four (P=0.0284). Tapentadol treatment was associated with a reduction in nausea, dizziness, vomiting, and constipation compared to oxycodone (P values not reported) (Stegman et al, 2008).
  - A three-month safety study by Hale et al demonstrated a lower incidence of treatment-related adverse events with tapentadol compared to oxycodone, while also significantly lowering the incidence of withdrawal symptoms (17 vs 29%; P≤0.05) (Hale et al, 2009).
  - A short-term (ten day) study in patients with low back pain and associated radicular leg pain demonstrated that pain relief with tapentadol was non-inferior to that of oxycodone. In this study, tapentadol was associated with a lower incidence of vomiting and constipation (Biondi et al, 2013).
- The effectiveness of the extended-release formulation of tapentadol has been demonstrated in several clinical trials:
  - In a 12-week trial of adults with OA of the knee, significant pain relief was achieved with tapentadol ER compared to placebo (LSM difference, -0.7; 95% CI, -1.04 to -0.33). Oxycodone controlled-release (CR) reduced the average pain intensity compared to placebo for the overall maintenance period (LSM difference vs placebo, -0.3), but was not statistically significantly lower at week 12 of the maintenance period (LSM, -0.3; P value not reported). There was no significant difference in the proportion of patients in the tapentadol group and the placebo group achieving a ≥30% reduction in average pain intensity at week 12 of the maintenance period (43 vs 35.9%, respectively; P=0.058). Significantly fewer patients in the oxycodone CR group achieved this improvement compared to placebo (24.9 vs 35.9%; P=0.002). A higher percentage of patients achieved a ≥50% reduction in average pain intensity from baseline at week 12 with tapentadol ER compared to placebo (32 vs 24.3%; P=0.027), while significantly fewer oxycodone CR-treated patients achieved this improvement compared to placebo (17.3 vs 24.3%; P=0.023) (Afilalo et al, 2010).
  - Buynak et al evaluated tapentadol ER compared to oxycodone ER and placebo in adults with moderate to severe lower back pain. The mean change in pain intensity from baseline to week 12 was significantly greater for tapentadol ER (LSM difference, -0.8; P<0.001) and oxycodone CR (LSM difference, -0.9; P<0.001) compared to placebo. The mean change in pain intensity from baseline over the entire maintenance period

was -2.8 for the tapentadol ER group and -2.1 for the placebo group (LSM difference, -0.7; P<0.001) (Buynak et al, 2010).
    - Schwartz et al evaluated tapentadol ER in adults with painful diabetic peripheral neuropathy in a 12-week, randomized withdrawal trial. Patients were titrated to an optimal dose of tapentadol ER during a three-week open-label phase; subsequently, patients with at least a one-point reduction in pain intensity were randomized to continue tapentadol ER or switch to placebo during a 12-week double-blind phase. The LSM change in average pain intensity from the start of the double-blind treatment period to week 12 was 1.4 in the placebo group, indicating a worsening in pain intensity, and 0 in the tapentadol ER group, indicating no change in pain intensity (LSM difference, -1.3; 95% CI, -1.7 to -0.92; P<0.001). From pre-titration to week 12 of double-blind treatment, a ≥30% improvement in pain intensity was observed in 53.6% of tapentadol ER-treated patients and 42.2% of placebo-treated patients (P=0.017). A ≥50% improvement in pain intensity was observed in 37.8% of tapentadol ER-treated patients and 27.6% of placebo-treated patients (P=0.028) (Schwartz et al, 2011).
    - A second, 12-week, randomized withdrawal trial of tapentadol ER in adults with painful diabetic peripheral neuropathy was performed by Vinik et al. In this trial, the mean change in average pain intensity from the start of the double-blind treatment period to week 12 was 1.3 in the placebo group, indicating a worsening in pain intensity, and 0.28 in the tapentadol ER group (LSM difference, -0.95; 95% CI, -1.42 to -0.49; P<0.001). From pre-titration to week 12 of double-blind treatment, a ≥30% improvement in pain intensity was observed in 55.4% of tapentadol ER-treated patients and 45.4% of placebo-treated patients (P=0.032). A ≥50% improvement in pain intensity was observed in 40.4% of tapentadol ER-treated patients and 28.9% of placebo-treated patients (P=0.015) (Vinik et al, 2014).
    - Kress et al evaluated tapentadol ER compared to placebo and morphine CR for managing moderate to severe malignant tumor-related pain. Patients were randomized and titrated to an optimal dose of tapentadol ER (100 mg to 250 mg twice daily) or morphine sulfate CR (40 mg to 100 mg twice daily) over two weeks. Patients who completed titration and had adequate pain control continued into a four-week maintenance period during which patients who received morphine CR continued on the same medication and patients who received tapentadol ER were re-randomized to continue tapentadol ER or switch to placebo. Criteria for response during each phase were based on completion of the phase, a pain intensity score <5, and a mean total daily dose of ≤20 mg/day of rescue medication (morphine sulfate immediate release). Based on responder rates at the end of titration, tapentadol ER was determined to be non-inferior to morphine sulfate CR (76% vs 83%, respectively). During the titration phase, incidences of treatment-related adverse events were 50% with tapentadol ER and 63.9% with morphine CR; nausea, vomiting, and dry mouth occurred less commonly with tapentadol ER than with morphine CR. During the maintenance phase, the adjusted responder rate was significantly higher with tapentadol ER (64.3%) than with placebo (47.1%) (P=0.02). (Kress et al, 2014).
    - Imanaka et al evaluated tapentadol ER compared to oxycodone CR in Japanese and Korean patients with cancer-related pain. The primary efficacy endpoint, mean change in average pain intensity on an 11-point scale, was -2.69 and -2.57 in the tapentadol ER and oxycodone CR groups, respectively. Tapentadol was demonstrated to be non-inferior to oxycodone CR for the primary endpoint. The percentage of patients responding with ≥30% reduction in pain intensity was 63.5% and 59% in the tapentadol ER and oxycodone CR groups, respectively, and the percentage responding with a ≥50% improvement was 50% and 42.4%, respectively. In this study, tapentadol was also associated with a slightly lower incidence of some gastrointestinal adverse events than oxycodone CR (Imanaka et al, 2013).
    - In a pooled analysis of three studies of patients with pain due to OA or nonmalignant lower back pain, tapentadol ER was significantly more effective compared to placebo over a three week treatment phase (LSM difference, -0.6; 95% CI, -0.8 to -0.39; P<0.001) and for the overall 12 week maintenance period (-0.5; 95% CI, -0.73 to -0.34; P<0.001). A similar analgesic effect was reported in patients receiving oxycodone CR; however, the responder rate was higher with tapentadol ER (P<0.001). Moreover, a significantly higher proportion of patients receiving tapentadol ER achieved a ≥30% and ≥50% improvement in pain intensity from baseline compared to oxycodone CR and placebo (P<0.001 for both) (Lange et al, 2010).
- No published studies were identified that compared the analgesic efficacy of tramadol and tapentadol.

Guidelines

- Current consensus guidelines for the management of low back pain recommend the use of opioids or tramadol in patients with severe pain that has not responded to treatment with acetaminophen or NSAIDs (Chou et al, 2007).
- Tramadol may be an initial treatment option along with topical capsaicin and topical or oral NSAIDs for osteoarthritis of the hand, knee or hips (Hochberg et al, 2012).
- Guidelines established by the European Federation of Neurological Societies and the American Academy of Neurology generally recommend the use of tramadol as a second-line therapy for the treatment of various polyneuropathies (Attal et al, 2010; Bril et al, 2011).
- A practice guideline from the American College of Occupational and Environmental Medicine (ACOEM) notes that tramadol may be a better option than more potent opioids for management of chronic noncancer pain. However, it notes that with long-term use, especially at higher doses, it may be considered equivalent to other opioids (Hegmann et al, 2014).
- Based on an updated systematic review and meta-analysis, the Special Interest Group on Neuropathic Pain (NeuPSIG) of the International Association for the Study of Pain gives tramadol a weak recommendation for use in the management of neuropathic pain, recommending it as a second-line agent. Medications with a strong recommendation for use (first-line agents) include gabapentin, pregabalin, duloxetine, venlafaxine, and tricyclic antidepressants. Tapentadol has an inconclusive recommendation for neuropathic pain based on inconsistent findings (Finnerup et al, 2015).
- The Canadian Pain Society also recommends tramadol as a second-line agent for management of chronic neuropathic pain, and recommends tapentadol as a fourth-line agent. First-line agents include gabapentin, pregabalin, serotonin noradrenaline reuptake inhibitors, and tricyclic antidepressants (Moulin et al, 2014).
- The specific role of immediate- or extended-release tapentadol has not been incorporated into most currently available treatment guidelines, and in most cases no preference is given to one single opioid over another.

SAFETY SUMMARY

- NUCYNTA ER is included in the Extended Release/Long Acting (ER/LA) Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). The REMS consists of a medication guide, elements to assure safe use, and a timetable for submission of assessments of the REMS. The goal of the REMS is to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of ER/LA opioid analgesics while maintaining patient access to pain medications (FDA, 2016).
- Tapentadol is a Schedule II controlled substance, and tapentadol-containing products carry a Boxed Warning regarding the risks of addiction, abuse, and misuse; life-threatening respiratory depression; accidental ingestion; interaction with benzodiazepines and other central nervous system (CNS) depressants; and neonatal opioid withdrawal syndrome (NOWS). Tramadol is a Schedule IV controlled substance, and ULTRAM, ULTRAM ER, and ULTRACET carry Boxed Warnings regarding these same risks, with the addition of concomitant use of cytochrome P450 (CYP) inducers and inhibitors.
- ULTRACET has a Boxed Warning noting that acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death.
- Tapentadol- and tramadol-containing products are generally contraindicated in patients with significant respiratory depression, acute or severe bronchial asthma where resuscitation is unfeasible, known or suspected gastrointestinal obstruction, hypersensitivity, and with concurrent use of monoamine oxidase inhibitors (MAOIs) within the last 14 days.
- The prescribing information for both tramadol and tapentadol contain warnings regarding the risk of seizures and serotonin syndrome in patients using concomitant serotonergic drugs. Based on data reported to the National Poison Data System, tramadol is associated with a greater risk of seizures than tapentadol (Tsutaoka et al, 2015).
- Both tramadol and tapentadol have warnings related to respiratory depression and CNS depression, and may have additive effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause CNS depression. However, tramadol appears to be associated with reduced cardiovascular and respiratory side effects when compared to opioids and appears to possess a low potential for abuse and psychological/physical dependence when used short term. However, cases of abuse and dependence have occurred, particularly in patients with a history of opioid abuse and those utilizing the tramadol containing products long term (Leppert et al, 2005). Based on data reported to the National Poison Data System,

tapentadol was associated with more toxic effects and severe outcomes than tramadol, consistent with an opioid agonist (Tsutaoka et al, 2015).

- Tramadol- and tapentadol-containing products may produce adrenal insufficiency, severe hypotension, and increased intracranial pressure.
- Tapentadol may be associated with lower rates of gastrointestinal adverse events compared to other available opioid products. Tramadol is associated with a higher risk of vomiting than tapentadol (Tsutaoka et al, 2015).
- Notable drug interactions associated with tramadol and/or tapentadol include:
    - Concomitant use with MAOIs may lead to an increased risk of seizures or serotonin syndrome; use only with great caution.
    - Additive serotonergic effects may occur when co-administered with serotonergic drugs.
    - CYP3A4 and/or CYP2D6 inhibitors may reduce the metabolism of tramadol, thereby increasing the risk of adverse events. Carbamazepine increases tramadol metabolism and may significantly reduce its analgesic efficacy.
    - Tapentadol may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
NUCYNTA NUCYNTA ER (tapentadol)	Immediate release (IR) tablet: 50 mg 75 mg 100 mg Extended-release (ER) tablet: 50 mg 100 mg 150 mg 200 mg 250 mg Oral solution: 20 mg/mL (not marketed)	Acute Pain: IR tablet and oral solution: initial, 50 mg, 75 mg, or 100 mg every four to six hours Chronic pain, Neuropathic pain: ER tablet: initial, 50 mg twice daily; maintenance, titrate to adequate analgesia	Max dose: IR tablet and oral solution: 700 mg on first day, 600 mg on subsequent days ER tablet: 500 mg/day IR tablet and oral solution: On first day of dosing, second dose may be administered as soon as 1 hour after the first dose if adequate pain relief is not attained with the first dose	May be given with or without food ER tablets: Advise patients to swallow whole and not to cut, chew, dissolve, or crush the tablet
ULTRAM ULTRAM ER CONZIP RYZOLT (tramadol)	Tablet: 50 mg ER tablet: 100 mg 200 mg 300 mg ER capsule: 100 mg 150 mg 200 mg 300 mg	Management of moderate to moderately severe pain in adults: IR tablet: initial, 25 to 50 mg in the morning titrated to four times daily; maintenance, 50 to 100 mg every four to six hours as needed Chronic pain: ER capsule, ER tablet (patients not currently on tramadol IR	Max dose: IR: 400 mg/day ER: 300 mg/day	Administer without regard to meals ER capsules and ER tablets: Advise patients to swallow whole and not to cut, chew, dissolve, or crush the capsule or tablet.

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		products): initial, 100 mg daily and titrated to pain relief ER capsule, ER tablet (patients currently on tramadol IR products): initial, calculate the 24-hour tramadol IR dose and round down to nearest 100 mg increment and administer daily		
ULTRACET (tramadol/ acetamino-phen)	Tablet: 37.5 mg/325 mg	Short-term (five days or less) management of acute pain: Tablet: initial, two tablets every four to six hours as needed for five days or less	Max dose: Eight tablets daily	Take without regard to food; take with food if GI upset occurs

ER=extended release, IR=immediate release

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
NUCYNTA NUCYNTA ER (tapentadol)	Consider starting elderly patients with the lower range of recommended doses	Safety and efficacy have not been established in pediatric patients younger than 18 years; use is not recommended in this population	Mild to moderate: No dosage adjustment is recommended Severe: Use is not recommended	Mild: No dosage adjustment is recommended Moderate: IR: 50 mg with the interval between doses no less than every 8 hours. Further treatment should reflect maintenance of analgesia with acceptable tolerability, to be achieved by either shortening or lengthening the dosing interval, max 3 doses in 24 hours (150 mg per 24 hours). ER: 50 mg	Pregnancy Category C Unknown whether excreted in breast milk; use is not recommended

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
				administered no more frequently than once every 24 hours, max 100 mg/day Severe: Use is not recommended	
ULTRAM ULTRAM ER CONZIP RYZOLT (tramadol)	Elderly >65 years: Use caution and initiate at the lower end of the dosing range; refer to adult dosing Elderly >75 years: IR: Do not exceed 300 mg/day; see dosing adjustments for renal and hepatic impairment ER: Use with great caution; see dosing for adults, renal, and hepatic impairment	Safety and efficacy have not been established	IR: CrCl <30 mL/minute: Administer 50 to 100 mg every 12 hours (max 200 mg/day) ER: Should not be used in patients with CrCl <30 mL/minute	IR: Recommended dose in patients with cirrhosis: 50 mg every 12 hours ER: Should not be used in patients with severe (Child-Pugh class C) hepatic dysfunction (ULTRAM ER, CONZIP) or any degree of hepatic dysfunction (RYZOLT [generic])	Pregnancy Category C (RYZOLT) Unclassified† (ULTRAM, ULTRAM ER, and CONZIP) Prolonged use of opioids during pregnancy may cause NOWS. Available data in pregnant women are insufficient to inform a drug-associated risk for major birth defects and miscarriage. Excreted in breast milk; use is not recommended
ULTRACET (tramadol/ acetaminophen)	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients	Safety and efficacy in pediatric patients ≤16 years of age have not been established	CrCl<30 mL/minute: Maximum of two tablets every 12 hours.	Not recommended	Unclassified† Available data in pregnant women are insufficient to inform a drug-associated risk for major birth defects and miscarriage. Excreted in breast milk; use is not recommended.

CrCl=creatinine clearance, ER=extended release, IR=immediate release

*Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
†In accordance with the FDA's Pregnancy and Lactation Labeling Rule (PLLR), this product is not currently assigned a Pregnancy Category. Consult product prescribing information for details.

CONCLUSION

- Tramadol (ULTRAM) and tapentadol (NUCYNTA) are both centrally-acting opioid analgesics that produce analgesia through opioid agonist properties and by blocking the reuptake of norepinephrine and serotonin.
- Both tramadol and tapentadol are available in extended-release formulations, and tramadol is also available in combination with acetaminophen. Tramadol is available generically in immediate-release (IR) and extended-release formulations as well as in combination with acetaminophen. Currently, there is no generic available for tapentadol-containing products.
- Clinical studies have generally demonstrated that tramadol and tapentadol are effective in the management of moderate-to-moderately severe chronic pain and for the relief of moderate-to-severe conditions of acute pain including low back pain, osteoarthritis, and diabetic peripheral neuropathy. Clinical studies evaluating tapentadol (both IR and ER) have generally demonstrated significant pain relief compared to placebo with a similar analgesic profile compared to oxycodone (both IR and ER). Furthermore, both formulations of tapentadol may be associated with a more favorable adverse event profile compared to oxycodone. There is a risk of seizures with both tramadol and tapentadol products; however, the risk appears to be higher with tramadol. Tapentadol products are classified as Schedule II controlled substances, and tramadol-containing products are classified as schedule IV controlled substances.
- Guidelines for the treatment of low back pain recommend opioids or tramadol in patients with severe pain that has not responded to treatment with acetaminophen or NSAIDs (Chou et al, 2007). Tramadol may be considered an initial treatment option along with topical capsaicin and topical or oral NSAIDs for osteoarthritis of the hand, knee or hips (Hochberg et al, 2012). Guidelines established by the European Federation of Neurological Societies and the American Academy of Neurology generally recommend tramadol as a second-line therapy for the treatment of polyneuropathies (Attal et al, 2010, Bril et al, 2011). Guidelines from the International Association for the Study of Pain and the Canadian Pain Society recommend tramadol as a second-line agent for neuropathic pain (Finnerup et al, 2015; Moulin et al, 2014). A practice guideline from the American College of Occupational and Environmental Medicine states that tramadol may be a better option than more potent opioids for management of chronic noncancer pain, but may be an equivalent choice when used long-term (Hegmann et al, 2014). The role of immediate- or extended-release tapentadol is not specifically incorporated into most currently available treatment guidelines, and in most cases no preference is given to one single opioid over another.

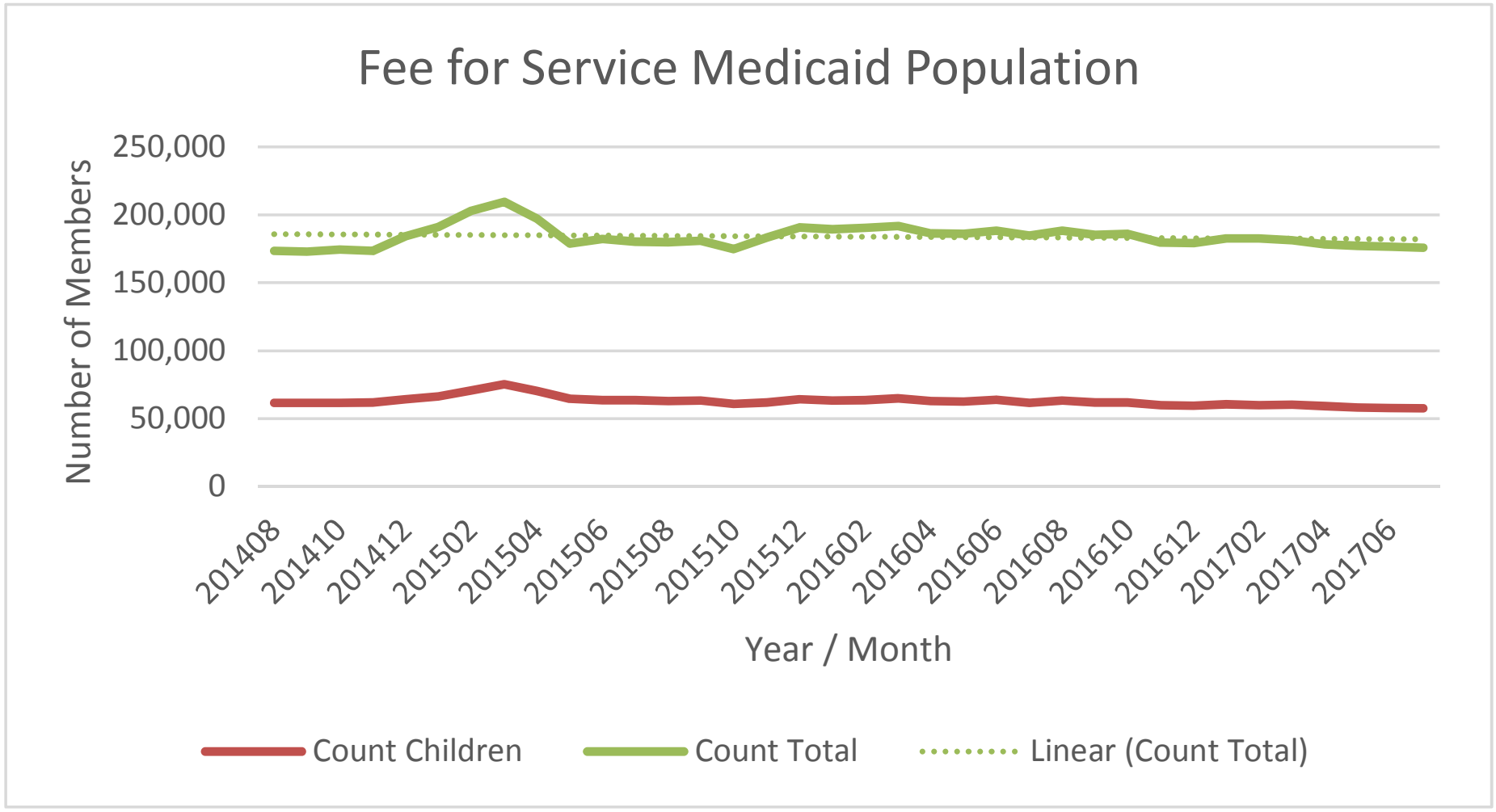
REFERENCES

- Afilalo M, Etropolski MS, Kuperwasser B, et al. Efficacy and safety of tapentadol extended release compared to oxycodone controlled release for the management of moderate to severe chronic pain related to osteoarthritis of the knee: a randomized, double-blind, placebo- and active-controlled phase III study. Clin Drug Investig. 2010;30(8):489-505.
- Alfano G, Grieco M, Forino A, et al. Analgesia with paracetamol/tramadol vs. paracetamol/codeine in one day-surgery: a randomized open study. Eur Rev Med Pharmacol Sci. 2011 Feb;15(2):205-10.
- Attal N, Cruccu G, Baron R, et al. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. Eur J Neurol. 2010 Sep;17(9):1113-e88.
- Baumann TJ, Herndon CM, Strickland JM. Pain Management. In: Talbert RL, DiPiro JT, Matzke GR, Posey LM, Wells BG, Yee GC, eds. Pharmacotherapy: A Pathophysiologic Approach. 9th ed. New York: McGraw-Hill; 2014.
- Beaulieu AD, Peloso P, Bensen W, et al. A randomized, double-blind, 8-week crossover study of once-daily controlled-release tramadol versus immediate-release tramadol taken as needed for chronic noncancer pain. Clin Ther. 2007;29:49-60.
- Biondi D, Xiang J, Benson C, et al. Tapentadol immediate release versus oxycodone immediate release for treatment of acute low back pain. Pain Physician. 2013;16:E237-E246.
- Bril V, England J, Franklin GM, et al. Evidence-based guideline: treatment of painful diabetic neuropathy: report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Neurology. 2011 May 17:76(20):1758-65.
- Burch F, Fishman R, Messina N, et al. A comparison of the analgesic efficacy of Tramadol Contramid OAD versus placebo in patients with pain due to osteoarthritis. J Pain Symptom Manage. 2007 Sep;34(3):328-38.
- Buynak R, Shapiro DY, Okamoto A, et al. Efficacy and safety of tapentadol extended release for the management of chronic low back pain: results of a prospective, randomized, double-blind, placebo- and active-controlled Phase III study. Expert Opin Pharmacother. 2010 Aug;11(11):1787-804.
- Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. Ann Int Med. 2007 Oct 2;147(7):478-91.
- CONZIP prescribing information. Vertical Pharmaceuticals, Inc. Sayerville, NJ. December 2016.
- Courtney MJ, Cabraal D. Tramadol vs. diclofenac for post tonsillectomy analgesia. Arch Otolaryngol Head Neck Surg. 2001;127:385-8.

- Daniels SE, Upmalis D, Okamoto A, et al. A randomized, double-blind, phase III study comparing multiple doses of tapentadol IR, oxycodone IR, and placebo for postoperative (bunionectomy) pain. Current Medical Research and Opinion. 2009;25(3):765-76.
- DeLemos BP, Xiang J, Benson C, et al. Tramadol hydrochloride extended-release once-daily in the treatment of osteoarthritis of the knee and/or hip: a double-blind, randomized, dose-ranging trial. Am J Ther. 2011 May;18(3):216-26.
- Drugs@FDA [database on the Internet]. Rockville (MD): Food and Drug Administration (US), Center for Drug Evaluation and Research; 2017. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed March 13, 2017.
- Federal Register. 2014;79(127):37623-37629. Available at: http://www.gpo.gov/fdsys/pkg/FR-2014-07-02/pdf/2014-15548.pdf. Accessed March 13, 2017.
- Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015;14:162-73.
- Fishman RL, Kistler CJ, Ellerbusch MT, et al. Efficacy and safety of 12 weeks of osteoarthritic pain therapy with once-daily tramadol (Tramadol Contramid® OAD). J Opioid Manag. 2007 Sep-Oct;3(5):273-80.
- Fleischmann RM, Caldwell JR, Roth SH, et al. Tramadol for the treatment of joint pain associated with osteoarthritis: A randomized, double-blind, placebo-controlled trial. Curr Ther Res Clin Exp. 2001;62:113-8.
- Food and Drug Administration. Extended-release (ER) and long-acting (LA) opioid analgesics risk evaluation and mitigation strategy (REMS). Available at: https://www.accessdata.fda.gov/drugsatfda_docs/rems/ERLA_2016-09-30_REMS_Document%20.pdf. June 2016 update. Accessed March 24, 2017.
- Fricke JR, Karim R, Jordan D, Rosenthal N. A double-blind, single-dose comparison of the analgesic efficacy of tramadol/acetaminophen combination tablets, hydrocodone/acetaminophen combination tablets, and placebo after oral surgery. Clin Ther. 2002;24:953-68.
- Hale M, Upmalis D, Okamoto A, et al. Tolerability of tapentadol immediate release in patients with lower back pain or osteoarthritis of the hip or knee over 90 days: a randomized, double-blind study. Curr Med Res Opin. 2009;25(5):1095-104.
- Hartrick C, Van Hove I, Stegman JU, et al. Efficacy and tolerability of tapentadol immediate release and oxycodone HCl immediate release in patients awaiting primary joint replacement surgery for end-stage joint disease: a 10-day, phase III, randomized, double-blind, active- and placebo-controlled study. Clinical Therapeutics. 2009;31(2):260-71.
- Hegmann KT, Weiss MS, Bowden K, et al. ACOEM Practice Guidelines: Opioids for treatment of acute, subacute, chronic, and postoperative pain. J Occup Environ Med. 2014;56(12):e143-59.
- Hochberg MC, Altman RD, April KT, et al; American College of Rheumatology. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2012 Apr;64(4):455-74.
- Imanaka K, Tominaga Y, Etropolski M, et al. Efficacy and safety of oral tapentadol extended release in Japanese and Korean patients with moderate to severe, chronic malignant tumor-related pain. Curr Med Res Opin. 2013;29(10):1399-409.
- International Association for the Study of Pain. IASP Taxonomy, 2012. Available at: http://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698#Pain. Accessed March 13, 2017.
- Karlsson M, Berggren AC. Efficacy and safety of low-dose transdermal buprenorphine patches (5, 10, and 20 microg/h) versus prolonged-release tramadol tablets (75, 100, 150, and 200 mg) in patients with chronic osteoarthritis pain: a 12-week, randomized, open-label, controlled, parallel-group noninferiority study. Clin Ther. 2009 Mar;31(3):503-13.
- Kean WF, Bouchard S, Roderich Gossen E. Women with pain due to osteoarthritis: the efficacy and safety of a once-daily formulation of tramadol. Pain Med. 2009 Sep;10(6):1001-11.
- Kleinert R, Lange C, Steup A, et al. Single dose analgesic efficacy of tapentadol in postsurgical dental pain: the results of a randomized, double-blind, placebo-controlled study. Anesth Analg. 2008;107:2048-55.
- Kress HG, Koch ED, Kosturski H, et al. Tapentadol prolonged release for managing moderate to severe, chronic malignant tumor-related pain. Pain Physician. 2014; 17:329-343.
- Lange B, Kuperwasser B, Okamoto A, et al. Efficacy and safety of tapentadol prolonged release for chronic osteoarthritis pain and low back pain. Adv Ther. 2010 Jun;27(6):381-99.
- Lee YK, Ko JS, Rhim HY, et al. Acute postoperative pain relief with immediate-release tapentadol: randomized, double-blind, placebo-controlled study conducted in South Korea. Curr Med Res Opin. 2014;30:2561-70.
- Leppert W, Luczak J. The role of tramadol in cancer pain treatment-a review. Support Care Cancer. 2005;13:5-17.
- Moulin DE, Boulanger A, Clark AJ, et al. Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. Pain Res Manag. 2014;19(6):328-35.
- Mullican WS, Lacy JR. Tramadol/acetaminophen combination tablets and codeine/acetaminophen combination capsules for the management of chronic pain: A comparative trial. Clin Ther. 2001;23:1429-45.
- NUCYNTA ER prescribing information. Janssen Pharmaceuticals, Inc. Titusville, NJ. December 2016.
- NUCYNTA (immediate-release oral tablet) prescribing information. Janssen Pharmaceuticals, Inc. Titusville, NJ. December 2016.
- NUCYNTA (oral solution) prescribing information. Janssen Pharmaceuticals. Titusville, NJ. December 2016.
- O'Donnell JB, Ekman EF, Spalding WM, et al. The effectiveness of a weak opioid medication versus a cyclo-oxygenase-2 (COX-2) selective non-steroidal anti-inflammatory drug in treating flare-up of chronic low-back pain: results from two randomized, double-blind, 6-week studies. J Int Med Res. 2009 Nov-Dec;37(6):1789-802.
- Park KS, Choi JJ, Kim WU, et al. The efficacy of tramadol/acetaminophen combination tablets (Ultracet®) as add-on and maintenance therapy in knee osteoarthritis pain inadequately controlled by nonsteroidal anti-inflammatory drug (NSAID). Clin Rheumatol. 2012 Feb;31(2):317-23.
- Ruoff GE, Rosenthal N, Jordan D, et al. Tramadol/acetaminophen combination tablets for the treatment of chronic lower back pain: A multicenter, randomized, double-blind, placebo-controlled outpatient study. Clin Ther. 2003;25:1123-41.
- Schwartz S, Etropolski M, Shapiro DY, et al. Safety and efficacy of tapentadol ER in patients with painful diabetic peripheral neuropathy: results of a randomized-withdrawal, placebo-controlled trial. Curr Med Res Opin. 2011 Jan;27(1):151-62.
- Stegman JU, Weber H, Steup A, et al. The efficacy and tolerability of multiple-dose tapentadol immediate release for the relief of acute pain following orthopedic (bunionectomy) surgery. Curr Med Res Opin. 2008;24(11):3185-96.
- Tramadol hydrochloride extended-release tablets prescribing information [generic RYZOLT]. Par Pharmaceuticals. Spring Valley, NY. January 2017.

- Tsutaoka BT, Ho RY, Fung SM, Kearney TE. Comparative toxicity of tapentadol and tramadol utilizing data reported to the National Poison Data System. Ann Pharmacother. 2015;49(12):1311-6.
- ULTRACET prescribing information. Janssen Pharmaceuticals, Inc. Titusville, NJ. December 2016.
- ULTRAM prescribing information. Janssen Pharmaceuticals, Inc. Titusville, NJ. December 2016.
- ULTRAM ER prescribing information. Janssen Pharmaceuticals, Inc. Titusville, NJ. December 2016.
- Vinik AI, Shapiro DY, Rauschkolb C, et al. A randomized withdrawal, placebo-controlled study evaluating the efficacy and tolerability of tapentadol extended release in patients with chronic painful diabetic peripheral neuropathy. Diabetes Care. 2014;37:2302-9.
- Wild JE, Grond S, Kuperwasser B, et al. Long-term safety and tolerability of tapentadol extended release for the management of chronic low back pain or osteoarthritis pain. Pain Pract. 2010 Sept-Oct;10(5):416-27.

Publication Date: March 24, 2017


Fee for Service Medicaid Population
Number of Members
250,000
200,000
150,000
100,000
50,000
0
201408
201410
201412
201502
201504
201506
201508
201510
201512
201602
201604
201606
201608
201610
201612
201702
201704
201706
Year / Month
Count Children
Count Total
Linear (Count Total)

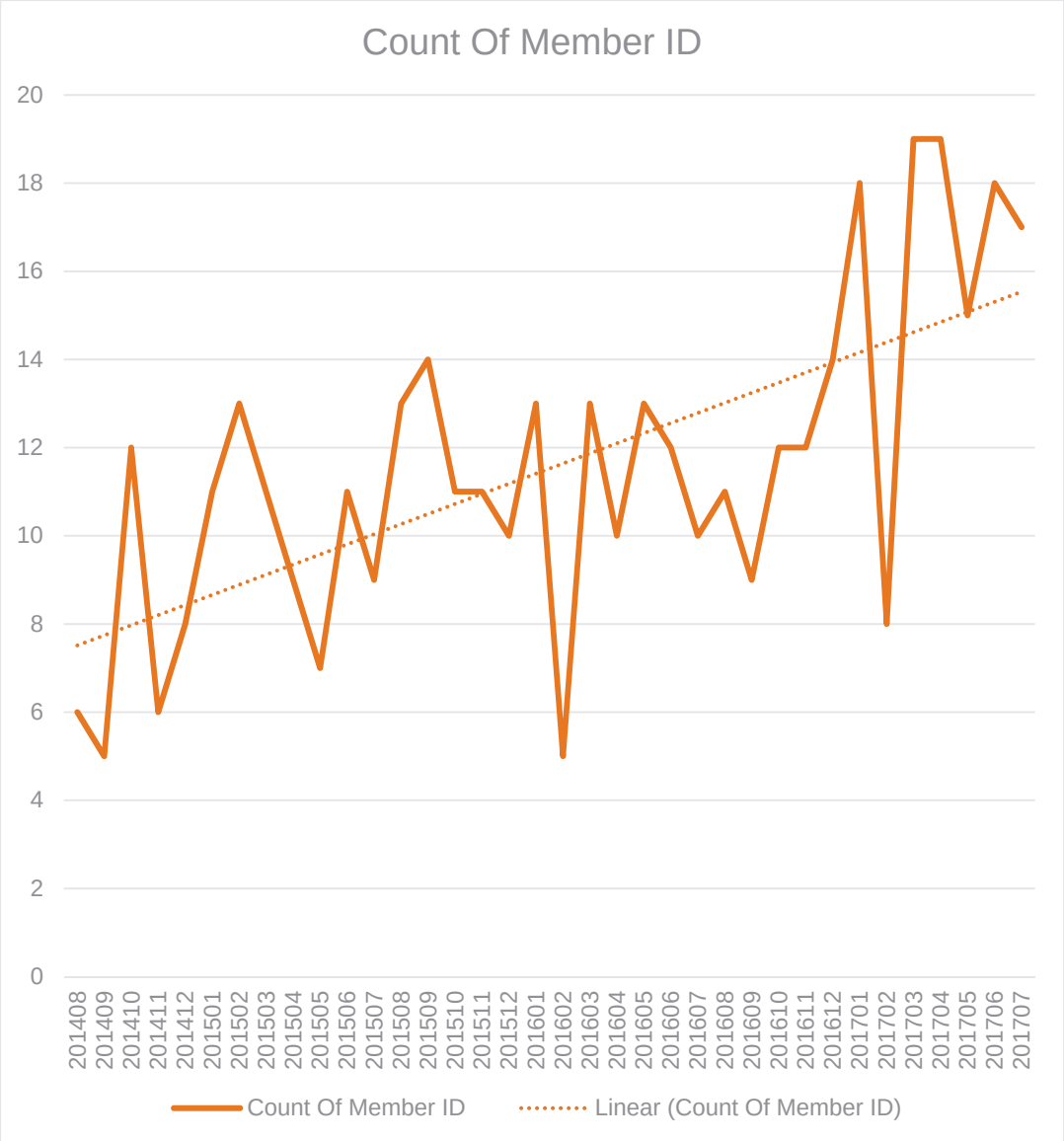
Nevada Medicaid

Psychotropic Medication Utilization in Children

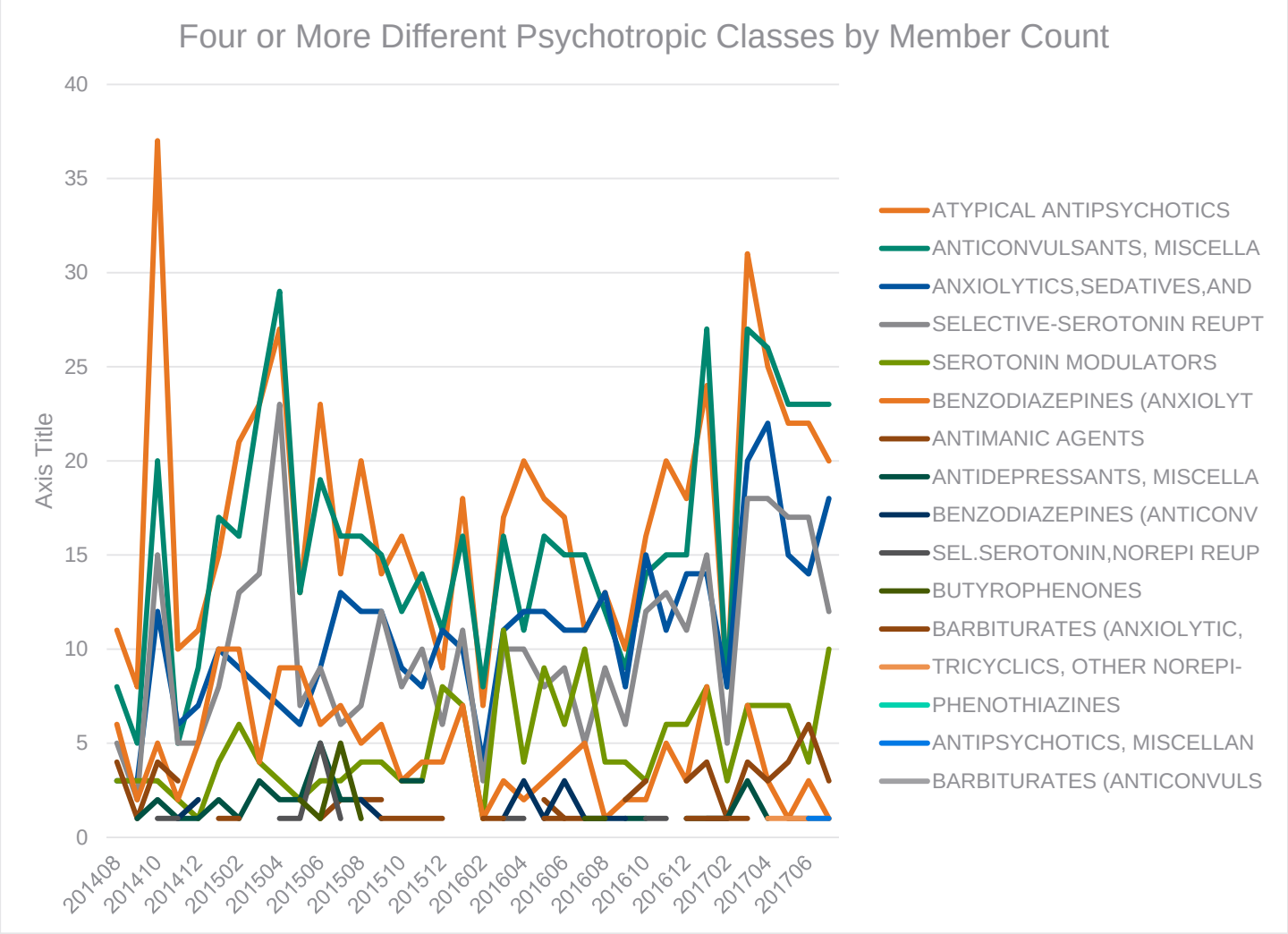
Four or more psychotropics require prior authorization

The chart below shows the count of recipients under the age of 18 receiving 4 our more psychotropic agents:

Year / Month Filled	Count Of Member ID
201408	6
201409	5
201410	12
201411	6
201412	8
201501	11
201502	13
201503	11
201504	9
201505	7
201506	11
201507	9
201508	13
201509	14
201510	11
201511	11
201512	10
201601	13
201602	5
201603	13
201604	10
201605	13
201606	12
201607	10
201608	11
201609	9
201610	12
201611	12
201612	14
201701	18
201702	8
201703	19
201704	19
201705	15
201706	18
201707	17



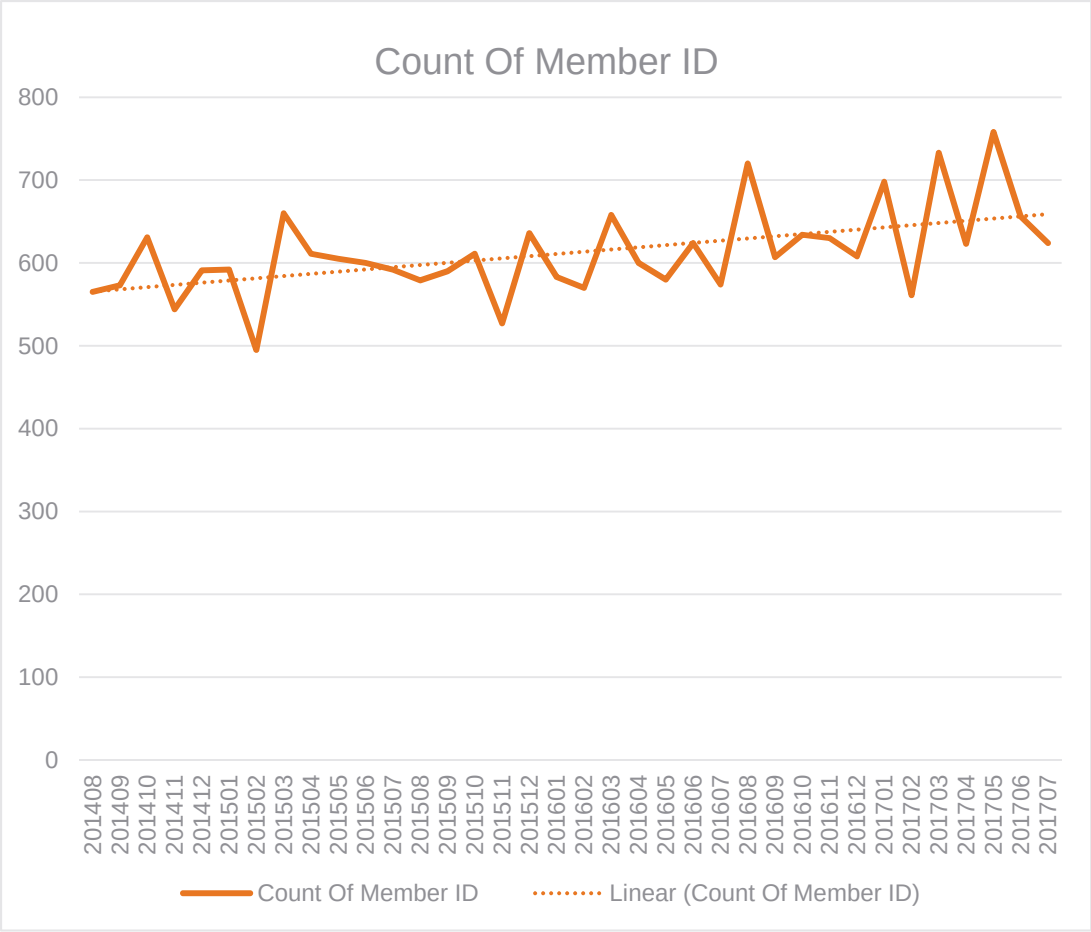
The chart below shows the number of recipients over the past year receiving four or more psychotropic medications.



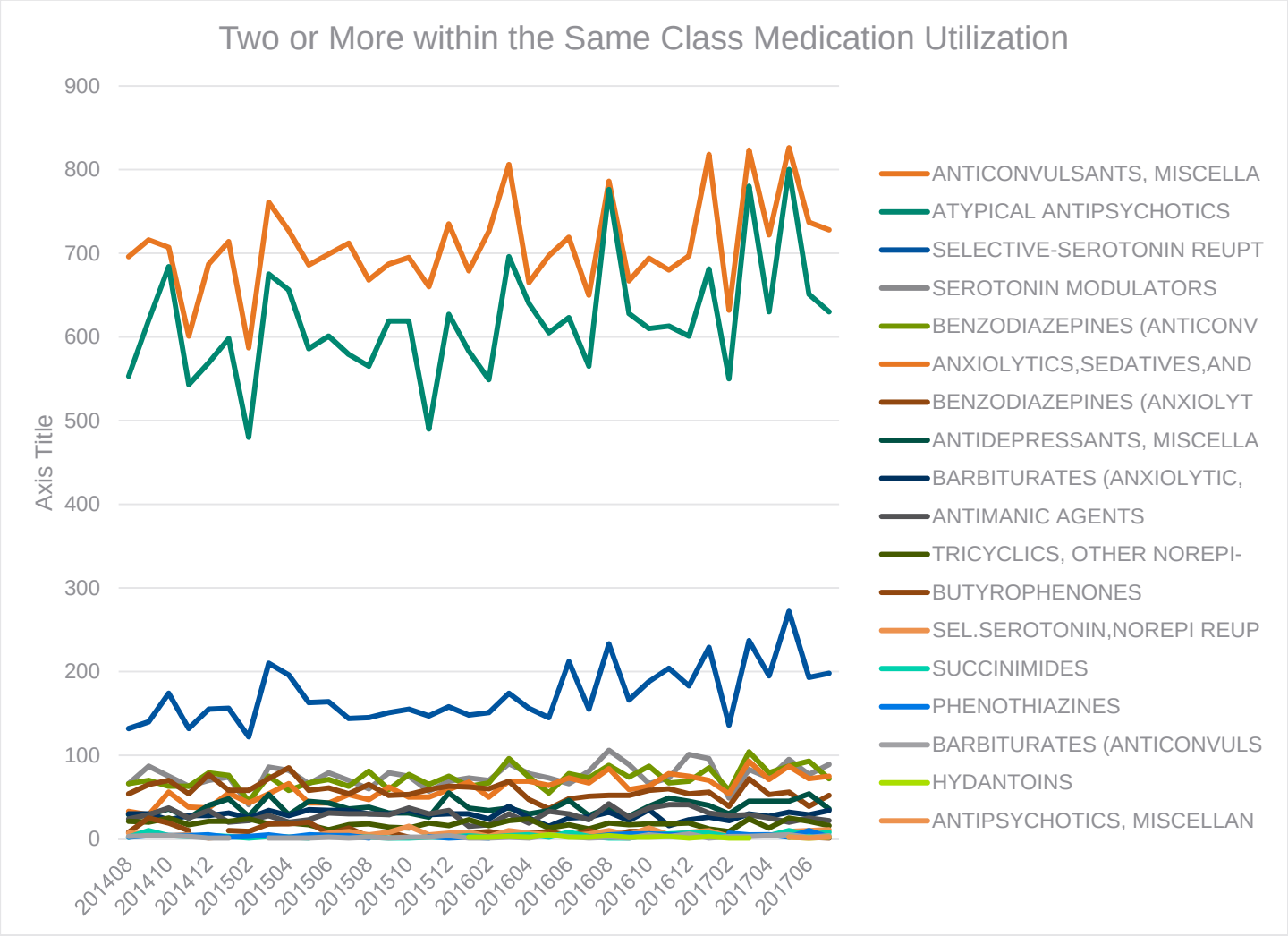
Two or more medications within the same class require prior authorization

The chart below shows the members under the age of 18 receiving more than one agent per class.

Year Month Filled	Count Of Member ID
201408	565
201409	573
201410	631
201411	544
201412	591
201501	592
201502	495
201503	660
201504	611
201505	605
201506	600
201507	592
201508	579
201509	590
201510	611
201511	527
201512	636
201601	583
201602	570
201603	658
201604	600
201605	580
201606	624
201607	574
201608	720
201609	607
201610	634
201611	630
201612	608
201701	698
201702	561
201703	733
201704	623
201705	758
201706	656
201707	624



The chart below shows the number of members under the age of 18 on multiple agents within the same class



Top 10 Members by Claim Count

August 2015 - July 2017

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
00000100108	**78**	**5333**	**2235**	**$ 3,192.63**
201508	**2**	**180**	**60**	**$ 100.07**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 41.94
MORPHINE SUL TAB 30MG ER	1	60	30	$ 58.13
201509	**4**	**231**	**97**	**$ 127.07**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 41.94
MORPHINE SUL TAB 15MG ER	1	30	30	$ 18.38
MORPHINE SUL TAB 30MG ER	1	60	30	$ 58.13
OXYCODONE TAB 5MG	1	21	7	$ 8.62
201510	**3**	**210**	**90**	**$ 118.45**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 41.94
MORPHINE SUL TAB 15MG ER	1	30	30	$ 18.38
MORPHINE SUL TAB 30MG ER	1	60	30	$ 58.13
201511	**3**	**210**	**90**	**$ 113.28**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 35.71
MORPHINE SUL TAB 15MG ER	1	30	30	$ 22.04
MORPHINE SUL TAB 30MG ER	1	60	30	$ 55.53
201512	**3**	**210**	**90**	**$ 111.00**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 33.91
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.79
MORPHINE SUL TAB 30MG ER	1	60	30	$ 55.30
201601	**3**	**210**	**90**	**$ 111.61**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 32.72
MORPHINE SUL TAB 15MG ER	1	30	30	$ 22.68
MORPHINE SUL TAB 30MG ER	1	60	30	$ 56.21
201602	**3**	**210**	**90**	**$ 110.25**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 33.90
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.89
MORPHINE SUL TAB 30MG ER	1	60	30	$ 54.46
201603	**3**	**210**	**90**	**$ 110.23**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 35.57
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.66
MORPHINE SUL TAB 30MG ER	1	60	30	$ 53.00
201604	**3**	**210**	**90**	**$ 109.43**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 32.85
MORPHINE SUL TAB 15MG ER	1	30	30	$ 22.04
MORPHINE SUL TAB 30MG ER	1	60	30	$ 54.54
201605	**3**	**210**	**90**	**$ 107.82**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 35.34
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.76
MORPHINE SUL TAB 30MG ER	1	60	30	$ 50.72

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201606	**6**	**420**	**180**	**$ 257.35**
HYDROCO/APAP TAB 10-325MG	1	120	30	$ 32.14
MORPHINE SUL TAB 15MG ER	2	60	60	$ 42.50
MORPHINE SUL TAB 30MG ER	2	120	60	$ 98.43
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 84.28
201607	**3**	**210**	**90**	**$ 149.58**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.18
MORPHINE SUL TAB 30MG ER	1	60	30	$ 48.04
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 80.36
201608	**3**	**210**	**90**	**$ 153.87**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.65
MORPHINE SUL TAB 30MG ER	1	60	30	$ 49.74
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 82.48
201609	**3**	**210**	**90**	**$ 153.87**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.65
MORPHINE SUL TAB 30MG ER	1	60	30	$ 49.74
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 82.48
201610	**3**	**210**	**90**	**$ 146.55**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 21.53
MORPHINE SUL TAB 30MG ER	1	60	30	$ 44.87
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 80.15
201611	**3**	**210**	**90**	**$ 144.92**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 20.32
MORPHINE SUL TAB 30MG ER	1	60	30	$ 44.87
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 79.73
201612	**3**	**210**	**90**	**$ 139.86**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 19.96
MORPHINE SUL TAB 30MG ER	1	60	30	$ 44.58
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 75.32
201701	**3**	**210**	**90**	**$ 136.60**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 20.07
MORPHINE SUL TAB 30MG ER	1	60	30	$ 44.87
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 71.66
201702	**3**	**210**	**90**	**$ 127.83**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 19.75
MORPHINE SUL TAB 30MG ER	1	60	30	$ 37.86
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 70.22
201703	**3**	**210**	**90**	**$ 128.03**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 19.34
MORPHINE SUL TAB 30MG ER	1	60	30	$ 37.86
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 70.83
201704	**5**	**282**	**93**	**$ 172.91**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 18.62

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
MORPHINE SUL TAB 30MG ER	1	60	30	$ 37.86
OXYCOD/APAP TAB 10-325MG	3	192	33	$ 116.43
201705	**4**	**230**	**95**	**$ 130.62**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 18.62
MORPHINE SUL TAB 30MG ER	1	60	30	$ 37.86
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 61.53
OXYCOD/APAP TAB 5-325MG	1	20	5	$ 12.61
201706	**4**	**330**	**120**	**$ 179.00**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 18.69
MORPHINE SUL TAB 30MG ER	1	60	30	$ 36.95
OXYCOD/APAP TAB 10-325MG	2	240	60	$ 123.36
201707	**2**	**90**	**60**	**$ 52.43**
MORPHINE SUL TAB 15MG ER	1	30	30	$ 18.06
MORPHINE SUL TAB 30MG ER	1	60	30	$ 34.37
11112116747	**95**	**2808**	**475**	**$ 2,926.52**
201508	**3**	**90**	**15**	**$ 57.15**
APAP/CODEINE TAB 300-30MG	1	30	5	$ 9.20
BUT/APAP/CAF CAP CODEINE	1	30	5	$ 38.04
OXYCOD/APAP TAB 5-325MG	1	30	5	$ 9.91
201509	**1**	**30**	**5**	**$ 38.04**
BUT/APAP/CAF CAP CODEINE	1	30	5	$ 38.04
201510	**2**	**60**	**10**	**$ 79.48**
BUT/APAP/CAF CAP CODEINE	2	60	10	$ 79.48
201511	**2**	**60**	**10**	**$ 81.97**
BUT/APAP/CAF CAP CODEINE	2	60	10	$ 81.97
201512	**3**	**90**	**15**	**$ 122.37**
BUT/APAP/CAF CAP CODEINE	3	90	15	$ 122.37
201601	**1**	**10**	**3**	**$ 8.83**
HYDROCO/APAP TAB 5-325MG	1	10	3	$ 8.83
201602	**1**	**30**	**5**	**$ 42.08**
BUT/APAP/CAF CAP CODEINE	1	30	5	$ 42.08
201603	**2**	**60**	**10**	**$ 82.70**
BUT/APAP/CAF CAP CODEINE	2	60	10	$ 82.70
201604	**1**	**30**	**5**	**$ 41.50**
BUT/APAP/CAF CAP CODEINE	1	30	5	$ 41.50
201605	**2**	**60**	**10**	**$ 82.18**
BUT/APAP/CAF CAP CODEINE	2	60	10	$ 82.18
201606	**1**	**30**	**5**	**$ 41.38**
BUT/APAP/CAF CAP CODEINE	1	30	5	$ 41.38
201607	**2**	**60**	**10**	**$ 82.76**
BUT/APAP/CAF CAP CODEINE	2	60	10	$ 82.76
201608	**2**	**60**	**10**	**$ 82.92**
BUT/APAP/CAF CAP CODEINE	2	60	10	$ 82.92

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201609	**3**	**90**	**15**	**$ 124.85**
BUT/APAP/CAF CAP CODEINE	3	90	15	$ 124.85
201610	**4**	**142**	**27**	**$ 84.79**
APAP/CODEINE TAB 300-30MG	1	30	8	$ 14.61
BUT/APAP/CAF CAP CODEINE	1	30	5	$ 41.58
OXYCOD/APAP TAB 5-325MG	2	82	14	$ 28.60
201611	**7**	**166**	**30**	**$ 197.59**
APAP/CODEINE TAB 300-30MG	1	20	4	$ 13.13
APAP/CODEINE TAB 300-60MG	1	20	4	$ 11.31
BUT/APAP/CAF CAP CODEINE	4	120	20	$ 167.18
HYDROCO/APAP TAB 5-325MG	1	6	2	$ 5.97
201612	**4**	**120**	**20**	**$ 142.26**
APAP/CODEINE TAB 300-60MG	1	30	5	$ 17.12
BUT/APAP/CAF CAP CODEINE	3	90	15	$ 125.14
201701	**4**	**120**	**20**	**$ 92.68**
APAP/CODEINE TAB 300-60MG	3	90	15	$ 51.20
BUT/APAP/CAF CAP CODEINE	1	30	5	$ 41.48
201702	**8**	**240**	**40**	**$ 233.30**
APAP/CODEINE TAB 300-60MG	4	120	20	$ 67.84
BUT/APAP/CAF CAP CODEINE	4	120	20	$ 165.46
201703	**9**	**270**	**45**	**$ 249.03**
APAP/CODEINE TAB 300-60MG	5	150	25	$ 84.95
BUT/APAP/CAF CAP CODEINE	4	120	20	$ 164.08
201704	**9**	**270**	**45**	**$ 276.36**
APAP/CODEINE TAB 300-60MG	4	120	20	$ 67.77
BUT/APAP/CAF CAP CODEINE	5	150	25	$ 208.59
201705	**6**	**180**	**30**	**$ 169.95**
APAP/CODEINE TAB 300-60MG	3	90	15	$ 49.14
BUT/APAP/CAF CAP CODEINE	3	90	15	$ 120.81
201706	**8**	**240**	**40**	**$ 228.10**
APAP/CODEINE TAB 300-60MG	4	120	20	$ 66.76
BUT/APAP/CAF CAP CODEINE	4	120	20	$ 161.34
201707	**10**	**300**	**50**	**$ 284.25**
APAP/CODEINE TAB 300-60MG	5	150	25	$ 84.15
BUT/APAP/CAF CAP CODEINE	5	150	25	$ 200.10
11113147562	**78**	**6477**	**2313**	**$ 4,862.60**
201508	**4**	**480**	**120**	**$ 346.38**
HYDROCO/APAP TAB 10-325MG	1	240	30	$ 79.13
MORPHINE SUL TAB 60MG ER	2	120	60	$ 191.48
OXYCODONE TAB 20MG	1	120	30	$ 75.77
201509	**3**	**270**	**87**	**$ 275.13**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 58.13
MORPHINE SUL TAB 60MG ER	1	90	27	$ 141.23

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 20MG	1	120	30	$ 75.77
201510	**4**	**372**	**108**	**$ 289.90**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 58.13
MORPHINE SUL TAB 60MG ER	1	72	18	$ 98.61
OXYCODONE TAB 20MG	2	240	60	$ 133.16
201511	**3**	**240**	**90**	**$ 231.86**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 128.50
MORPHINE SUL TAB 30MG ER	1	60	30	$ 55.53
OXYCODONE TAB 20MG	1	120	30	$ 47.83
201512	**2**	**180**	**60**	**$ 179.54**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 128.50
OXYCODONE TAB 30MG	1	120	30	$ 51.04
201601	**3**	**300**	**90**	**$ 239.71**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 128.50
OXYCODONE TAB 30MG	2	240	60	$ 111.21
201602	**3**	**240**	**90**	**$ 196.55**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 54.46
MORPHINE SUL TAB 60MG ER	1	60	30	$ 88.37
OXYCODONE TAB 30MG	1	120	30	$ 53.72
201603	**5**	**360**	**150**	**$ 336.44**
MORPHINE SUL TAB 30MG ER	2	120	60	$ 107.54
MORPHINE SUL TAB 60MG ER	2	120	60	$ 176.74
OXYCODONE TAB 30MG	1	120	30	$ 52.16
201604	**3**	**240**	**90**	**$ 194.88**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 50.72
MORPHINE SUL TAB 60MG ER	1	60	30	$ 88.37
OXYCODONE TAB 30MG	1	120	30	$ 55.79
201605	**3**	**240**	**90**	**$ 192.29**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 50.49
MORPHINE SUL TAB 60MG ER	1	60	30	$ 88.37
OXYCODONE TAB 30MG	1	120	30	$ 53.43
201606	**3**	**240**	**90**	**$ 192.29**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 50.49
MORPHINE SUL TAB 60MG ER	1	60	30	$ 88.37
OXYCODONE TAB 30MG	1	120	30	$ 53.43
201607	**3**	**240**	**90**	**$ 182.27**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 47.94
MORPHINE SUL TAB 60MG ER	1	60	30	$ 78.22
OXYCODONE TAB 30MG	1	120	30	$ 56.11
201608	**3**	**240**	**90**	**$ 179.95**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 48.04
MORPHINE SUL TAB 60MG ER	1	60	30	$ 78.22
OXYCODONE TAB 30MG	1	120	30	$ 53.69

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201609	**3**	**240**	**90**	**$ 181.07**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 49.74
MORPHINE SUL TAB 60MG ER	1	60	30	$ 78.22
OXYCODONE TAB 30MG	1	120	30	$ 53.11
201610	**3**	**240**	**90**	**$ 175.96**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 49.36
MORPHINE SUL TAB 60MG ER	1	60	30	$ 78.22
OXYCODONE TAB 30MG	1	120	30	$ 48.38
201611	**3**	**240**	**90**	**$ 176.94**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 44.87
MORPHINE SUL TAB 60MG ER	1	60	30	$ 78.22
OXYCODONE TAB 30MG	1	120	30	$ 53.85
201612	**3**	**240**	**90**	**$ 171.32**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 44.58
MORPHINE SUL TAB 60MG ER	1	60	30	$ 78.22
OXYCODONE TAB 30MG	1	120	30	$ 48.52
201701	**3**	**240**	**90**	**$ 170.62**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 44.58
MORPHINE SUL TAB 60MG ER	1	60	30	$ 74.61
OXYCODONE TAB 30MG	1	120	30	$ 51.43
201702	**6**	**480**	**180**	**$ 298.63**
MORPHINE SUL TAB 30MG ER	2	120	60	$ 75.72
MORPHINE SUL TAB 60MG ER	2	120	60	$ 124.91
OXYCODONE TAB 30MG	2	240	60	$ 98.00
201703	**3**	**225**	**86**	**$ 146.06**
MORPHINE SUL TAB 30MG ER	1	60	30	$ 37.86
MORPHINE SUL TAB 60MG ER	1	60	30	$ 62.75
OXYCODONE TAB 30MG	1	105	26	$ 45.45
201704	**3**	**225**	**86**	**$ 130.70**
MORPHINE SUL TAB 15MG ER	1	60	30	$ 27.07
MORPHINE SUL TAB 60MG ER	1	60	30	$ 61.96
OXYCODONE TAB 30MG	1	105	26	$ 41.67
201705	**3**	**225**	**86**	**$ 122.51**
MORPHINE SUL TAB 15MG ER	1	60	30	$ 27.20
MORPHINE SUL TAB 60MG ER	1	60	30	$ 53.64
OXYCODONE TAB 30MG	1	105	26	$ 41.67
201706	**3**	**240**	**90**	**$ 130.09**
MORPHINE SUL TAB 15MG ER	1	60	30	$ 27.20
MORPHINE SUL TAB 60MG ER	1	60	30	$ 54.11
OXYCODONE TAB 30MG	1	120	30	$ 48.78
201707	**3**	**240**	**90**	**$ 121.51**
MORPHINE SUL TAB 15MG ER	1	60	30	$ 25.96
MORPHINE SUL TAB 60MG ER	1	60	30	$ 49.97

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 30MG	1	120	30	$ 45.58
11114292001	**117**	**7620**	**1291**	**$ 3,671.00**
201508	**5**	**195**	**41**	**$ 99.43**
METHADONE TAB 10MG	1	120	30	$ 20.01
OXYCOD/APAP TAB 10-325MG	4	75	11	$ 79.42
201509	**4**	**240**	**48**	**$ 134.01**
METHADONE TAB 10MG	1	120	30	$ 23.10
OXYCOD/APAP TAB 10-325MG	3	120	18	$ 110.91
201510	**5**	**280**	**55**	**$ 170.98**
METHADONE TAB 10MG	1	120	30	$ 23.10
OXYCOD/APAP TAB 10-325MG	4	160	25	$ 147.88
201511	**6**	**275**	**55**	**$ 177.24**
METHADONE TAB 10MG	1	120	30	$ 28.51
OXYCOD/APAP TAB 10-325MG	5	155	25	$ 148.73
201512	**6**	**280**	**45**	**$ 143.63**
METHADONE TAB 10MG	1	180	30	$ 31.67
OXYCOD/APAP TAB 10-325MG	5	100	15	$ 111.96
201601	**5**	**260**	**43**	**$ 131.14**
METHADONE TAB 10MG	1	180	30	$ 37.67
OXYCOD/APAP TAB 10-325MG	4	80	13	$ 93.47
201602	**6**	**280**	**45**	**$ 151.05**
METHADONE TAB 10MG	1	180	30	$ 36.98
OXYCOD/APAP TAB 10-325MG	5	100	15	$ 114.07
201603	**5**	**260**	**42**	**$ 125.45**
METHADONE TAB 10MG	1	180	30	$ 31.67
OXYCOD/APAP TAB 10-325MG	4	80	12	$ 93.78
201604	**6**	**280**	**47**	**$ 149.00**
METHADONE TAB 10MG	1	180	30	$ 31.67
OXYCOD/APAP TAB 10-325MG	5	100	17	$ 117.33
201605	**6**	**380**	**64**	**$ 212.35**
METHADONE TAB 10MG	1	180	30	$ 31.67
OXYCOD/APAP TAB 10-325MG	5	200	34	$ 180.68
201606	**4**	**300**	**49**	**$ 141.28**
METHADONE TAB 10MG	1	180	30	$ 33.70
OXYCOD/APAP TAB 10-325MG	3	120	19	$ 107.58
201607	**6**	**380**	**64**	**$ 208.87**
METHADONE TAB 10MG	1	180	30	$ 35.82
OXYCOD/APAP TAB 10-325MG	5	200	34	$ 173.05
201608	**5**	**340**	**57**	**$ 167.35**
METHADONE TAB 10MG	1	180	30	$ 31.67
OXYCOD/APAP TAB 10-325MG	4	160	27	$ 135.68
201609	**5**	**340**	**58**	**$ 169.26**
METHADONE TAB 10MG	1	180	30	$ 32.95

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCOD/APAP TAB 10-325MG	4	160	28	$ 136.31
201610	**6**	**380**	**63**	**$ 187.55**
METHADONE TAB 10MG	1	180	30	$ 31.67
OXYCOD/APAP TAB 10-325MG	5	200	33	$ 155.88
201611	**6**	**378**	**61**	**$ 194.45**
METHADONE TAB 10MG	1	180	30	$ 31.03
OXYCOD/APAP TAB 10-325MG	5	198	31	$ 163.42
201612	**3**	**366**	**61**	**$ 151.16**
METHADONE TAB 10MG	1	180	30	$ 31.67
OXYCOD/APAP TAB 10-325MG	2	186	31	$ 119.49
201701	**4**	**360**	**60**	**$ 153.28**
METHADONE TAB 10MG	1	180	30	$ 31.24
OXYCOD/APAP TAB 10-325MG	3	180	30	$ 122.04
201702	**4**	**360**	**60**	**$ 149.22**
METHADONE TAB 10MG	1	180	30	$ 28.62
OXYCOD/APAP TAB 10-325MG	3	180	30	$ 120.60
201703	**6**	**446**	**73**	**$ 189.52**
METHADONE TAB 10MG	2	222	37	$ 39.66
OXYCOD/APAP TAB 10-325MG	4	224	36	$ 149.86
201704	**2**	**140**	**22**	**$ 81.63**
OXYCOD/APAP TAB 10-325MG	2	140	22	$ 81.63
201705	**4**	**390**	**63**	**$ 112.86**
METHADONE TAB 10MG	1	180	30	$ 28.62
OXYCOD/APAP TAB 10-325MG	1	70	11	$ 40.52
OXYCODONE TAB 10MG	2	140	22	$ 43.72
201706	**4**	**390**	**63**	**$ 153.85**
METHADONE TAB 10MG	1	180	30	$ 28.62
OXYCOD/APAP TAB 10-325MG	3	210	33	$ 125.23
201707	**4**	**320**	**52**	**$ 116.44**
METHADONE TAB 10MG	2	180	30	$ 36.44
OXYCOD/APAP TAB 10-325MG	2	140	22	$ 80.00
22222264138	**120**	**1839**	**1409**	**$ 17,102.82**
201511	**4**	**75**	**45**	**$ 652.34**
SUBOXONE MIS 12-3MG	1	15	15	$ 213.31
SUBOXONE MIS 8-2MG	3	60	30	$ 439.03
201512	**4**	**100**	**65**	**$ 923.57**
SUBOXONE MIS 12-3MG	2	30	30	$ 426.62
SUBOXONE MIS 8-2MG	2	70	35	$ 496.95
201601	**3**	**75**	**45**	**$ 672.73**
SUBOXONE MIS 12-3MG	1	15	15	$ 223.46
SUBOXONE MIS 8-2MG	2	60	30	$ 449.27
201602	**3**	**72**	**51**	**$ 757.34**
SUBOXONE MIS 12-3MG	1	30	30	$ 436.75

Member		Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
SUBOXONE	MIS 8-2MG	2	42	21	$ 320.59
201603		**3**	**66**	**48**	**$ 714.45**
SUBOXONE	MIS 12-3MG	1	30	30	$ 436.75
SUBOXONE	MIS 8-2MG	2	36	18	$ 277.70
201604		**7**	**96**	**63**	**$ 969.59**
SUBOXONE	MIS 12-3MG	1	30	30	$ 436.75
SUBOXONE	MIS 8-2MG	6	66	33	$ 532.84
201605		**7**	**130**	**66**	**$ 846.00**
HYDROMORPHON	TAB 4MG	2	52	12	$ 25.42
SUBOXONE	MIS 12-3MG	1	30	30	$ 436.75
SUBOXONE	MIS 8-2MG	4	48	24	$ 383.83
201606		**6**	**129**	**72**	**$ 763.01**
HYDROMORPHON	TAB 4MG	1	40	7	$ 14.08
SUBOXONE	MIS 12-3MG	1	15	15	$ 223.46
SUBOXONE	MIS 2-0.5MG	1	14	14	$ 66.03
SUBOXONE	MIS 8-2MG	3	60	36	$ 459.44
201607		**3**	**63**	**54**	**$ 586.95**
SUBOXONE	MIS 12-3MG	1	15	30	$ 223.46
SUBOXONE	MIS 8-2MG	2	48	24	$ 363.49
201608		**7**	**117**	**102**	**$ 880.99**
SUBOXONE	MIS 12-3MG	1	15	30	$ 223.46
SUBOXONE	MIS 2-0.5MG	3	42	42	$ 198.09
SUBOXONE	MIS 8-2MG	3	60	30	$ 459.44
201609		**8**	**122**	**90**	**$ 1,077.20**
SUBOXONE	MIS 12-3MG	1	30	30	$ 436.75
SUBOXONE	MIS 2-0.5MG	2	28	28	$ 132.06
SUBOXONE	MIS 8-2MG	5	64	32	$ 508.39
201610		**8**	**107**	**90**	**$ 863.82**
SUBOXONE	MIS 12-3MG	1	15	30	$ 223.46
SUBOXONE	MIS 2-0.5MG	2	28	28	$ 132.06
SUBOXONE	MIS 8-2MG	5	64	32	$ 508.30
201611		**9**	**122**	**98**	**$ 992.35**
SUBOXONE	MIS 12-3MG	2	17	31	$ 262.59
SUBOXONE	MIS 2-0.5MG	2	29	29	$ 136.05
SUBOXONE	MIS 8-2MG	5	76	38	$ 593.71
201612		**9**	**103**	**54**	**$ 978.75**
SUBOXONE	MIS 12-3MG	1	28	9	$ 409.17
SUBOXONE	MIS 2-0.5MG	1	15	15	$ 69.83
SUBOXONE	MIS 8-2MG	7	60	30	$ 499.75
201701		**6**	**83**	**87**	**$ 819.60**
SUBOXONE	MIS 12-3MG	2	30	38	$ 447.84
SUBOXONE	MIS 2-0.5MG	1	15	15	$ 69.83
SUBOXONE	MIS 8-2MG	3	38	34	$ 301.93

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201702	**4**	**60**	**60**	**$ 713.20**
SUBOXONE MIS 12-3MG	2	30	30	$ 468.36
SUBOXONE MIS 8-2MG	2	30	30	$ 244.84
201703	**5**	**75**	**75**	**$ 947.38**
SUBOXONE MIS 12-3MG	3	45	45	$ 702.54
SUBOXONE MIS 8-2MG	2	30	30	$ 244.84
201704	**5**	**56**	**56**	**$ 694.01**
SUBOXONE MIS 12-3MG	3	30	30	$ 479.36
SUBOXONE MIS 8-2MG	2	26	26	$ 214.65
201705	**6**	**62**	**62**	**$ 681.36**
SUBOXONE MIS 12-3MG	3	21	21	$ 344.99
SUBOXONE MIS 8-2MG	3	41	41	$ 336.37
201706	**7**	**69**	**69**	**$ 879.03**
SUBOXONE MIS 12-3MG	5	39	39	$ 634.89
SUBOXONE MIS 8-2MG	2	30	30	$ 244.14
201707	**6**	**57**	**57**	**$ 689.15**
SUBOXONE MIS 12-3MG	4	27	27	$ 445.01
SUBOXONE MIS 8-2MG	2	30	30	$ 244.14
27483344445	**78**	**13409**	**2138**	**$ 14,769.05**
201508	**1**	**60**	**30**	**$ 999.26**
NUCYNTA ER TAB 250MG	1	60	30	$ 999.26
201509	**3**	**480**	**90**	**$ 1,210.70**
MORPHINE SUL TAB 30MG	1	240	30	$ 61.75
NUCYNTA ER TAB 250MG	1	60	30	$ 999.26
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 149.69
201510	**2**	**420**	**43**	**$ 211.44**
MORPHINE SUL TAB 30MG	1	240	13	$ 61.75
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 149.69
201511	**2**	**240**	**60**	**$ 1,071.21**
NUCYNTA ER TAB 250MG	1	60	30	$ 953.91
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 117.30
201512	**3**	**480**	**85**	**$ 1,137.25**
MORPHINE SUL TAB 30MG	1	240	30	$ 66.04
NUCYNTA ER TAB 250MG	1	60	30	$ 953.91
OXYCOD/APAP TAB 10-325MG	1	180	25	$ 117.30
201601	**3**	**480**	**85**	**$ 1,233.84**
MORPHINE SUL TAB 30MG	1	240	30	$ 66.04
NUCYNTA ER TAB 250MG	1	60	30	$ 1,047.31
OXYCOD/APAP TAB 10-325MG	1	180	25	$ 120.49
201602	**3**	**480**	**90**	**$ 1,242.51**
ENDOCET TAB 10-325MG	1	180	30	$ 129.16
MORPHINE SUL TAB 30MG	1	240	30	$ 66.04
NUCYNTA ER TAB 250MG	1	60	30	$ 1,047.31

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201603	**4**	**660**	**105**	**$ 270.91**
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 131.12
TRAMADL/APAP TAB 37.5-325	1	120	15	$ 33.78
TRAMADOL HCL TAB 50MG	1	120	30	$ 13.19
201604	**4**	**690**	**110**	**$ 601.87**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 363.23
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 131.12
TRAMADOL HCL TAB 50MG	1	180	30	$ 14.70
201605	**4**	**690**	**110**	**$ 594.18**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 359.48
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 127.85
TRAMADOL HCL TAB 50MG	1	180	30	$ 14.03
201606	**6**	**1020**	**153**	**$ 1,102.83**
MORPHINE SUL TAB 200MG ER	2	180	60	$ 777.39
MORPHINE SUL TAB 30MG	2	480	43	$ 185.64
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 125.80
TRAMADOL HCL TAB 50MG	1	180	30	$ 14.00
201607	**3**	**510**	**90**	**$ 528.51**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 391.58
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 121.34
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.59
201608	**3**	**660**	**90**	**$ 223.76**
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 115.45
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.49
201609	**4**	**750**	**110**	**$ 566.06**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 339.47
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 118.63
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.14
201610	**5**	**989**	**122**	**$ 604.60**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 366.41
MORPHINE SUL TAB 30MG	1	239	12	$ 92.47
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 115.15
TRAMADOL HCL TAB 50MG	2	480	60	$ 30.57
201611	**4**	**750**	**120**	**$ 549.02**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 326.35
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 114.51
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.34

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201612	**4**	**750**	**120**	**$ 522.66**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 306.80
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 107.89
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.15
201701	**4**	**750**	**117**	**$ 490.51**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 282.26
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	27	$ 100.25
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.18
201702	**4**	**750**	**98**	**$ 490.51**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 282.26
MORPHINE SUL TAB 30MG	1	240	13	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	25	$ 100.25
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.18
201704	**2**	**240**	**60**	**$ 171.63**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72
MORPHINE SUL TAB 30MG	1	150	30	$ 48.91
201705	**3**	**540**	**60**	**$ 221.57**
MORPHINE SUL TAB 30MG	1	240	30	$ 72.16
OXYCOD/APAP TAB 10-325MG	2	300	30	$ 149.41
201706	**3**	**450**	**80**	**$ 320.69**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 261.74
MORPHINE SUL TAB 30MG	1	180	20	$ 45.04
TRAMADOL HCL TAB 50MG	1	180	30	$ 13.91
201707	**4**	**570**	**110**	**$ 403.53**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 283.61
MORPHINE SUL TAB 30MG	1	180	30	$ 45.04
OXYCOD/APAP TAB 10-325MG	1	120	20	$ 61.15
TRAMADOL HCL TAB 50MG	1	180	30	$ 13.73
44447412422	**81**	**5443**	**935**	**$ 2,259.16**
201508	**2**	**216**	**36**	**$ 96.99**
HYDROCO/APAP TAB 10-325MG	1	36	6	$ 15.91
OXYCODONE TAB 30MG	1	180	30	$ 81.08
201509	**2**	**216**	**36**	**$ 96.99**
HYDROCO/APAP TAB 10-325MG	1	36	6	$ 15.91
OXYCODONE TAB 30MG	1	180	30	$ 81.08
201510	**2**	**216**	**36**	**$ 96.99**
HYDROCO/APAP TAB 10-325MG	1	36	6	$ 15.91
OXYCODONE TAB 30MG	1	180	30	$ 81.08
201511	**6**	**324**	**57**	**$ 149.29**
HYDROCO/APAP TAB 10-325MG	2	72	13	$ 35.12
OXYCODONE TAB 20MG	1	32	6	$ 20.21

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 30MG	1	180	30	$ 72.66
TRAMADOL HCL TAB 50MG	2	40	8	$ 21.30
201512	**3**	**396**	**64**	**$ 169.07**
HYDROCO/APAP TAB 10-325MG	1	36	4	$ 17.29
OXYCODONE TAB 30MG	2	360	60	$ 151.78
201601	**1**	**150**	**25**	**$ 65.33**
OXYCODONE TAB 30MG	1	150	25	$ 65.33
201602	**2**	**156**	**36**	**$ 71.51**
HYDROCO/APAP TAB 10-325MG	1	36	6	$ 17.79
OXYCODONE TAB 30MG	1	120	30	$ 53.72
201603	**2**	**156**	**25**	**$ 71.51**
HYDROCO/APAP TAB 10-325MG	1	36	5	$ 17.79
OXYCODONE TAB 30MG	1	120	20	$ 53.72
201604	**2**	**141**	**23**	**$ 63.88**
HYDROCO/APAP TAB 10-325MG	1	36	5	$ 16.97
OXYCODONE TAB 30MG	1	105	18	$ 46.91
201605	**4**	**312**	**50**	**$ 144.66**
HYDROCO/APAP TAB 10-325MG	2	72	10	$ 35.44
OXYCODONE TAB 30MG	2	240	40	$ 109.22
201606	**2**	**156**	**25**	**$ 70.19**
HYDROCO/APAP TAB 10-325MG	1	36	5	$ 16.76
OXYCODONE TAB 30MG	1	120	20	$ 53.43
201607	**4**	**312**	**50**	**$ 143.54**
HYDROCO/APAP TAB 10-325MG	2	72	10	$ 33.74
OXYCODONE TAB 30MG	2	240	40	$ 109.80
201608	**2**	**156**	**25**	**$ 70.78**
HYDROCO/APAP TAB 10-325MG	1	36	5	$ 17.09
OXYCODONE TAB 30MG	1	120	20	$ 53.69
201609	**3**	**192**	**30**	**$ 82.84**
HYDROCO/APAP TAB 10-325MG	2	72	10	$ 34.46
OXYCODONE TAB 30MG	1	120	20	$ 48.38
201610	**4**	**282**	**44**	**$ 126.10**
HYDROCO/APAP TAB 10-325MG	2	72	10	$ 33.64
OXYCODONE TAB 30MG	2	210	34	$ 92.46
201611	**2**	**126**	**20**	**$ 59.23**
HYDROCO/APAP TAB 10-325MG	1	36	5	$ 16.30
OXYCODONE TAB 30MG	1	90	15	$ 42.93
201612	**2**	**126**	**20**	**$ 55.57**
HYDROCO/APAP TAB 10-325MG	1	36	5	$ 16.64
OXYCODONE TAB 30MG	1	90	15	$ 38.93
201701	**5**	**390**	**42**	**$ 119.08**
HYDROCO/APAP TAB 10-325MG	2	72	10	$ 32.70
OXYCODONE TAB 15MG	3	318	32	$ 86.38

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201702	**4**	**202**	**25**	**$ 76.64**
HYDROCO/APAP TAB 10-325MG	2	72	10	$ 32.60
OXYCODONE TAB 15MG	2	130	15	$ 44.04
201703	**7**	**312**	**65**	**$ 107.67**
HYDROCO/APAP TAB 10-325MG	1	24	5	$ 14.19
OXYCODONE TAB 15MG	3	180	42	$ 60.66
TRAMADOL HCL TAB 50MG	3	108	18	$ 32.82
201704	**3**	**204**	**52**	**$ 56.21**
HYDROCO/APAP TAB 10-325MG	1	48	16	$ 18.22
OXYCODONE TAB 15MG	1	120	30	$ 27.03
TRAMADOL HCL TAB 50MG	1	36	6	$ 10.96
201705	**3**	**108**	**30**	**$ 46.89**
HYDROCO/APAP TAB 10-325MG	2	48	16	$ 28.29
OXYCODONE TAB 15MG	1	60	14	$ 18.60
201706	**8**	**342**	**73**	**$ 122.23**
HYDROCO/APAP TAB 10-325MG	4	102	20	$ 57.62
OXYCODONE TAB 15MG	3	180	38	$ 53.19
TRAMADOL HCL TAB 50MG	1	60	15	$ 11.42
201707	**6**	**252**	**46**	**$ 95.97**
HYDROCO/APAP TAB 10-325MG	3	72	14	$ 41.61
OXYCODONE TAB 15MG	3	180	32	$ 54.36
46770922223	**101**	**6171**	**1269**	**$ 2,948.29**
201508	**3**	**340**	**36**	**$ 199.46**
OXYCODONE TAB 15MG	1	60	5	$ 33.14
OXYCODONE TAB 20MG	1	80	14	$ 76.76
OXYCODONE TAB 30MG	1	200	17	$ 89.56
201509	**6**	**580**	**52**	**$ 283.30**
OXYCODONE TAB 15MG	3	180	17	$ 99.42
OXYCODONE TAB 30MG	3	400	35	$ 183.88
201510	**5**	**345**	**62**	**$ 177.18**
OXYCODONE TAB 15MG	3	145	34	$ 82.86
OXYCODONE TAB 30MG	2	200	28	$ 94.32
201511	**3**	**220**	**47**	**$ 89.80**
OXYCODONE TAB 15MG	2	120	30	$ 44.91
OXYCODONE TAB 30MG	1	100	17	$ 44.89
201512	**4**	**280**	**57**	**$ 118.96**
OXYCODONE TAB 15MG	2	120	30	$ 45.20
OXYCODONE TAB 20MG	1	40	7	$ 22.72
OXYCODONE TAB 30MG	1	120	20	$ 51.04
201601	**5**	**351**	**47**	**$ 175.60**
OXYCODONE TAB 15MG	1	60	15	$ 24.00
OXYCODONE TAB 30MG	4	291	32	$ 151.60
201602	**3**	**294**	**59**	**$ 117.20**

Member		Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE	TAB 15MG	1	120	30	$ 33.13
OXYCODONE	TAB 20MG	1	24	4	$ 18.74
OXYCODONE	TAB 30MG	1	150	25	$ 65.33
201603		**6**	**363**	**63**	**$ 172.18**
OXYCODONE	TAB 15MG	2	120	30	$ 43.44
OXYCODONE	TAB 20MG	1	18	6	$ 16.57
OXYCODONE	TAB 30MG	3	225	27	$ 112.17
201604		**4**	**270**	**44**	**$ 118.64**
OXYCODONE	TAB 15MG	2	120	30	$ 45.82
OXYCODONE	TAB 30MG	2	150	14	$ 72.82
201605		**4**	**270**	**44**	**$ 122.16**
OXYCODONE	TAB 15MG	2	120	30	$ 44.80
OXYCODONE	TAB 30MG	2	150	14	$ 77.36
201606		**3**	**360**	**41**	**$ 150.13**
OXYCODONE	TAB 15MG	1	60	15	$ 21.65
OXYCODONE	TAB 30MG	2	300	26	$ 128.48
201607		**3**	**180**	**43**	**$ 81.38**
OXYCODONE	TAB 15MG	2	105	29	$ 42.50
OXYCODONE	TAB 30MG	1	75	14	$ 38.88
201608		**5**	**315**	**70**	**$ 150.81**
OXYCODONE	TAB 15MG	2	90	28	$ 39.06
OXYCODONE	TAB 30MG	3	225	42	$ 111.75
201609		**4**	**212**	**49**	**$ 101.68**
OXYCODONE	TAB 15MG	2	85	21	$ 37.94
OXYCODONE	TAB 30MG	2	127	28	$ 63.74
201610		**5**	**220**	**67**	**$ 104.62**
OXYCODONE	TAB 15MG	3	126	39	$ 53.30
OXYCODONE	TAB 30MG	2	94	28	$ 51.32
201611		**4**	**156**	**51**	**$ 86.66**
OXYCODONE	TAB 15MG	2	72	23	$ 35.74
OXYCODONE	TAB 30MG	2	84	28	$ 50.92
201612		**6**	**180**	**64**	**$ 109.77**
OXYCODONE	TAB 15MG	2	72	28	$ 33.45
OXYCODONE	TAB 20MG	2	24	8	$ 28.12
OXYCODONE	TAB 30MG	2	84	28	$ 48.20
201701		**2**	**70**	**28**	**$ 39.63**
OXYCODONE	TAB 15MG	1	28	14	$ 15.02
OXYCODONE	TAB 30MG	1	42	14	$ 24.61
201702		**6**	**210**	**84**	**$ 117.06**
OXYCODONE	TAB 15MG	3	84	42	$ 45.78
OXYCODONE	TAB 30MG	3	126	42	$ 71.28
201703		**2**	**70**	**28**	**$ 39.34**
OXYCODONE	TAB 15MG	1	28	14	$ 15.24

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 30MG	1	42	14	$ 24.10
201704	**4**	**156**	**56**	**$ 79.02**
OXYCODONE TAB 15MG	2	72	28	$ 30.46
OXYCODONE TAB 30MG	2	84	28	$ 48.56
201705	**4**	**156**	**56**	**$ 75.48**
OXYCODONE TAB 15MG	2	72	28	$ 29.94
OXYCODONE TAB 30MG	2	84	28	$ 45.54
201706	**5**	**163**	**63**	**$ 89.14**
OXYCODONE TAB 15MG	2	72	28	$ 29.42
OXYCODONE TAB 20MG	1	7	7	$ 12.36
OXYCODONE TAB 30MG	2	84	28	$ 47.36
201707	**5**	**410**	**58**	**$ 149.09**
OXYCODONE TAB 15MG	2	140	35	$ 38.90
OXYCODONE TAB 30MG	3	270	23	$ 110.19
50155177779	**78**	**9286**	**2258**	**$ 4,679.91**
201508	**4**	**510**	**102**	**$ 279.87**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 45.62
MORPHINE SUL TAB 30MG ER	1	90	30	$ 84.81
OXYCODONE TAB 30MG	2	330	42	$ 149.44
201509	**3**	**345**	**81**	**$ 205.15**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 45.62
MORPHINE SUL TAB 30MG ER	1	90	30	$ 84.81
OXYCODONE TAB 30MG	1	165	21	$ 74.72
201510	**4**	**510**	**111**	**$ 279.87**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 45.62
MORPHINE SUL TAB 30MG ER	1	90	30	$ 84.81
OXYCODONE TAB 30MG	2	330	51	$ 149.44
201511	**3**	**216**	**65**	**$ 146.08**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 45.78
MORPHINE SUL TAB 30MG ER	1	90	30	$ 77.87
OXYCODONE TAB 30MG	1	36	5	$ 22.43
201512	**4**	**505**	**114**	**$ 264.12**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 45.03
MORPHINE SUL TAB 30MG ER	1	90	30	$ 79.23
OXYCODONE TAB 30MG	2	325	54	$ 139.86
201601	**3**	**360**	**90**	**$ 200.66**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 47.70
MORPHINE SUL TAB 30MG ER	1	90	30	$ 76.60
OXYCODONE TAB 30MG	1	180	30	$ 76.36
201602	**3**	**360**	**90**	**$ 196.11**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 45.33
MORPHINE SUL TAB 30MG ER	1	90	30	$ 74.42
OXYCODONE TAB 30MG	1	180	30	$ 76.36

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201603	**4**	**450**	**112**	**$ 240.33**
MORPHINE SUL TAB 15MG ER	2	180	60	$ 90.42
MORPHINE SUL TAB 30MG ER	1	90	30	$ 74.42
OXYCODONE TAB 30MG	1	180	22	$ 75.49
201604	**3**	**360**	**90**	**$ 194.82**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 44.94
MORPHINE SUL TAB 30MG ER	1	90	30	$ 76.73
OXYCODONE TAB 30MG	1	180	30	$ 73.15
201605	**3**	**360**	**90**	**$ 193.66**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 44.06
MORPHINE SUL TAB 30MG ER	1	90	30	$ 71.00
OXYCODONE TAB 30MG	1	180	30	$ 78.60
201606	**3**	**360**	**90**	**$ 188.43**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 42.74
MORPHINE SUL TAB 30MG ER	1	90	30	$ 70.64
OXYCODONE TAB 30MG	1	180	30	$ 75.05
201607	**3**	**360**	**90**	**$ 189.12**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 43.21
MORPHINE SUL TAB 30MG ER	1	90	30	$ 66.83
OXYCODONE TAB 30MG	1	180	30	$ 79.08
201608	**3**	**360**	**90**	**$ 187.05**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 44.62
MORPHINE SUL TAB 30MG ER	1	90	30	$ 66.98
OXYCODONE TAB 30MG	1	180	30	$ 75.45
201609	**3**	**360**	**90**	**$ 188.72**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 44.62
MORPHINE SUL TAB 30MG ER	1	90	30	$ 69.52
OXYCODONE TAB 30MG	1	180	30	$ 74.58
201610	**3**	**360**	**90**	**$ 177.07**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 40.63
MORPHINE SUL TAB 30MG ER	1	90	30	$ 68.96
OXYCODONE TAB 30MG	1	180	30	$ 67.48
201611	**3**	**360**	**90**	**$ 178.54**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 40.63
MORPHINE SUL TAB 30MG ER	1	90	30	$ 62.21
OXYCODONE TAB 30MG	1	180	30	$ 75.70
201612	**3**	**360**	**90**	**$ 169.03**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 39.55
MORPHINE SUL TAB 30MG ER	1	90	30	$ 61.78
OXYCODONE TAB 30MG	1	180	30	$ 67.70
201701	**3**	**360**	**90**	**$ 173.72**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 39.88
MORPHINE SUL TAB 30MG ER	1	90	30	$ 61.78

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 30MG	1	180	30	$ 72.06
201702	**3**	**360**	**90**	**$ 159.03**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 38.90
MORPHINE SUL TAB 30MG ER	1	90	30	$ 51.71
OXYCODONE TAB 30MG	1	180	30	$ 68.42
201703	**3**	**360**	**90**	**$ 159.26**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 37.69
MORPHINE SUL TAB 30MG ER	1	90	30	$ 51.71
OXYCODONE TAB 30MG	1	180	30	$ 69.86
201704	**3**	**360**	**90**	**$ 157.88**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 35.52
MORPHINE SUL TAB 30MG ER	1	90	30	$ 51.71
OXYCODONE TAB 30MG	1	180	30	$ 70.65
201705	**5**	**630**	**150**	**$ 260.28**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 36.98
MORPHINE SUL TAB 30MG ER	2	180	60	$ 94.96
OXYCODONE TAB 30MG	2	360	60	$ 128.34
201706	**3**	**360**	**90**	**$ 147.51**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 35.72
MORPHINE SUL TAB 30MG ER	1	90	30	$ 48.51
OXYCODONE TAB 30MG	1	180	30	$ 63.28
201707	**3**	**360**	**83**	**$ 143.60**
MORPHINE SUL TAB 15MG ER	1	90	30	$ 33.85
MORPHINE SUL TAB 30MG ER	1	90	30	$ 46.47
OXYCODONE TAB 30MG	1	180	23	$ 63.28
56292500001	**86**	**13770**	**1791**	**$ 6,035.45**
201508	**2**	**360**	**36**	**$ 156.38**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 43.17
HYDROCOD/IBU TAB 7.5-200	1	180	18	$ 113.21
201509	**4**	**720**	**66**	**$ 312.76**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 86.34
HYDROCOD/IBU TAB 7.5-200	2	360	30	$ 226.42
201510	**2**	**360**	**33**	**$ 156.38**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 43.17
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 113.21
201511	**4**	**720**	**66**	**$ 233.26**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	2	360	30	$ 136.10
201512	**4**	**720**	**66**	**$ 238.80**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	2	360	30	$ 141.64
201601	**2**	**360**	**33**	**$ 119.90**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 48.58

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 71.32
201602	**3**	**540**	**51**	**$ 166.64**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 69.48
201603	**2**	**360**	**33**	**$ 119.15**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 48.58
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 70.57
201604	**3**	**540**	**51**	**$ 165.81**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 68.65
201605	**3**	**540**	**66**	**$ 171.03**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 73.87
201606	**6**	**840**	**136**	**$ 425.47**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 100.80
BUT/ASA/CAF/ CAP COD 30MG	2	120	40	$ 184.58
HYDROCOD/IBU TAB 7.5-200	2	360	60	$ 140.09
201607	**2**	**360**	**36**	**$ 104.44**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
201608	**4**	**600**	**86**	**$ 275.54**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
BUT/ASA/CAF/ CAP COD 30MG	1	60	20	$ 98.52
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 72.58
201609	**3**	**420**	**68**	**$ 220.52**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 52.22
BUT/ASA/CAF/ CAP COD 30MG	1	60	20	$ 98.52
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 69.78
201610	**4**	**600**	**86**	**$ 272.74**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
BUT/ASA/CAF/ CAP COD 30MG	1	60	20	$ 98.52
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 69.78
201611	**5**	**660**	**106**	**$ 375.79**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
BUT/ASA/CAF/ CAP COD 30MG	2	120	40	$ 197.04
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 74.31
201612	**6**	**840**	**136**	**$ 441.92**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.32
BUT/ASA/CAF/ CAP COD 30MG	2	120	40	$ 197.04
HYDROCOD/IBU TAB 7.5-200	2	360	60	$ 140.56
201701	**4**	**630**	**96**	**$ 313.76**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 102.76
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 68.31

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201702	**4**	**630**	**96**	**$ 307.09**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 101.80
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 62.60
201703	**3**	**450**	**78**	**$ 256.36**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 51.07
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 62.60
201704	**4**	**630**	**96**	**$ 309.31**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 103.90
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 62.72
201705	**4**	**630**	**90**	**$ 302.46**
APAP/CODEINE TAB 300-60MG	2	360	30	$ 94.82
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 64.95
201706	**4**	**630**	**90**	**$ 304.88**
APAP/CODEINE TAB 300-60MG	2	360	30	$ 96.73
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 65.46
201707	**4**	**630**	**90**	**$ 285.06**
APAP/CODEINE TAB 300-60MG	2	360	30	$ 99.59
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 124.79
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 60.68
66662735498	**78**	**8105**	**2242**	**$ 12,468.08**
201508	**3**	**290**	**70**	**$ 417.65**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 232.87
MORPHINE SUL TAB 60MG ER	1	20	10	$ 35.09
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 149.69
201509	**3**	**360**	**90**	**$ 507.48**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 216.56
MORPHINE SUL TAB 60MG ER	1	90	30	$ 141.23
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 149.69
201510	**2**	**240**	**60**	**$ 295.65**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 145.96
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 149.69
201511	**3**	**240**	**90**	**$ 395.13**
MORPHINE SUL TAB 200MG ER	1	60	30	$ 218.73
MORPHINE SUL TAB 60MG ER	1	60	30	$ 88.37
OXYCOD/APAP TAB 10-325MG	1	120	30	$ 88.03
201512	**6**	**480**	**180**	**$ 911.28**
MORPHINE SUL TAB 200MG ER	2	120	60	$ 561.74
MORPHINE SUL TAB 60MG ER	2	120	60	$ 176.74

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCOD/APAP TAB 10-325MG	2	240	60	$ 172.80
201601	**3**	**300**	**90**	**$ 488.19**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 128.50
MORPHINE SUL TAB 200MG ER	1	60	30	$ 239.20
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 120.49
201602	**3**	**330**	**87**	**$ 548.03**
MORPHINE SUL TAB 100MG ER	1	90	27	$ 187.66
MORPHINE SUL TAB 200MG ER	1	60	30	$ 231.21
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 129.16
201603	**4**	**180**	**60**	**$ 289.55**
MORPHINE SUL TAB 100MG ER	1	15	15	$ 39.75
MORPHINE SUL TAB 200MG ER	1	45	15	$ 186.70
OXYCODONE TAB 30MG	2	120	30	$ 63.10
201604	**4**	**255**	**105**	**$ 436.69**
MORPHINE SUL TAB 100MG ER	2	90	60	$ 197.83
MORPHINE SUL TAB 200MG ER	1	45	15	$ 186.70
OXYCODONE TAB 30MG	1	120	30	$ 52.16
201605	**4**	**450**	**120**	**$ 618.82**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 128.50
MORPHINE SUL TAB 200MG ER	1	90	30	$ 359.48
OXYCODONE TAB 30MG	2	300	60	$ 130.84
201606	**3**	**330**	**90**	**$ 603.80**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 127.62
MORPHINE SUL TAB 200MG ER	1	90	30	$ 397.10
OXYCODONE TAB 30MG	1	180	30	$ 79.08
201607	**4**	**420**	**120**	**$ 969.82**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 122.50
MORPHINE SUL TAB 200MG ER	2	180	60	$ 771.87
OXYCODONE TAB 30MG	1	180	30	$ 75.45
201608	**3**	**330**	**90**	**$ 513.48**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 99.43
MORPHINE SUL TAB 200MG ER	1	90	30	$ 339.47
OXYCODONE TAB 30MG	1	180	30	$ 74.58
201609	**3**	**330**	**90**	**$ 506.38**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 99.43
MORPHINE SUL TAB 200MG ER	1	90	30	$ 339.47
OXYCODONE TAB 30MG	1	180	30	$ 67.48
201610	**3**	**330**	**90**	**$ 497.76**
MORPHINE SUL TAB 100MG ER	1	60	30	$ 99.43
MORPHINE SUL TAB 200MG ER	1	90	30	$ 326.35
OXYCODONE TAB 30MG	1	180	30	$ 71.98
201611	**3**	**360**	**90**	**$ 546.11**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
MORPHINE SUL TAB 200MG ER	1	90	30	$ 326.35
OXYCODONE TAB 30MG	1	180	30	$ 75.70
201612	**3**	**360**	**90**	**$ 518.56**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06
MORPHINE SUL TAB 200MG ER	1	90	30	$ 306.80
OXYCODONE TAB 30MG	1	180	30	$ 67.70
201701	**3**	**360**	**90**	**$ 494.74**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06
MORPHINE SUL TAB 200MG ER	1	90	30	$ 282.26
OXYCODONE TAB 30MG	1	180	30	$ 68.42
201702	**3**	**360**	**90**	**$ 473.40**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72
MORPHINE SUL TAB 200MG ER	1	90	30	$ 282.26
OXYCODONE TAB 30MG	1	180	30	$ 68.42
201703	**3**	**360**	**90**	**$ 518.93**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72
MORPHINE SUL TAB 200MG ER	1	90	30	$ 326.35
OXYCODONE TAB 30MG	1	180	30	$ 69.86
201704	**3**	**360**	**90**	**$ 508.27**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72
MORPHINE SUL TAB 200MG ER	1	90	30	$ 298.35
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 87.20
201705	**3**	**360**	**90**	**$ 457.47**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 107.51
MORPHINE SUL TAB 200MG ER	1	90	30	$ 261.74
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 88.22
201706	**3**	**360**	**90**	**$ 468.05**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 112.59
MORPHINE SUL TAB 200MG ER	1	90	30	$ 261.74
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 93.72
201707	**3**	**360**	**90**	**$ 482.84**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 112.59
MORPHINE SUL TAB 200MG ER	1	90	30	$ 283.61
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 86.64
77777867134	**78**	**6250**	**1476**	**$ 1,789.36**
201508	**4**	**240**	**60**	**$ 101.42**
METHADONE TAB 10MG	2	90	30	$ 20.96
OXYCODONE TAB 15MG	2	150	30	$ 80.46
201509	**6**	**360**	**87**	**$ 152.13**
METHADONE TAB 10MG	3	135	45	$ 31.44
OXYCODONE TAB 15MG	3	225	42	$ 120.69
201510	**4**	**240**	**59**	**$ 85.08**
METHADONE TAB 10MG	2	90	30	$ 20.96

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 15MG	2	150	29	$ 64.12
201511	**4**	**240**	**56**	**$ 103.13**
METHADONE TAB 10MG	2	90	30	$ 22.98
OXYCOD/APAP TAB 10-325MG	1	75	12	$ 54.81
OXYCODONE TAB 15MG	1	75	14	$ 25.34
201512	**4**	**235**	**55**	**$ 73.65**
METHADONE TAB 10MG	2	85	28	$ 22.23
OXYCODONE TAB 15MG	2	150	27	$ 51.42
201601	**4**	**240**	**60**	**$ 77.88**
METHADONE TAB 10MG	2	90	30	$ 22.98
OXYCODONE TAB 15MG	2	150	30	$ 54.90
201602	**5**	**315**	**68**	**$ 96.62**
METHADONE TAB 10MG	2	90	30	$ 22.98
OXYCODONE TAB 15MG	3	225	38	$ 73.64
201603	**5**	**285**	**73**	**$ 89.56**
METHADONE TAB 10MG	3	135	45	$ 38.87
OXYCODONE TAB 15MG	2	150	28	$ 50.69
201604	**4**	**240**	**56**	**$ 74.53**
METHADONE TAB 10MG	2	90	30	$ 22.98
OXYCODONE TAB 15MG	2	150	26	$ 51.55
201605	**4**	**240**	**56**	**$ 72.97**
METHADONE TAB 10MG	2	90	30	$ 22.98
OXYCODONE TAB 15MG	2	150	26	$ 49.99
201606	**4**	**240**	**58**	**$ 72.04**
METHADONE TAB 10MG	2	90	30	$ 22.98
OXYCODONE TAB 15MG	2	150	28	$ 49.06
201607	**3**	**315**	**61**	**$ 84.82**
METHADONE TAB 10MG	1	90	22	$ 18.22
OXYCODONE TAB 15MG	2	225	39	$ 66.60
201608	**2**	**240**	**60**	**$ 59.72**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	150	30	$ 41.50
201609	**2**	**240**	**60**	**$ 59.45**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	150	30	$ 41.23
201610	**2**	**240**	**55**	**$ 55.53**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	150	25	$ 37.31
201611	**2**	**255**	**60**	**$ 63.68**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	165	30	$ 45.46
201612	**2**	**255**	**57**	**$ 59.87**
METHADONE TAB 10MG	1	90	30	$ 18.22

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 15MG	1	165	27	$ 41.65
201701	**2**	**255**	**57**	**$ 56.99**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	165	27	$ 38.77
201702	**2**	**255**	**60**	**$ 58.47**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	165	30	$ 40.25
201703	**3**	**275**	**60**	**$ 70.99**
HYDROCO/APAP TAB 5-325MG	1	20	3	$ 12.75
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	165	27	$ 40.02
201704	**2**	**255**	**57**	**$ 51.57**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	165	27	$ 33.35
201705	**2**	**255**	**57**	**$ 51.57**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	1	165	27	$ 33.35
201706	**3**	**305**	**68**	**$ 65.65**
METHADONE TAB 10MG	1	90	30	$ 18.22
OXYCODONE TAB 15MG	2	215	38	$ 47.43
201707	**3**	**230**	**76**	**$ 52.04**
METHADONE TAB 10MG	2	110	46	$ 25.97
OXYCODONE TAB 15MG	1	120	30	$ 26.07
85993300003	**79**	**4943**	**1391**	**$ 24,834.80**
201508	**5**	**242**	**64**	**$ 969.71**
BUT/APAP/CAF CAP CODEINE	2	180	30	$ 218.82
FENTANYL DIS 25MCG/HR	1	2	4	$ 14.77
MORPHINE SUL TAB 100MG ER	1	15	15	$ 42.78
OXYCONTIN TAB 80MG CR	1	45	15	$ 693.34
201509	**4**	**240**	**60**	**$ 1,529.23**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 109.41
OXYCODONE TAB 15MG	1	60	15	$ 33.14
OXYCONTIN TAB 80MG CR	2	90	30	$ 1,386.68
201510	**2**	**135**	**30**	**$ 830.30**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 109.41
OXYCONTIN TAB 80MG CR	1	45	15	$ 720.89
201511	**4**	**276**	**67**	**$ 768.34**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 103.19
MORPHINE SUL TAB 100MG ER	1	21	7	$ 51.58
OXYCODONE TAB 15MG	1	120	30	$ 34.45
OXYCONTIN TAB 80MG CR	1	45	15	$ 579.12
201512	**5**	**390**	**90**	**$ 1,488.53**
BUT/APAP/CAF CAP CODEINE	2	180	30	$ 204.08

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE TAB 15MG	1	120	30	$ 35.03
OXYCONTIN TAB 80MG CR	2	90	30	$ 1,249.42
201601	**2**	**90**	**30**	**$ 1,181.28**
OXYCONTIN TAB 60MG CR	2	90	30	$ 1,181.28
201602	**3**	**240**	**60**	**$ 646.09**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 105.89
OXYCODONE TAB 15MG	1	120	30	$ 33.13
OXYCONTIN TAB 80MG CR	1	30	15	$ 507.07
201603	**4**	**240**	**60**	**$ 1,222.00**
BUT/APAP/CAF CAP CODEINE	2	180	30	$ 207.86
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,014.14
201604	**4**	**240**	**60**	**$ 1,221.21**
BUT/APAP/CAF CAP CODEINE	2	180	30	$ 207.07
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,014.14
201605	**2**	**120**	**30**	**$ 609.99**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 102.92
OXYCONTIN TAB 80MG CR	1	30	15	$ 507.07
201606	**6**	**420**	**120**	**$ 1,691.29**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 103.80
OXYCODONE TAB 15MG	2	240	60	$ 66.28
OXYCONTIN TAB 80MG CR	3	90	45	$ 1,521.21
201607	**3**	**180**	**60**	**$ 1,049.37**
OXYCODONE TAB 15MG	1	120	30	$ 35.23
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,014.14
201608	**2**	**120**	**45**	**$ 611.11**
BUT/APAP/CAF CAP CODEINE	1	90	30	$ 104.04
OXYCONTIN TAB 80MG CR	1	30	15	$ 507.07
201609	**3**	**180**	**60**	**$ 632.83**
BUT/APAP/CAF CAP CODEINE	1	90	30	$ 104.73
OXYCODONE TAB 15MG	1	60	15	$ 21.03
OXYCONTIN TAB 80MG CR	1	30	15	$ 507.07
201610	**3**	**240**	**60**	**$ 643.34**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 104.39
OXYCODONE TAB 15MG	1	120	30	$ 31.88
OXYCONTIN TAB 80MG CR	1	30	15	$ 507.07
201611	**2**	**60**	**30**	**$ 1,004.20**
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,004.20
201612	**2**	**150**	**45**	**$ 535.16**
OXYCODONE TAB 15MG	1	120	30	$ 33.06
OXYCONTIN TAB 80MG CR	1	30	15	$ 502.10
201701	**4**	**330**	**75**	**$ 742.50**
BUT/APAP/CAF CAP CODEINE	2	180	30	$ 208.36
OXYCODONE TAB 15MG	1	120	30	$ 32.04

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCONTIN TAB 80MG CR	1	30	15	$ 502.10
201702	**3**	**150**	**45**	**$ 1,205.19**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 104.09
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,101.10
201703	**4**	**180**	**60**	**$ 1,754.33**
BUT/APAP/CAF CAP CODEINE	1	90	15	$ 102.72
OXYCONTIN TAB 80MG CR	3	90	45	$ 1,651.61
201704	**3**	**180**	**60**	**$ 1,125.81**
OXYCODONE TAB 15MG	1	120	30	$ 27.03
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,098.78
201705	**3**	**180**	**60**	**$ 1,124.07**
OXYCODONE TAB 15MG	1	120	30	$ 25.29
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,098.78
201706	**3**	**180**	**60**	**$ 1,124.07**
OXYCODONE TAB 15MG	1	120	30	$ 25.29
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,098.78
201707	**3**	**180**	**60**	**$ 1,124.85**
OXYCODONE TAB 15MG	1	120	30	$ 26.07
OXYCONTIN TAB 80MG CR	2	60	30	$ 1,098.78
99990925934	**98**	**1084**	**531**	**$ 8,427.75**
201508	**4**	**70**	**35**	**$ 622.07**
SUBOXONE MIS 12-3MG	1	14	7	$ 205.77
SUBOXONE MIS 8-2MG	3	56	28	$ 416.30
201509	**5**	**72**	**36**	**$ 655.55**
SUBOXONE MIS 12-3MG	2	16	8	$ 239.24
SUBOXONE MIS 8-2MG	3	56	28	$ 416.31
201510	**5**	**58**	**36**	**$ 655.54**
SUBOXONE MIS 12-3MG	3	30	22	$ 445.01
SUBOXONE MIS 8-2MG	2	28	14	$ 210.53
201511	**3**	**49**	**29**	**$ 257.61**
HYDROCO/APAP TAB 5-325MG	1	16	4	$ 12.58
SUBOXONE MIS 8-2MG	2	33	25	$ 245.03
201601	**1**	**16**	**4**	**$ 12.52**
HYDROCO/APAP TAB 5-325MG	1	16	4	$ 12.52
201604	**2**	**34**	**17**	**$ 26.14**
HYDROCO/APAP TAB 7.5-325	2	34	17	$ 26.14
201605	**2**	**40**	**20**	**$ 27.16**
HYDROCO/APAP TAB 7.5-325	2	40	20	$ 27.16
201606	**1**	**6**	**3**	**$ 53.06**
SUBOXONE MIS 8-2MG	1	6	3	$ 53.06
201607	**7**	**66**	**33**	**$ 537.02**
SUBOXONE MIS 8-2MG	7	66	33	$ 537.02
201608	**7**	**64**	**32**	**$ 526.46**

Member		Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
SUBOXONE	MIS 8-2MG	7	64	32	$ 526.46
201609		**7**	**66**	**33**	**$ 542.63**
SUBOXONE	MIS 8-2MG	7	66	33	$ 542.63
201610		**8**	**64**	**32**	**$ 537.65**
SUBOXONE	MIS 8-2MG	8	64	32	$ 537.65
201611		**7**	**64**	**32**	**$ 527.97**
SUBOXONE	MIS 8-2MG	7	64	32	$ 527.97
201612		**7**	**74**	**37**	**$ 599.75**
SUBOXONE	MIS 8-2MG	7	74	37	$ 599.75
201701		**6**	**60**	**30**	**$ 494.34**
SUBOXONE	MIS 8-2MG	6	60	30	$ 494.34
201702		**6**	**60**	**25**	**$ 509.98**
SUBOXONE	MIS 8-2MG	6	60	25	$ 509.98
201703		**9**	**74**	**31**	**$ 645.25**
SUBOXONE	MIS 8-2MG	9	74	31	$ 645.25
201704		**3**	**19**	**7**	**$ 170.25**
SUBOXONE	MIS 8-2MG	3	19	7	$ 170.25
201705		**2**	**60**	**28**	**$ 465.58**
SUBOXONE	MIS 8-2MG	2	60	28	$ 465.58
201706		**6**	**68**	**31**	**$ 561.22**
SUBOXONE	MIS 8-2MG	6	68	31	$ 561.22
Grand Total		**1245**	**92538**	**21754**	**$ 109,967.42**

Top 10 Members by Total Quantity

August 2015 - July 2017

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
00007154616	**29**	**54356**	**830**	**$ 6,483.03**
201604	**1**	**120**	**2**	**$ 25.15**
HYDROCO/APAP SOL 7.5-325	1	120	2	$ 25.15
201606	**2**	**3874**	**60**	**$ 526.94**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 456.30
MORPHINE SUL TAB 30MG ER	1	90	30	$ 70.64
201607	**2**	**3874**	**60**	**$ 397.85**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 331.02
MORPHINE SUL TAB 30MG ER	1	90	30	$ 66.83
201608	**2**	**3874**	**61**	**$ 506.79**
HYDROCO/APAP SOL 7.5-325	1	3784	31	$ 439.81
MORPHINE SUL TAB 30MG ER	1	90	30	$ 66.98
201609	**2**	**3874**	**61**	**$ 496.84**
HYDROCO/APAP SOL 7.5-325	1	3784	31	$ 427.32
MORPHINE SUL TAB 30MG ER	1	90	30	$ 69.52
201610	**2**	**3874**	**60**	**$ 550.20**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 481.24
MORPHINE SUL TAB 30MG ER	1	90	30	$ 68.96
201611	**2**	**3874**	**61**	**$ 517.64**
HYDROCO/APAP SOL 7.5-325	1	3784	31	$ 455.43
MORPHINE SUL TAB 30MG ER	1	90	30	$ 62.21
201612	**2**	**3874**	**45**	**$ 505.22**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 443.44
MORPHINE SUL TAB 30MG ER	1	90	15	$ 61.78
201701	**2**	**3874**	**60**	**$ 463.38**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 401.17
MORPHINE SUL TAB 30MG ER	1	90	30	$ 62.21
201702	**2**	**3874**	**60**	**$ 505.33**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 453.62
MORPHINE SUL TAB 30MG ER	1	90	30	$ 51.71
201703	**2**	**3874**	**60**	**$ 475.93**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 424.22
MORPHINE SUL TAB 30MG ER	1	90	30	$ 51.71
201704	**2**	**3874**	**60**	**$ 357.75**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 306.04
MORPHINE SUL TAB 30MG ER	1	90	30	$ 51.71
201705	**2**	**3874**	**60**	**$ 456.97**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 405.26
MORPHINE SUL TAB 30MG ER	1	90	30	$ 51.71
201706	**2**	**3874**	**60**	**$ 344.07**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 293.74
MORPHINE SUL TAB 30MG ER	1	90	30	$ 50.33

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201707	**2**	**3874**	**60**	**$ 352.97**
HYDROCO/APAP SOL 7.5-325	1	3784	30	$ 306.50
MORPHINE SUL TAB 30MG ER	1	90	30	$ 46.47
27483344445	**78**	**13409**	**2138**	**$ 14,769.05**
201508	**1**	**60**	**30**	**$ 999.26**
NUCYNTA ER TAB 250MG	1	60	30	$ 999.26
201509	**3**	**480**	**90**	**$ 1,210.70**
MORPHINE SUL TAB 30MG	1	240	30	$ 61.75
NUCYNTA ER TAB 250MG	1	60	30	$ 999.26
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 149.69
201510	**2**	**420**	**43**	**$ 211.44**
MORPHINE SUL TAB 30MG	1	240	13	$ 61.75
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 149.69
201511	**2**	**240**	**60**	**$ 1,071.21**
NUCYNTA ER TAB 250MG	1	60	30	$ 953.91
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 117.30
201512	**3**	**480**	**85**	**$ 1,137.25**
MORPHINE SUL TAB 30MG	1	240	30	$ 66.04
NUCYNTA ER TAB 250MG	1	60	30	$ 953.91
OXYCOD/APAP TAB 10-325MG	1	180	25	$ 117.30
201601	**3**	**480**	**85**	**$ 1,233.84**
MORPHINE SUL TAB 30MG	1	240	30	$ 66.04
NUCYNTA ER TAB 250MG	1	60	30	$ 1,047.31
OXYCOD/APAP TAB 10-325MG	1	180	25	$ 120.49
201602	**3**	**480**	**90**	**$ 1,242.51**
ENDOCET TAB 10-325MG	1	180	30	$ 129.16
MORPHINE SUL TAB 30MG	1	240	30	$ 66.04
NUCYNTA ER TAB 250MG	1	60	30	$ 1,047.31
201603	**4**	**660**	**105**	**$ 270.91**
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 131.12
TRAMADL/APAP TAB 37.5-325	1	120	15	$ 33.78
TRAMADOL HCL TAB 50MG	1	120	30	$ 13.19
201604	**4**	**690**	**110**	**$ 601.87**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 363.23
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 131.12
TRAMADOL HCL TAB 50MG	1	180	30	$ 14.70
201605	**4**	**690**	**110**	**$ 594.18**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 359.48
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 127.85
TRAMADOL HCL TAB 50MG	1	180	30	$ 14.03
201606	**6**	**1020**	**153**	**$ 1,102.83**

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
MORPHINE SUL TAB 200MG ER	2	180	60	$ 777.39
MORPHINE SUL TAB 30MG	2	480	43	$ 185.64
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 125.80
TRAMADOL HCL TAB 50MG	1	180	30	$ 14.00
201607	**3**	**510**	**90**	**$ 528.51**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 391.58
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 121.34
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.59
201608	**3**	**660**	**90**	**$ 223.76**
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 115.45
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.49
201609	**4**	**750**	**110**	**$ 566.06**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 339.47
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 118.63
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.14
201610	**5**	**989**	**122**	**$ 604.60**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 366.41
MORPHINE SUL TAB 30MG	1	239	12	$ 92.47
OXYCOD/APAP TAB 10-325MG	1	180	20	$ 115.15
TRAMADOL HCL TAB 50MG	2	480	60	$ 30.57
201611	**4**	**750**	**120**	**$ 549.02**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 326.35
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 114.51
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.34
201612	**4**	**750**	**120**	**$ 522.66**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 306.80
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	30	$ 107.89
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.15
201701	**4**	**750**	**117**	**$ 490.51**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 282.26
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	27	$ 100.25
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.18
201702	**4**	**750**	**98**	**$ 490.51**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 282.26
MORPHINE SUL TAB 30MG	1	240	13	$ 92.82
OXYCOD/APAP TAB 10-325MG	1	180	25	$ 100.25
TRAMADOL HCL TAB 50MG	1	240	30	$ 15.18
201704	**2**	**240**	**60**	**$ 171.63**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
MORPHINE SUL TAB 30MG	1	150	30	$ 48.91
201705	**3**	**540**	**60**	**$ 221.57**
MORPHINE SUL TAB 30MG	1	240	30	$ 72.16
OXYCOD/APAP TAB 10-325MG	2	300	30	$ 149.41
201706	**3**	**450**	**80**	**$ 320.69**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 261.74
MORPHINE SUL TAB 30MG	1	180	20	$ 45.04
TRAMADOL HCL TAB 50MG	1	180	30	$ 13.91
201707	**4**	**570**	**110**	**$ 403.53**
MORPHINE SUL TAB 200MG ER	1	90	30	$ 283.61
MORPHINE SUL TAB 30MG	1	180	30	$ 45.04
OXYCOD/APAP TAB 10-325MG	1	120	20	$ 61.15
TRAMADOL HCL TAB 50MG	1	180	30	$ 13.73
44448546720	**52**	**13260**	**1462**	**$ 4,575.78**
201508	**2**	**510**	**55**	**$ 208.64**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 51.24
OXYCODONE TAB 30MG	1	360	30	$ 157.40
201509	**2**	**510**	**47**	**$ 208.64**
HYDROCO/APAP TAB 10-325MG	1	150	17	$ 51.24
OXYCODONE TAB 30MG	1	360	30	$ 157.40
201510	**2**	**510**	**55**	**$ 208.64**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 51.24
OXYCODONE TAB 30MG	1	360	30	$ 157.40
201511	**2**	**510**	**55**	**$ 177.25**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 42.09
OXYCODONE TAB 30MG	1	360	30	$ 135.16
201512	**2**	**510**	**60**	**$ 172.63**
HYDROCO/APAP TAB 10-325MG	1	150	30	$ 39.84
OXYCODONE TAB 30MG	1	360	30	$ 132.79
201601	**2**	**510**	**60**	**$ 188.78**
HYDROCO/APAP TAB 10-325MG	1	150	30	$ 38.35
OXYCODONE TAB 30MG	1	360	30	$ 150.43
201602	**2**	**510**	**60**	**$ 182.38**
HYDROCO/APAP TAB 10-325MG	1	150	30	$ 39.84
OXYCODONE TAB 30MG	1	360	30	$ 142.54
201603	**4**	**1020**	**115**	**$ 357.39**
HYDROCO/APAP TAB 10-325MG	2	300	55	$ 80.45
OXYCODONE TAB 30MG	2	720	60	$ 276.94
201604	**2**	**510**	**55**	**$ 188.66**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 41.63
OXYCODONE TAB 30MG	1	360	30	$ 147.03
201605	**2**	**510**	**55**	**$ 177.57**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 37.63
OXYCODONE TAB 30MG	1	360	30	$ 139.94

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201606	**2**	**510**	**55**	**$ 177.57**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 37.63
OXYCODONE TAB 30MG	1	360	30	$ 139.94
201607	**2**	**510**	**60**	**$ 186.10**
HYDROCO/APAP TAB 10-325MG	1	150	30	$ 38.10
OXYCODONE TAB 30MG	1	360	30	$ 148.00
201608	**2**	**510**	**55**	**$ 179.73**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 39.00
OXYCODONE TAB 30MG	1	360	30	$ 140.73
201609	**2**	**510**	**55**	**$ 178.59**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 39.60
OXYCODONE TAB 30MG	1	360	30	$ 138.99
201610	**2**	**510**	**55**	**$ 164.84**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 40.05
OXYCODONE TAB 30MG	1	360	30	$ 124.79
201611	**2**	**510**	**55**	**$ 176.95**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 35.73
OXYCODONE TAB 30MG	1	360	30	$ 141.22
201612	**2**	**510**	**60**	**$ 162.37**
HYDROCO/APAP TAB 10-325MG	1	150	30	$ 37.15
OXYCODONE TAB 30MG	1	360	30	$ 125.22
201701	**4**	**1020**	**120**	**$ 332.44**
HYDROCO/APAP TAB 10-325MG	2	300	60	$ 71.83
OXYCODONE TAB 30MG	2	720	60	$ 260.61
201702	**2**	**510**	**55**	**$ 162.37**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 35.71
OXYCODONE TAB 30MG	1	360	30	$ 126.66
201703	**2**	**510**	**55**	**$ 166.45**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 35.32
OXYCODONE TAB 30MG	1	360	30	$ 131.13
201704	**2**	**510**	**55**	**$ 152.89**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 34.72
OXYCODONE TAB 30MG	1	360	30	$ 118.17
201705	**2**	**510**	**55**	**$ 153.45**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 35.28
OXYCODONE TAB 30MG	1	360	30	$ 118.17
201706	**2**	**510**	**55**	**$ 161.77**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 35.76
OXYCODONE TAB 30MG	1	360	30	$ 126.01
201707	**2**	**510**	**55**	**$ 149.68**
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 33.29
OXYCODONE TAB 30MG	1	360	30	$ 116.39
44449536649	**35**	**12755**	**1035**	**$ 4,230.27**
201511	**1**	**10**	**30**	**$ 65.30**

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
201512	**1**	**10**	**30**	**$ 65.30**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
201601	**1**	**10**	**30**	**$ 65.30**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
201602	**1**	**10**	**30**	**$ 65.30**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
201603	**1**	**10**	**30**	**$ 65.30**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
201604	**2**	**460**	**60**	**$ 178.07**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	450	30	$ 112.77
201605	**1**	**10**	**30**	**$ 65.30**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
201606	**2**	**910**	**60**	**$ 280.66**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	900	30	$ 215.36
201607	**2**	**910**	**60**	**$ 280.66**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	900	30	$ 215.36
201608	**2**	**910**	**60**	**$ 272.09**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	900	30	$ 206.79
201609	**2**	**910**	**60**	**$ 269.33**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	900	30	$ 204.03
201610	**2**	**910**	**60**	**$ 269.31**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	900	30	$ 204.01
201611	**2**	**910**	**60**	**$ 244.26**
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	900	30	$ 178.96
201612	**3**	**915**	**75**	**$ 294.41**
FENTANYL DIS 25MCG/HR	1	5	15	$ 27.85
FENTANYL DIS 50MCG/HR	1	10	30	$ 65.30
OXYCODONE SOL 5MG/5ML	1	900	30	$ 201.26
201701	**2**	**910**	**60**	**$ 289.30**
FENTANYL DIS 75MCG/HR	1	10	30	$ 95.39
OXYCODONE SOL 5MG/5ML	1	900	30	$ 193.91
201702	**2**	**910**	**60**	**$ 277.78**
FENTANYL DIS 75MCG/HR	1	10	30	$ 91.38
OXYCODONE SOL 5MG/5ML	1	900	30	$ 186.40
201703	**2**	**910**	**60**	**$ 289.72**
FENTANYL DIS 75MCG/HR	1	10	30	$ 92.00

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
OXYCODONE SOL 5MG/5ML	1	900	30	$ 197.72
201704	**2**	**910**	**60**	**$ 277.77**
FENTANYL DIS 75MCG/HR	1	10	30	$ 92.77
OXYCODONE SOL 5MG/5ML	1	900	30	$ 185.00
201705	**2**	**1110**	**60**	**$ 328.67**
FENTANYL DIS 75MCG/HR	1	10	30	$ 92.46
OXYCODONE SOL 5MG/5ML	1	1100	30	$ 236.21
201706	**2**	**1110**	**60**	**$ 286.44**
FENTANYL DIS 75MCG/HR	1	10	30	$ 95.39
OXYCODONE SOL 5MG/5ML	1	1100	30	$ 191.05
55550664914	**16**	**19161**	**219**	**$ 2,057.70**
201508	**2**	**2600**	**32**	**$ 278.64**
HYDROCO/APAP SOL 7.5-325	2	2600	32	$ 278.64
201509	**1**	**1300**	**14**	**$ 139.32**
HYDROCO/APAP SOL 7.5-325	1	1300	14	$ 139.32
201510	**2**	**2600**	**28**	**$ 278.64**
HYDROCO/APAP SOL 7.5-325	2	2600	28	$ 278.64
201511	**1**	**1300**	**14**	**$ 141.72**
HYDROCO/APAP SOL 7.5-325	1	1300	14	$ 141.72
201512	**3**	**2261**	**29**	**$ 224.75**
HYDROCO/APAP SOL 7.5-325	2	2246	27	$ 212.27
HYDROCO/APAP TAB 5-325MG	1	15	2	$ 12.48
201601	**2**	**2600**	**28**	**$ 284.18**
HYDROCO/APAP SOL 7.5-325	2	2600	28	$ 284.18
201602	**2**	**2600**	**30**	**$ 284.18**
HYDROCO/APAP SOL 7.5-325	2	2600	30	$ 284.18
201603	**2**	**2600**	**29**	**$ 284.18**
HYDROCO/APAP SOL 7.5-325	2	2600	29	$ 284.18
201604	**1**	**1300**	**15**	**$ 142.09**
HYDROCO/APAP SOL 7.5-325	1	1300	15	$ 142.09
56292500001	**86**	**13770**	**1791**	**$ 6,035.45**
201508	**2**	**360**	**36**	**$ 156.38**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 43.17
HYDROCOD/IBU TAB 7.5-200	1	180	18	$ 113.21
201509	**4**	**720**	**66**	**$ 312.76**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 86.34
HYDROCOD/IBU TAB 7.5-200	2	360	30	$ 226.42
201510	**2**	**360**	**33**	**$ 156.38**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 43.17
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 113.21
201511	**4**	**720**	**66**	**$ 233.26**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	2	360	30	$ 136.10
201512	**4**	**720**	**66**	**$ 238.80**

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	2	360	30	$ 141.64
201601	**2**	**360**	**33**	**$ 119.90**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 48.58
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 71.32
201602	**3**	**540**	**51**	**$ 166.64**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 69.48
201603	**2**	**360**	**33**	**$ 119.15**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 48.58
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 70.57
201604	**3**	**540**	**51**	**$ 165.81**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	1	180	15	$ 68.65
201605	**3**	**540**	**66**	**$ 171.03**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 97.16
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 73.87
201606	**6**	**840**	**136**	**$ 425.47**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 100.80
BUT/ASA/CAF/ CAP COD 30MG	2	120	40	$ 184.58
HYDROCOD/IBU TAB 7.5-200	2	360	60	$ 140.09
201607	**2**	**360**	**36**	**$ 104.44**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
201608	**4**	**600**	**86**	**$ 275.54**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
BUT/ASA/CAF/ CAP COD 30MG	1	60	20	$ 98.52
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 72.58
201609	**3**	**420**	**68**	**$ 220.52**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 52.22
BUT/ASA/CAF/ CAP COD 30MG	1	60	20	$ 98.52
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 69.78
201610	**4**	**600**	**86**	**$ 272.74**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
BUT/ASA/CAF/ CAP COD 30MG	1	60	20	$ 98.52
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 69.78
201611	**5**	**660**	**106**	**$ 375.79**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.44
BUT/ASA/CAF/ CAP COD 30MG	2	120	40	$ 197.04
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 74.31
201612	**6**	**840**	**136**	**$ 441.92**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 104.32
BUT/ASA/CAF/ CAP COD 30MG	2	120	40	$ 197.04
HYDROCOD/IBU TAB 7.5-200	2	360	60	$ 140.56
201701	**4**	**630**	**96**	**$ 313.76**

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
APAP/CODEINE TAB 300-60MG	2	360	36	$ 102.76
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 68.31
201702	**4**	**630**	**96**	**$ 307.09**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 101.80
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 62.60
201703	**3**	**450**	**78**	**$ 256.36**
APAP/CODEINE TAB 300-60MG	1	180	18	$ 51.07
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 62.60
201704	**4**	**630**	**96**	**$ 309.31**
APAP/CODEINE TAB 300-60MG	2	360	36	$ 103.90
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 62.72
201705	**4**	**630**	**90**	**$ 302.46**
APAP/CODEINE TAB 300-60MG	2	360	30	$ 94.82
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 64.95
201706	**4**	**630**	**90**	**$ 304.88**
APAP/CODEINE TAB 300-60MG	2	360	30	$ 96.73
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 142.69
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 65.46
201707	**4**	**630**	**90**	**$ 285.06**
APAP/CODEINE TAB 300-60MG	2	360	30	$ 99.59
BUT/ASA/CAF/ CAP COD 30MG	1	90	30	$ 124.79
HYDROCOD/IBU TAB 7.5-200	1	180	30	$ 60.68
66666846275	**49**	**13350**	**1470**	**$ 2,488.23**
201508	**2**	**540**	**60**	**$ 81.57**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 42.50
METHADONE TAB 10MG	1	270	30	$ 39.07
201509	**1**	**270**	**30**	**$ 42.50**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 42.50
201510	**2**	**540**	**60**	**$ 81.57**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 42.50
METHADONE TAB 10MG	1	270	30	$ 39.07
201511	**2**	**540**	**60**	**$ 91.65**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 47.17
METHADONE TAB 10MG	1	270	30	$ 44.48
201512	**2**	**570**	**64**	**$ 95.76**
HYDROCO/APAP TAB 10-325MG	1	300	34	$ 51.28
METHADONE TAB 10MG	1	270	30	$ 44.48
201601	**2**	**570**	**64**	**$ 117.97**
HYDROCO/APAP TAB 10-325MG	1	300	34	$ 66.54

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
METHADONE TAB 10MG	1	270	30	$ 51.43
201602	**2**	**570**	**64**	**$ 119.88**
HYDROCO/APAP TAB 10-325MG	1	300	34	$ 69.50
METHADONE TAB 10MG	1	270	30	$ 50.38
201603	**2**	**540**	**60**	**$ 118.76**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 67.33
METHADONE TAB 10MG	1	270	30	$ 51.43
201604	**2**	**540**	**60**	**$ 111.32**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 61.20
METHADONE TAB 10MG	1	270	30	$ 50.12
201605	**2**	**570**	**64**	**$ 124.52**
HYDROCO/APAP TAB 10-325MG	1	300	34	$ 73.09
METHADONE TAB 10MG	1	270	30	$ 51.43
201606	**2**	**540**	**60**	**$ 105.06**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 59.60
METHADONE TAB 10MG	1	270	30	$ 45.46
201607	**2**	**540**	**60**	**$ 109.08**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 60.44
METHADONE TAB 10MG	1	270	30	$ 48.64
201608	**2**	**540**	**60**	**$ 107.38**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 60.44
METHADONE TAB 10MG	1	270	30	$ 46.94
201609	**4**	**1080**	**120**	**$ 212.13**
HYDROCO/APAP TAB 10-325MG	2	540	60	$ 125.21
METHADONE TAB 10MG	2	540	60	$ 86.92
201610	**1**	**270**	**30**	**$ 41.46**
METHADONE TAB 10MG	1	270	30	$ 41.46
201611	**2**	**540**	**60**	**$ 99.01**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 56.18
METHADONE TAB 10MG	1	270	30	$ 42.83
201612	**3**	**810**	**90**	**$ 157.39**
HYDROCO/APAP TAB 10-325MG	2	540	60	$ 115.61
METHADONE TAB 10MG	1	270	30	$ 41.78
201701	**2**	**540**	**52**	**$ 97.72**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 56.13
METHADONE TAB 10MG	1	270	22	$ 41.59
201702	**1**	**270**	**30**	**$ 56.13**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 56.13
201703	**3**	**810**	**90**	**$ 144.01**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 55.45
METHADONE TAB 10MG	2	540	60	$ 88.56
201704	**2**	**540**	**52**	**$ 93.92**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 54.37
METHADONE TAB 10MG	1	270	22	$ 39.55

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201705	**2**	**540**	**60**	**$ 95.61**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 55.36
METHADONE TAB 10MG	1	270	30	$ 40.25
201706	**1**	**270**	**30**	**$ 51.79**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 51.79
201707	**3**	**810**	**90**	**$ 132.04**
HYDROCO/APAP TAB 10-325MG	1	270	30	$ 51.79
METHADONE TAB 10MG	2	540	60	$ 80.25
88889918278	**72**	**17540**	**1939**	**$ 9,899.05**
201508	**5**	**790**	**130**	**$ 374.32**
FENTANYL DIS 100MCG/H	1	10	30	$ 244.49
HYDROCO/APAP TAB 10-325MG	1	240	30	$ 38.31
HYDROMORPHON TAB 4MG	1	180	30	$ 26.99
METHADONE TAB 10MG	2	360	40	$ 64.53
201509	**6**	**690**	**115**	**$ 362.60**
FENTANYL DIS 100MCG/H	2	10	30	$ 246.45
HYDROCO/APAP TAB 10-325MG	2	320	40	$ 54.25
HYDROMORPHON TAB 4MG	1	90	15	$ 15.88
METHADONE TAB 10MG	1	270	30	$ 46.02
201510	**6**	**690**	**112**	**$ 350.38**
FENTANYL DIS 100MCG/H	1	10	30	$ 238.87
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 25.72
HYDROMORPHON TAB 4MG	3	170	27	$ 35.28
METHADONE TAB 10MG	1	360	30	$ 50.51
201511	**4**	**400**	**71**	**$ 205.68**
FENTANYL DIS 100MCG/H	1	10	30	$ 122.09
HYDROCO/APAP TAB 10-325MG	1	150	25	$ 30.72
METHADONE TAB 10MG	1	200	13	$ 35.59
OXYCODONE TAB 10MG	1	40	3	$ 17.28
201512	**3**	**870**	**69**	**$ 676.78**
METHADONE CON 10MG/ML	1	630	30	$ 444.03
MORPHINE SUL TAB 100MG ER	1	90	30	$ 187.66
MORPHINE SUL TAB 30MG	1	150	9	$ 45.09
201601	**4**	**630**	**110**	**$ 324.26**
HYDROCO/APAP TAB 10-325MG	2	300	50	$ 70.56
MORPHINE SUL TAB 100MG ER	1	90	30	$ 187.66
MORPHINE SUL TAB 30MG	1	240	30	$ 66.04
201602	**3**	**1260**	**76**	**$ 931.11**
METHADONE CON 10MG/ML	1	930	16	$ 650.63
MORPHINE SUL TAB 100MG ER	1	90	30	$ 187.66
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201603	**3**	**1050**	**94**	**$ 802.33**
METHADONE CON 10MG/ML	1	720	34	$ 521.85
MORPHINE SUL TAB 100MG ER	1	90	30	$ 187.66

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201604	**2**	**330**	**60**	**$ 280.48**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 187.66
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201605	**3**	**1020**	**93**	**$ 781.01**
METHADONE CON 10MG/ML	1	690	33	$ 500.53
MORPHINE SUL TAB 100MG ER	1	90	30	$ 187.66
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201606	**1**	**90**	**30**	**$ 187.66**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 187.66
201607	**3**	**1020**	**93**	**$ 772.01**
METHADONE CON 10MG/ML	1	690	33	$ 500.53
MORPHINE SUL TAB 100MG ER	1	90	30	$ 178.66
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201608	**3**	**1020**	**93**	**$ 724.65**
METHADONE CON 10MG/ML	1	690	33	$ 487.77
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201609	**2**	**330**	**60**	**$ 238.04**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06
MORPHINE SUL TAB 30MG	1	240	30	$ 93.98
201610	**3**	**1020**	**93**	**$ 724.65**
METHADONE CON 10MG/ML	1	690	33	$ 487.77
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201611	**1**	**240**	**30**	**$ 92.82**
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201612	**3**	**960**	**90**	**$ 683.12**
METHADONE CON 10MG/ML	1	630	30	$ 446.24
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201701	**3**	**960**	**90**	**$ 279.19**
METHADONE CON 10MG/ML	1	630	30	$ 42.31
MORPHINE SUL TAB 100MG ER	1	90	30	$ 144.06
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201702	**3**	**960**	**90**	**$ 257.85**
METHADONE CON 10MG/ML	1	630	30	$ 42.31
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72
MORPHINE SUL TAB 30MG	1	240	30	$ 92.82
201703	**3**	**960**	**90**	**$ 237.19**
METHADONE CON 10MG/ML	1	630	30	$ 42.31
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72
MORPHINE SUL TAB 30MG	1	240	30	$ 72.16
201704	**3**	**960**	**90**	**$ 237.19**

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
METHADONE CON 10MG/ML	1	630	30	$ 42.31
MORPHINE SUL TAB 100MG ER	1	90	30	$ 122.72
MORPHINE SUL TAB 30MG	1	240	30	$ 72.16
201705	**3**	**960**	**90**	**$ 206.48**
METHADONE CON 10MG/ML	1	630	30	$ 42.31
MORPHINE SUL TAB 100MG ER	1	90	30	$ 107.51
MORPHINE SUL TAB 30MG	1	240	30	$ 56.66
201706	**2**	**330**	**70**	**$ 169.25**
MORPHINE SUL TAB 100MG ER	1	90	30	$ 112.59
MORPHINE SUL TAB 30MG	1	240	40	$ 56.66
90209455556	**27**	**28500**	**760**	**$ 3,658.65**
201508	**1**	**1260**	**30**	**$ 164.87**
METHADONE TAB 10MG	1	1260	30	$ 164.87
201509	**1**	**1260**	**30**	**$ 164.87**
METHADONE TAB 10MG	1	1260	30	$ 164.87
201510	**1**	**1260**	**30**	**$ 164.87**
METHADONE TAB 10MG	1	1260	30	$ 164.87
201511	**1**	**1260**	**30**	**$ 170.28**
METHADONE TAB 10MG	1	1260	30	$ 170.28
201512	**1**	**1260**	**30**	**$ 170.28**
METHADONE TAB 10MG	1	1260	30	$ 170.28
201601	**1**	**1260**	**30**	**$ 170.28**
METHADONE TAB 10MG	1	1260	30	$ 170.28
201602	**1**	**1260**	**30**	**$ 170.28**
METHADONE TAB 10MG	1	1260	30	$ 170.28
201603	**1**	**1170**	**30**	**$ 158.85**
METHADONE TAB 10MG	1	1170	30	$ 158.85
201604	**1**	**1170**	**30**	**$ 158.85**
METHADONE TAB 10MG	1	1170	30	$ 158.85
201605	**2**	**2160**	**60**	**$ 294.82**
METHADONE TAB 10MG	2	2160	60	$ 294.82
201606	**1**	**1080**	**30**	**$ 147.41**
METHADONE TAB 10MG	1	1080	30	$ 147.41
201607	**1**	**1080**	**30**	**$ 147.41**
METHADONE TAB 10MG	1	1080	30	$ 147.41
201608	**1**	**1080**	**30**	**$ 146.88**
METHADONE TAB 10MG	1	1080	30	$ 146.88
201609	**2**	**1110**	**36**	**$ 155.84**
HYDROCO/APAP TAB 10-325MG	1	30	6	$ 16.06
METHADONE TAB 10MG	1	1080	30	$ 139.78
201610	**1**	**1080**	**30**	**$ 135.33**
METHADONE TAB 10MG	1	1080	30	$ 135.33
201611	**1**	**1080**	**30**	**$ 135.33**
METHADONE TAB 10MG	1	1080	30	$ 135.33

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
201612	**1**	**1080**	**30**	**$ 140.83**
METHADONE TAB 10MG	1	1080	30	$ 140.83
201701	**1**	**1080**	**30**	**$ 120.87**
METHADONE TAB 10MG	1	1080	30	$ 120.87
201702	**2**	**1110**	**34**	**$ 136.15**
HYDROCO/APAP TAB 10-325MG	1	30	4	$ 15.28
METHADONE TAB 10MG	1	1080	30	$ 120.87
201703	**1**	**1080**	**30**	**$ 120.87**
METHADONE TAB 10MG	1	1080	30	$ 120.87
201704	**1**	**1080**	**30**	**$ 120.87**
METHADONE TAB 10MG	1	1080	30	$ 120.87
201705	**1**	**1080**	**30**	**$ 120.87**
METHADONE TAB 10MG	1	1080	30	$ 120.87
201706	**1**	**1080**	**30**	**$ 120.87**
METHADONE TAB 10MG	1	1080	30	$ 120.87
201707	**1**	**1080**	**30**	**$ 120.87**
METHADONE TAB 10MG	1	1080	30	$ 120.87
91274577778	**26**	**36456**	**662**	**$ 4,286.90**
201508	**1**	**1500**	**30**	**$ 219.24**
HYDROCO/APAP SOL 7.5-325	1	1500	30	$ 219.24
201509	**1**	**1500**	**25**	**$ 219.24**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 219.24
201510	**1**	**1500**	**25**	**$ 219.24**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 219.24
201511	**1**	**1500**	**25**	**$ 161.96**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 161.96
201512	**1**	**1500**	**33**	**$ 138.35**
HYDROCO/APAP SOL 7.5-325	1	1500	33	$ 138.35
201601	**1**	**1500**	**25**	**$ 182.61**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 182.61
201602	**2**	**3000**	**50**	**$ 369.19**
HYDROCO/APAP SOL 7.5-325	2	3000	50	$ 369.19
201603	**1**	**1500**	**25**	**$ 189.47**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 189.47
201604	**1**	**1500**	**25**	**$ 189.47**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 189.47
201605	**1**	**1500**	**34**	**$ 162.39**
HYDROCO/APAP SOL 7.5-325	1	1500	34	$ 162.39
201606	**1**	**120**	**30**	**$ 30.65**
HYDROCO/APAP TAB 7.5-325	1	120	30	$ 30.65
201607	**2**	**1520**	**29**	**$ 193.27**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 180.48
HYDROCO/APAP TAB 5-325MG	1	20	4	$ 12.79
201608	**1**	**1500**	**25**	**$ 175.53**

Member	Sum of Count Of RxClaim Nbr	Sum of Sum Of Metric Decimal Qty	Sum of Sum Of Days Supply	Sum of Sum Of Phr Due Amt
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 175.53
201609	**1**	**1500**	**25**	**$ 189.47**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 189.47
201610	**1**	**1500**	**25**	**$ 186.68**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 186.68
201611	**1**	**1500**	**25**	**$ 186.68**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 186.68
201612	**1**	**1500**	**25**	**$ 165.17**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 165.17
201701	**1**	**1500**	**25**	**$ 185.96**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 185.96
201702	**1**	**1500**	**25**	**$ 185.96**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 185.96
201703	**1**	**1500**	**25**	**$ 174.30**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 174.30
201704	**1**	**1500**	**25**	**$ 166.79**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 166.79
201705	**1**	**1500**	**25**	**$ 122.58**
HYDROCO/APAP SOL 7.5-325	1	1500	25	$ 122.58
201706	**1**	**1366**	**23**	**$ 112.54**
HYDROCO/APAP SOL 7.5-325	1	1366	23	$ 112.54
201707	**1**	**1950**	**33**	**$ 160.16**
HYDROCO/APAP SOL 7.5-325	1	1950	33	$ 160.16
Grand Total	**470**	**222557**	**12306**	**$ 58,484.11**

Top Prescribers from Each Class and Their Prescribing Trends
August 2015 - July 2017

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
Presc 1	**1,827**	**1,955**	**57,048**	**166,119**	**$ 105,959.72**
BUTRANS DIS 5MCG/HR	1	1	28	4	$ 245.48
ENDOCET TAB 10-325MG	2	2	60	240	$ 167.44
ENDOCET TAB 5-325MG	2	2	60	240	$ 57.24
FENTANYL DIS 12MCG/HR	4	4	120	55	$ 808.24
FENTANYL DIS 25MCG/HR	30	31	914	325	$ 1,541.76
FENTANYL DIS 50MCG/HR	15	16	480	160	$ 1,026.38
HYDROCO/APAP TAB 10-325MG	168	176	5,172	18,158	$ 5,267.55
HYDROCO/APAP TAB 5-325MG	142	150	4,378	9,830	$ 2,908.35
HYDROCO/APAP TAB 7.5-325	69	74	2,128	7,102	$ 1,859.77
HYSINGLA ER TAB 20 MG	3	3	90	90	$ 715.32
HYSINGLA ER TAB 30 MG	17	18	540	540	$ 5,882.39
METHADONE TAB 10MG	55	59	1,550	4,740	$ 1,075.43
MORPHINE SUL CAP 60MG ER	1	1	30	60	$ 429.64
MORPHINE SUL TAB 15MG ER	258	272	8,150	17,163	$ 8,907.27
MORPHINE SUL TAB 30MG ER	153	161	4,814	12,194	$ 9,476.71
MORPHINE SUL TAB 60MG ER	42	46	1,335	3,225	$ 4,360.24
OPANA ER TAB 20MG	23	25	750	1,500	$ 12,558.26
OXYCOD/APAP TAB 10-325MG	334	362	10,480	37,833	$ 25,915.55
OXYCOD/APAP TAB 5-325MG	82	91	2,614	9,142	$ 2,191.97
OXYCOD/APAP TAB 7.5-325	90	97	2,759	10,288	$ 6,462.74
OXYCODONE TAB 10MG	67	72	2,073	6,409	$ 2,102.92
OXYCODONE TAB 10MG ER	1	1	30	60	$ 116.44
OXYCODONE TAB 15MG	46	50	1,484	5,440	$ 1,595.55
OXYCODONE TAB 20MG ER	3	4	51	102	$ 382.37
OXYCODONE TAB 5MG	110	120	3,474	10,257	$ 2,384.34
OXYCONTIN TAB 20MG CR	10	12	360	720	$ 3,642.96
OXYCONTIN TAB 30MG CR	1	1	30	60	$ 432.03
OXYMORPHONE TAB 10MG ER	3	3	64	192	$ 685.19
OXYMORPHONE TAB 15MG ER	6	7	210	420	$ 1,696.41
TRAMADOL HCL TAB 50MG	89	94	2,820	9,570	$ 1,063.78
Presc 10	**1,662**	**1,964**	**46,800**	**151,922**	**$ 59,932.47**
BUT/APAP/CAF CAP CODEINE	1	1	5	30	$ 42.13
BUTRANS DIS 5MCG/HR	1	1	28	4	$ 245.48
ENDOCET TAB 10-325MG	1	1	30	60	$ 46.32
HYDROCO/APAP TAB 10-325MG	412	486	11,623	37,300	$ 11,318.67
HYDROCO/APAP TAB 5-325MG	217	256	6,374	17,706	$ 4,885.21
HYDROCO/APAP TAB 7.5-325	61	71	1,668	5,043	$ 1,331.78
HYDROMORPHON TAB 2MG	13	14	347	1,208	$ 247.99
HYDROMORPHON TAB 4MG	1	1	30	120	$ 22.29
METHADONE TAB 10MG	5	6	138	286	$ 75.13
METHADONE TAB 5MG	5	5	129	178	$ 53.75
MORPHINE SUL TAB 15MG ER	17	18	433	776	$ 405.02
MORPHINE SUL TAB 30MG ER	4	4	110	190	$ 186.42
OXYCOD/APAP TAB 10-325MG	366	437	10,459	36,242	$ 24,182.43
OXYCOD/APAP TAB 5-325MG	75	92	2,142	6,385	$ 1,564.44
OXYCOD/APAP TAB 7.5-325	17	22	508	1,540	$ 918.24
OXYCODONE CAP 5MG	1	1	30	120	$ 30.42

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OXYCODONE CON 100/5ML	6	6	160	300	$ 1,421.66
OXYCODONE TAB 10MG	269	330	7,478	27,752	$ 8,141.38
OXYCODONE TAB 15MG	95	104	2,417	9,174	$ 3,074.03
OXYCODONE TAB 5MG	71	82	2,074	6,158	$ 1,461.10
TRAMADOL HCL TAB 50MG	24	26	617	1,350	$ 278.58
Presc 11	**574**	**615**	**3,040**	**12,225**	**$ 7,699.67**
APAP/CODEINE TAB 300-30MG	84	87	427	1,724	$ 1,009.66
HYDROCO/APAP TAB 5-325MG	255	267	1,323	5,299	$ 3,310.65
HYDROCO/APAP TAB 7.5-325	190	209	1,020	4,090	$ 2,578.14
HYDROCOD/IBU TAB 7.5-200	1	2	9	35	$ 31.99
OXYCOD/APAP TAB 5-325MG	24	28	132	530	$ 324.72
OXYCOD/APAP TAB 7.5-325	18	20	94	377	$ 380.53
OXYCOD/ASA TAB	1	1	5	20	$ 22.48
OXYCODONE TAB 15MG	1	1	30	150	$ 41.50
Presc 12	**3,044**	**3,131**	**92,601**	**280,893**	**$ 303,429.10**
APAP/CODEINE TAB 300-60MG	9	10	208	416	$ 180.57
BUPRENORPHIN DIS 10MCG/HR	2	2	58	8	$ 655.80
BUT/APAP/CAF CAP CODEINE	20	20	600	1,320	$ 2,066.64
BUTRANS DIS 10MCG/HR	3	3	84	12	$ 1,036.55
BUTRANS DIS 15MCG/HR	13	13	366	52	$ 6,634.21
EMBEDA CAP 20-0.8MG	1	1	30	30	$ 184.40
EMBEDA CAP 30-1.2MG	4	4	120	120	$ 1,111.22
ENDOCET TAB 10-325MG	2	2	60	240	$ 149.59
ENDOCET TAB 7.5-325	46	46	1,380	4,750	$ 3,527.91
FENTANYL DIS 100MCG/H	1	1	30	10	$ 115.48
FENTANYL DIS 12MCG/HR	1	1	30	10	$ 150.11
FENTANYL DIS 25MCG/HR	3	3	60	20	$ 101.44
FENTANYL DIS 50MCG/HR	11	11	332	110	$ 702.07
HYDROCO/APAP TAB 10-325MG	458	470	14,007	47,535	$ 14,090.80
HYDROCO/APAP TAB 5-325MG	31	31	925	2,510	$ 693.94
HYDROCO/APAP TAB 7.5-325	386	391	11,624	38,719	$ 10,012.80
HYDROMORPHON TAB 2MG	45	46	1,253	3,184	$ 743.51
HYDROMORPHON TAB 4MG	123	129	3,650	8,205	$ 2,045.65
HYSINGLA ER TAB 20 MG	4	4	120	120	$ 935.70
HYSINGLA ER TAB 30 MG	5	5	150	150	$ 1,714.65
HYSINGLA ER TAB 60 MG	1	1	30	30	$ 627.64
METHADONE TAB 10MG	100	103	3,048	12,645	$ 2,524.81
METHADONE TAB 5MG	30	31	840	1,920	$ 554.35
MORPHINE SUL TAB 15MG	1	1	30	60	$ 17.32
MORPHINE SUL TAB 15MG ER	139	143	4,232	8,790	$ 4,552.32
MORPHINE SUL TAB 30MG ER	102	106	3,169	7,748	$ 6,418.13
NUCYNTA TAB 50MG	13	13	390	1,560	$ 6,992.52
OPANA ER TAB 15MG	20	21	630	1,620	$ 10,650.39
OPANA ER TAB 20MG	59	60	1,770	3,540	$ 29,531.91
OPANA ER TAB 30MG	26	28	840	1,650	$ 19,613.23
OXYCOD/APAP TAB 10-325MG	684	709	21,154	73,677	$ 50,635.18
OXYCOD/APAP TAB 5-325MG	36	37	1,110	2,940	$ 781.72
OXYCOD/APAP TAB 7.5-325	357	368	10,850	36,352	$ 21,747.29
OXYCODONE TAB 10MG	12	12	360	960	$ 311.83
OXYCODONE TAB 15MG	1	1	30	60	$ 20.06

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OXYCODONE TAB 20MG	1	1	30	60	$ 31.61
OXYCODONE TAB 30MG ER	1	1	30	60	$ 419.12
OXYCODONE TAB 40MG ER	12	14	420	870	$ 6,652.92
OXYCODONE TAB 5MG	7	8	224	462	$ 127.46
OXYCONTIN TAB 10MG CR	13	13	390	840	$ 2,504.13
OXYCONTIN TAB 15MG CR	85	87	2,610	5,760	$ 25,789.13
OXYCONTIN TAB 20MG CR	32	32	958	2,036	$ 10,918.86
OXYCONTIN TAB 30MG CR	51	54	1,620	3,270	$ 25,619.11
OXYCONTIN TAB 40MG CR	5	5	150	330	$ 2,890.71
OXYMORPHONE TAB 15MG ER	8	8	240	480	$ 2,019.38
OXYMORPHONE TAB 20MG ER	18	18	540	1,080	$ 6,068.73
OXYMORPHONE TAB 30MG ER	1	1	30	60	$ 594.61
OXYMORPHONE TAB 40MG ER	16	16	480	960	$ 9,906.44
OXYMORPHONE TAB HCL 10MG	41	42	1,227	3,351	$ 8,009.94
TRAMADOL HCL TAB 50MG	4	4	82	201	$ 45.21
Presc 13	**1,490**	**1,582**	**45,270**	**158,495**	**$ 169,452.45**
DURAGESIC DIS 50MCG/HR	3	3	90	30	$ 1,866.99
EMBEDA CAP 20-0.8MG	12	12	360	390	$ 2,377.82
EMBEDA CAP 30-1.2MG	15	15	450	630	$ 5,794.37
EMBEDA CAP 50-2MG	3	4	120	240	$ 2,902.16
EMBEDA CAP 80-3.2MG	10	11	270	540	$ 9,990.96
ENDOCET TAB 10-325MG	5	6	155	590	$ 398.35
FENTANYL DIS 100MCG/H	28	29	869	345	$ 3,967.96
FENTANYL DIS 25MCG/HR	2	2	60	20	$ 93.33
FENTANYL DIS 37.5MCG	2	2	60	20	$ 869.42
FENTANYL DIS 50MCG/HR	53	56	1,670	695	$ 4,369.95
FENTANYL DIS 75MCG/HR	33	34	1,018	385	$ 3,995.42
HYDROCO/APAP TAB 10-325MG	237	246	7,145	27,650	$ 7,815.23
HYDROCO/APAP TAB 7.5-325	62	65	1,867	6,231	$ 1,576.97
HYDROMORPHON TAB 32MG ER	6	7	210	210	$ 9,405.96
HYDROMORPHON TAB 4MG	21	25	361	2,180	$ 438.47
HYDROMORPHON TAB 8MG	7	8	209	820	$ 433.11
HYSINGLA ER TAB 20 MG	2	2	60	60	$ 476.88
METHADONE TAB 10MG	17	20	591	2,064	$ 445.98
MORPHINE SUL CAP 20MG ER	1	1	30	30	$ 117.99
MORPHINE SUL CAP 30MG ER	14	14	420	420	$ 1,584.38
MORPHINE SUL CAP 60MG ER	1	1	30	60	$ 413.81
MORPHINE SUL TAB 15MG	77	81	2,320	8,010	$ 2,234.87
MORPHINE SUL TAB 15MG ER	59	63	1,859	5,220	$ 2,582.91
MORPHINE SUL TAB 30MG	14	14	420	1,620	$ 552.94
MORPHINE SUL TAB 30MG ER	80	85	2,540	6,789	$ 5,212.81
MORPHINE SUL TAB 60MG ER	32	34	1,005	2,700	$ 2,997.47
NUCYNTA TAB 50MG	2	2	60	300	$ 1,539.12
OXYCOD/APAP TAB 10-325MG	231	241	6,913	28,079	$ 18,210.02
OXYCOD/APAP TAB 7.5-325	2	2	60	210	$ 126.10
OXYCODONE TAB 10MG	13	13	380	1,530	$ 421.34
OXYCODONE TAB 15MG	138	145	4,254	18,600	$ 5,494.21
OXYCODONE TAB 20MG ER	6	6	180	360	$ 1,684.86
OXYCODONE TAB 30MG	220	247	6,719	35,417	$ 15,039.35
OXYCODONE TAB 40MG ER	4	4	120	240	$ 1,881.35

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OXYCONTIN TAB 10MG CR	4	4	120	210	$ 663.01
OXYCONTIN TAB 20MG CR	6	7	210	420	$ 2,512.33
OXYCONTIN TAB 30MG CR	16	16	480	960	$ 7,367.72
OXYCONTIN TAB 40MG CR	21	23	690	1,410	$ 13,342.77
OXYCONTIN TAB 60MG CR	22	23	690	2,070	$ 28,152.31
TRAMADOL HCL TAB 50MG	9	9	205	740	$ 101.45
Presc 14	**2,138**	**2,439**	**64,655**	**221,892**	**$ 509,924.66**
APAP/CODEINE TAB 300-30MG	1	1	16	32	$ 14.90
BUPRENORPHIN SUB 8MG	2	2	60	75	$ 115.94
BUTRANS DIS 10MCG/HR	1	1	28	4	$ 363.69
BUTRANS DIS 20MCG/HR	1	1	28	4	$ 634.73
EMBEDA CAP 20-0.8MG	2	2	60	90	$ 558.66
EMBEDA CAP 30-1.2MG	1	1	30	30	$ 273.51
EXALGO TAB 16MG	1	1	30	30	$ 770.83
FENTANYL DIS 25MCG/HR	3	3	90	30	$ 136.59
HYDROCO/APAP TAB 10-325MG	208	216	6,069	27,805	$ 7,450.15
HYDROCO/APAP TAB 5-325MG	12	12	360	1,440	$ 325.11
HYDROCO/APAP TAB 7.5-325	9	9	270	1,050	$ 270.40
HYDROMORPHON TAB 2MG	10	11	205	1,110	$ 200.91
HYDROMORPHON TAB 4MG	65	69	2,035	7,050	$ 1,346.35
HYDROMORPHON TAB 8MG	41	42	1,260	4,860	$ 2,274.44
HYSINGLA ER TAB 20 MG	2	2	60	60	$ 476.88
HYSINGLA ER TAB 30 MG	2	2	60	60	$ 685.94
METHADONE TAB 10MG	102	108	3,225	19,140	$ 3,424.72
MORPHINE SUL CAP 60MG ER	2	2	60	120	$ 833.03
MORPHINE SUL CAP 80MG ER	4	4	120	240	$ 2,274.79
MORPHINE SUL TAB 100MG ER	10	11	330	420	$ 893.57
MORPHINE SUL TAB 15MG	8	8	240	960	$ 282.77
MORPHINE SUL TAB 15MG ER	28	30	885	1,935	$ 1,011.35
MORPHINE SUL TAB 30MG	3	3	90	300	$ 121.99
MORPHINE SUL TAB 30MG ER	78	82	2,460	6,060	$ 4,788.30
MORPHINE SUL TAB 60MG ER	76	79	2,370	5,790	$ 7,628.59
OPANA ER TAB 30MG	3	3	90	180	$ 2,107.41
OPANA ER TAB 40MG	3	3	90	180	$ 2,746.35
OXYCOD/APAP TAB 10-325MG	191	199	5,826	22,714	$ 13,612.70
OXYCOD/APAP TAB 5-325MG	3	3	90	300	$ 67.63
OXYCOD/APAP TAB 7.5-325	22	23	665	3,000	$ 1,855.87
OXYCODONE TAB 10MG	83	88	2,534	10,373	$ 2,870.07
OXYCODONE TAB 15MG	236	261	7,467	35,034	$ 9,921.48
OXYCODONE TAB 20MG	47	49	1,410	5,528	$ 2,399.45
OXYCODONE TAB 30MG	202	219	6,560	19,530	$ 9,046.98
OXYCODONE TAB 40MG ER	14	15	450	930	$ 7,541.13
OXYCODONE TAB 5MG	20	21	525	2,250	$ 468.66
OXYCONTIN TAB 20MG CR	5	5	150	360	$ 2,099.42
OXYCONTIN TAB 30MG CR	17	18	540	1,350	$ 10,572.46
OXYCONTIN TAB 40MG CR	38	42	1,260	3,270	$ 30,855.71
OXYCONTIN TAB 60MG CR	24	24	720	1,440	$ 19,655.21
OXYCONTIN TAB 80MG CR	5	5	150	300	$ 5,258.54
OXYMORPHONE TAB 10MG ER	2	2	50	100	$ 281.85
OXYMORPHONE TAB 20MG ER	2	2	60	120	$ 723.22

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OXYMORPHONE TAB 30MG ER	1	1	30	60	$ 262.46
OXYMORPHONE TAB 40MG ER	2	2	60	120	$ 1,040.77
OXYMORPHONE TAB HCL 10MG	46	49	1,409	6,110	$ 13,805.14
OXYMORPHONE TAB HCL 5MG	10	10	227	510	$ 818.98
SUBOXONE MIS 12-3MG	4	4	45	90	$ 1,311.29
SUBOXONE MIS 2-0.5MG	55	57	1,665	3,165	$ 13,321.30
SUBOXONE MIS 4-1MG	17	18	516	943	$ 6,976.72
SUBOXONE MIS 8-2MG	333	531	9,267	15,730	$ 119,591.01
SUBSYS SPR 200MCG	4	4	110	480	$ 25,986.12
SUBSYS SPR 400MCG	6	6	180	720	$ 68,534.46
SUBSYS SPR 600MCG	6	6	180	720	$ 98,191.02
TRAMADOL HCL TAB 50MG	65	67	1,888	7,590	$ 843.11
Presc 15	**1,847**	**1,887**	**53,830**	**178,236**	**$ 87,302.00**
APAP/CODEINE TAB 300-60MG	1	1	30	90	$ 31.01
BUTRANS DIS 10MCG/HR	1	1	30	4	$ 308.12
ENDOCET TAB 10-325MG	1	1	30	120	$ 89.49
ENDOCET TAB 7.5-325	1	1	30	90	$ 57.57
FENTANYL DIS 12MCG/HR	4	4	75	25	$ 374.81
FENTANYL DIS 25MCG/HR	14	14	366	122	$ 608.06
FENTANYL DIS 37.5MCG	1	1	15	5	$ 221.28
FENTANYL DIS 50MCG/HR	14	15	422	140	$ 909.75
HYDROCO/APAP TAB 10-325MG	564	578	16,598	61,517	$ 18,393.24
HYDROCO/APAP TAB 5-325MG	31	32	787	2,296	$ 684.40
HYDROCO/APAP TAB 7.5-325	55	55	1,575	5,085	$ 1,325.36
HYDROCOD/IBU TAB 7.5-200	2	2	60	240	$ 128.37
METHADONE TAB 10MG	43	43	1,259	3,761	$ 829.40
METHADONE TAB 5MG	6	6	180	450	$ 118.69
MORPHINE SUL TAB 100MG ER	4	4	120	240	$ 558.91
MORPHINE SUL TAB 15MG	11	11	330	810	$ 233.76
MORPHINE SUL TAB 15MG ER	209	215	6,150	12,638	$ 6,485.81
MORPHINE SUL TAB 30MG	2	2	60	240	$ 76.22
MORPHINE SUL TAB 30MG ER	64	67	1,920	4,690	$ 4,161.23
MORPHINE SUL TAB 60MG ER	20	22	585	1,245	$ 1,899.69
NUCYNTA TAB 50MG	3	3	90	210	$ 1,008.76
NUCYNTA TAB 75MG	4	4	120	450	$ 2,317.92
OPANA ER TAB 10MG	7	7	195	330	$ 1,599.11
OPANA ER TAB 30MG	3	3	90	180	$ 2,122.23
OXYCOD/APAP TAB 10-325MG	308	310	9,114	34,463	$ 24,107.87
OXYCOD/APAP TAB 5-325MG	10	10	270	990	$ 235.16
OXYCOD/APAP TAB 7.5-325	43	45	1,236	4,204	$ 2,735.30
OXYCODONE TAB 10MG	230	234	6,847	25,625	$ 7,372.53
OXYCODONE TAB 15MG	88	90	2,655	9,945	$ 3,528.50
OXYCODONE TAB 30MG	7	8	225	705	$ 337.80
OXYCODONE TAB 5MG	14	14	365	1,310	$ 285.55
OXYMORPHONE TAB 15MG ER	1	1	15	60	$ 253.84
OXYMORPHONE TAB 30MG ER	2	2	60	180	$ 1,473.03
OXYMORPHONE TAB 5MG ER	5	5	150	300	$ 454.40
TRAMADL/APAP TAB 37.5-325	4	4	75	180	$ 82.72
TRAMADOL HCL TAB 100MG ER	2	2	51	51	$ 149.73
TRAMADOL HCL TAB 50MG	63	65	1,500	4,645	$ 707.24

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
VICODIN HP TAB 10-300MG	5	5	150	600	$ 1,035.14
Presc 16	**988**	**1,603**	**24,425**	**65,401**	**$ 189,289.90**
APAP/CODEINE TAB 300-30MG	13	14	209	1,190	$ 288.43
APAP/CODEINE TAB 300-60MG	6	6	162	600	$ 196.60
BUNAVAIL MIS 6.3-1MG	2	2	28	56	$ 815.53
HYDROCO/APAP TAB 10-325MG	129	132	3,639	14,290	$ 4,053.60
HYDROCO/APAP TAB 5-325MG	73	74	1,206	4,250	$ 1,362.26
HYDROCO/APAP TAB 7.5-300	1	1	6	40	$ 60.04
HYDROCO/APAP TAB 7.5-325	17	18	490	977	$ 337.15
HYDROMORPHON TAB 2MG	2	2	35	110	$ 27.57
HYDROMORPHON TAB 4MG	2	2	17	80	$ 28.16
METHADONE TAB 10MG	10	10	225	600	$ 175.32
MORPHINE SUL TAB 15MG	6	7	194	583	$ 145.22
MORPHINE SUL TAB 30MG	2	2	60	180	$ 52.26
OXYCOD/APAP TAB 10-325MG	33	36	884	4,566	$ 2,783.84
OXYCOD/APAP TAB 5-325MG	23	25	636	1,898	$ 510.20
OXYCOD/APAP TAB 7.5-325	9	9	181	810	$ 439.73
OXYCODONE TAB 10MG	1	1	30	90	$ 26.53
OXYCODONE TAB 15MG	2	2	46	150	$ 52.79
OXYCODONE TAB 30MG	4	5	69	276	$ 147.96
SUBOXONE MIS 12-3MG	118	207	3,027	3,029	$ 45,820.98
SUBOXONE MIS 2-0.5MG	9	14	231	261	$ 1,184.58
SUBOXONE MIS 4-1MG	26	29	698	698	$ 5,277.07
SUBOXONE MIS 8-2MG	385	876	10,010	15,987	$ 123,876.45
TRAMADOL HCL TAB 50MG	115	129	2,342	14,680	$ 1,627.63
Presc 17	**1,862**	**1,898**	**56,496**	**190,994**	**$ 96,302.85**
APAP/CODEINE TAB 300-30MG	2	2	60	120	$ 34.54
APAP/CODEINE TAB 300-60MG	4	4	120	360	$ 121.16
ENDOCET TAB 10-325MG	4	4	120	420	$ 306.60
ENDOCET TAB 7.5-325	1	1	30	90	$ 95.40
HYDROCO/APAP TAB 10-300MG	1	1	25	150	$ 234.87
HYDROCO/APAP TAB 10-325MG	501	509	15,203	54,242	$ 15,859.47
HYDROCO/APAP TAB 5-325MG	78	82	2,412	6,029	$ 1,655.26
HYDROCO/APAP TAB 7.5-325	66	67	1,978	6,024	$ 1,622.79
HYDROCOD/IBU TAB 10-200MG	3	3	90	330	$ 1,060.33
HYDROCOD/IBU TAB 7.5-200	6	6	180	660	$ 344.98
METHADONE TAB 10MG	14	14	372	2,035	$ 394.92
MORPHINE SUL TAB 15MG	23	24	720	2,280	$ 617.90
MORPHINE SUL TAB 15MG ER	97	99	2,958	6,546	$ 3,298.49
MORPHINE SUL TAB 30MG ER	125	129	3,852	8,784	$ 7,319.94
MORPHINE SUL TAB 60MG ER	6	6	180	480	$ 714.16
NUCYNTA TAB 50MG	1	1	30	120	$ 518.62
OPANA ER TAB 10MG	1	1	30	60	$ 297.78
OPANA ER TAB 20MG	4	4	120	240	$ 1,956.16
OPANA ER TAB 30MG	1	1	30	60	$ 702.47
OXYCOD/APAP TAB 10-325MG	440	446	13,279	51,140	$ 34,823.78
OXYCOD/APAP TAB 5-325MG	42	44	1,320	3,540	$ 947.51
OXYCOD/APAP TAB 7.5-325	82	84	2,520	7,740	$ 5,337.30
OXYCODONE TAB 10MG	156	158	4,717	16,948	$ 4,917.23
OXYCODONE TAB 15MG	111	115	3,426	15,149	$ 5,027.85

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OXYCODONE TAB 5MG	17	17	510	1,290	$ 318.90
OXYMORPHONE TAB 10MG ER	11	11	330	660	$ 2,057.71
OXYMORPHONE TAB 15MG ER	2	2	60	120	$ 451.15
OXYMORPHONE TAB 20MG ER	4	4	120	240	$ 1,120.68
OXYMORPHONE TAB 5MG ER	3	3	90	180	$ 304.52
OXYMORPHONE TAB 7.5MG ER	4	4	120	240	$ 530.72
OXYMORPHONE TAB HCL 5MG	4	4	115	460	$ 520.37
SUBOXONE MIS 8-2MG	2	2	14	42	$ 333.66
TRAMADOL HCL TAB 50MG	44	44	1,305	4,035	$ 516.88
ZUBSOLV SUB 8.6-2.1	2	2	60	180	$ 1,938.75
Presc 18	**2,598**	**2,755**	**76,451**	**261,697**	**$ 132,465.23**
APAP/CODEINE TAB 300-30MG	3	3	21	63	$ 37.71
HYDROCO/APAP TAB 10-325MG	957	1,007	28,289	101,431	$ 30,462.46
HYDROCO/APAP TAB 5-325MG	59	60	1,647	5,618	$ 1,390.82
HYDROCO/APAP TAB 7.5-325	83	89	2,078	7,303	$ 1,978.15
HYDROMORPHON TAB 2MG	14	14	388	1,432	$ 270.35
HYDROMORPHON TAB 4MG	20	20	600	2,040	$ 389.18
HYDROMORPHON TAB 8MG	4	5	150	570	$ 287.18
LORCET HD TAB 10-325MG	1	1	30	120	$ 47.35
METHADONE TAB 10MG	42	43	1,255	7,440	$ 1,318.23
METHADONE TAB 5MG	9	9	270	540	$ 147.10
MORPHINE SUL TAB 100MG ER	8	8	240	480	$ 1,080.38
MORPHINE SUL TAB 15MG	31	33	960	2,880	$ 851.03
MORPHINE SUL TAB 15MG ER	90	95	2,600	5,680	$ 2,977.41
MORPHINE SUL TAB 30MG ER	170	177	5,180	10,773	$ 8,928.19
MORPHINE SUL TAB 60MG ER	11	11	330	750	$ 1,024.54
NUCYNTA ER TAB 100MG	12	12	360	720	$ 6,302.49
NUCYNTA ER TAB 50MG	8	8	240	480	$ 2,278.25
NUCYNTA TAB 50MG	8	8	240	480	$ 2,085.35
OPANA ER TAB 10MG	1	1	30	60	$ 278.07
OPANA ER TAB 40MG	1	2	60	120	$ 1,830.90
OPANA ER TAB 5MG	1	1	30	60	$ 147.09
OXYCOD/APAP TAB 10-325MG	592	633	17,683	64,980	$ 43,970.44
OXYCOD/APAP TAB 5-325MG	46	50	1,157	3,489	$ 986.54
OXYCOD/APAP TAB 7.5-325	59	66	1,691	5,883	$ 3,501.11
OXYCODONE TAB 10MG	203	228	5,920	20,015	$ 6,171.51
OXYCODONE TAB 15MG	60	62	1,835	7,440	$ 2,271.12
OXYCODONE TAB 30MG	5	5	148	592	$ 274.81
OXYCODONE TAB 5MG	19	20	590	2,250	$ 476.53
OXYCONTIN TAB 20MG CR	19	20	584	1,168	$ 6,313.44
OXYCONTIN TAB 30MG CR	4	4	120	240	$ 1,768.07
OXYCONTIN TAB 40MG CR	2	2	60	120	$ 1,061.82
OXYCONTIN TAB 60MG CR	1	1	30	60	$ 749.70
OXYMORPHONE TAB HCL 5MG	1	1	30	60	$ 108.14
TRAMADOL HCL TAB 50MG	54	56	1,605	6,360	$ 699.77
Presc 19	**1,870**	**1,934**	**55,346**	**165,034**	**$ 149,635.29**
APAP/CODEINE TAB 300-60MG	2	3	90	180	$ 72.43
BUT/APAP/CAF CAP CODEINE	10	10	267	554	$ 733.82
BUTRANS DIS 15MCG/HR	5	6	168	24	$ 2,609.79
EMBEDA CAP 30-1.2MG	3	3	90	150	$ 1,358.78

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
ENDOCET TAB 10-325MG	1	1	19	79	$ 62.39
ENDOCET TAB 7.5-325	13	14	397	1,178	$ 1,001.39
HYDROCO/APAP TAB 10-325MG	315	322	9,281	31,309	$ 9,532.79
HYDROCO/APAP TAB 5-325MG	45	45	1,307	3,084	$ 901.29
HYDROCO/APAP TAB 7.5-325	354	368	10,357	31,847	$ 8,654.20
HYDROMORPHON TAB 2MG	18	18	480	1,380	$ 296.54
HYDROMORPHON TAB 4MG	53	55	1,601	4,794	$ 991.78
HYDROMORPHON TAB 8MG	1	1	30	30	$ 21.15
HYSINGLA ER TAB 20 MG	3	3	74	148	$ 1,156.64
HYSINGLA ER TAB 30 MG	1	1	30	30	$ 313.91
METHADONE TAB 10MG	37	37	1,077	4,230	$ 888.02
METHADONE TAB 5MG	4	4	105	240	$ 77.40
MORPHINE SUL CAP 20MG ER	1	1	20	60	$ 216.46
MORPHINE SUL TAB 15MG	3	3	90	270	$ 85.92
MORPHINE SUL TAB 15MG ER	157	162	4,542	10,845	$ 5,629.38
MORPHINE SUL TAB 30MG ER	46	48	1,385	3,078	$ 2,502.54
NUCYNTA ER TAB 50MG	11	11	330	660	$ 3,319.81
NUCYNTA TAB 50MG	4	4	120	240	$ 1,209.50
OPANA ER TAB 10MG	1	1	30	60	$ 297.78
OPANA ER TAB 15MG	5	5	150	420	$ 2,674.87
OPANA ER TAB 20MG	2	2	60	120	$ 964.15
OPANA ER TAB 30MG	18	19	570	1,140	$ 13,631.63
OXYCOD/APAP TAB 10-325MG	310	325	9,322	31,746	$ 22,608.12
OXYCOD/APAP TAB 5-325MG	25	25	734	1,992	$ 522.01
OXYCOD/APAP TAB 7.5-325	227	237	6,790	20,985	$ 13,653.72
OXYCODONE TAB 10MG	13	13	342	994	$ 338.49
OXYCODONE TAB 15MG	5	5	150	540	$ 157.70
OXYCODONE TAB 20MG	1	1	30	60	$ 31.08
OXYCODONE TAB 20MG ER	1	1	30	60	$ 290.28
OXYCODONE TAB 30MG	1	1	30	120	$ 51.43
OXYCODONE TAB 40MG ER	6	6	180	420	$ 2,995.56
OXYCODONE TAB 5MG	20	20	600	1,620	$ 385.40
OXYCONTIN TAB 10MG CR	2	2	60	180	$ 503.72
OXYCONTIN TAB 15MG CR	19	20	554	1,272	$ 5,787.03
OXYCONTIN TAB 20MG CR	31	31	930	2,070	$ 11,488.86
OXYCONTIN TAB 30MG CR	18	18	508	1,046	$ 8,171.05
OXYCONTIN TAB 40MG CR	13	14	420	1,260	$ 11,284.81
OXYMORPHONE TAB 15MG ER	15	16	480	930	$ 3,752.18
OXYMORPHONE TAB 20MG ER	6	6	180	360	$ 1,778.49
OXYMORPHONE TAB 40MG ER	3	3	90	180	$ 1,398.19
OXYMORPHONE TAB 5MG ER	2	2	44	88	$ 195.20
OXYMORPHONE TAB HCL 10MG	23	25	750	1,500	$ 3,789.40
SUBOXONE MIS 8-2MG	2	2	60	120	$ 897.90
TRAMADOL HCL TAB 50MG	13	13	362	1,221	$ 151.82
VICODIN HP TAB 10-300MG	1	1	30	120	$ 198.49
Presc 2	**1,358**	**1,417**	**39,863**	**217,538**	**$ 106,836.07**
APAP/CODEINE TAB 300-60MG	15	17	509	3,960	$ 1,021.34
EMBEDA CAP 50-2MG	1	1	14	14	$ 168.57
FENTANYL DIS 100MCG/H	4	5	120	40	$ 851.90
FENTANYL DIS 25MCG/HR	8	10	249	85	$ 422.69

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
FENTANYL DIS 50MCG/HR	9	9	245	85	$ 557.84
FENTANYL DIS 75MCG/HR	16	16	480	160	$ 1,681.83
HYDROCO/APAP TAB 10-325MG	419	433	12,444	78,917	$ 19,395.95
HYDROCO/APAP TAB 5-325MG	4	4	104	540	$ 130.22
HYDROCO/APAP TAB 7.5-325	24	25	704	3,590	$ 801.40
HYDROMORPHON TAB 4MG	19	22	499	3,250	$ 532.25
HYDROMORPHON TAB 8MG	10	11	254	1,525	$ 590.06
METHADONE TAB 10MG	85	89	2,628	18,912	$ 3,274.15
MORPHINE SUL CAP 30MG ER	15	15	450	450	$ 2,021.01
MORPHINE SUL TAB 100MG ER	21	21	630	1,740	$ 3,085.48
MORPHINE SUL TAB 15MG	2	2	60	360	$ 94.21
MORPHINE SUL TAB 30MG	41	41	1,040	6,960	$ 2,506.12
MORPHINE SUL TAB 30MG ER	62	63	1,878	4,560	$ 3,460.91
MORPHINE SUL TAB 60MG ER	44	45	1,268	3,577	$ 4,663.53
OXYCOD/APAP TAB 10-325MG	151	155	4,306	26,150	$ 17,104.94
OXYCOD/APAP TAB 5-325MG	10	10	178	1,100	$ 261.01
OXYCOD/APAP TAB 7.5-325	37	37	1,085	5,370	$ 3,048.67
OXYCODONE TAB 10MG	80	84	2,385	14,580	$ 3,655.30
OXYCODONE TAB 15MG	64	67	1,883	10,524	$ 2,782.24
OXYCODONE TAB 20MG	35	38	1,063	6,351	$ 3,083.59
OXYCODONE TAB 30MG	77	83	2,400	9,360	$ 4,174.83
OXYCONTIN TAB 20MG CR	1	1	30	60	$ 340.65
OXYCONTIN TAB 30MG CR	29	33	964	2,618	$ 20,804.10
OXYCONTIN TAB 40MG CR	3	4	60	180	$ 1,744.62
OXYCONTIN TAB 60MG CR	3	3	90	270	$ 3,565.99
TRAMADOL HCL TAB 50MG	69	73	1,843	12,250	$ 1,010.67
Presc 20	**1,207**	**1,263**	**34,401**	**112,627**	**$ 74,955.05**
BUT/APAP/CAF CAP CODEINE	2	2	30	180	$ 941.06
BUTRANS DIS 15MCG/HR	1	1	28	4	$ 416.88
BUTRANS DIS 20MCG/HR	1	1	28	4	$ 536.01
ENDOCET TAB 10-325MG	4	4	120	450	$ 331.95
FENTANYL DIS 12MCG/HR	1	1	30	10	$ 153.87
FENTANYL DIS 25MCG/HR	8	8	210	75	$ 364.82
FENTANYL DIS 50MCG/HR	3	3	91	30	$ 190.49
FENTANYL DIS 75MCG/HR	1	2	30	10	$ 157.96
HYDROCO/APAP TAB 10-325MG	310	321	8,656	31,536	$ 9,827.27
HYDROCO/APAP TAB 5-325MG	34	36	708	2,057	$ 649.94
HYDROCO/APAP TAB 7.5-325	38	39	952	2,873	$ 870.76
HYDROMORPHON TAB 8MG	3	3	90	270	$ 121.56
METHADONE TAB 10MG	23	23	685	2,700	$ 553.12
METHADONE TAB 5MG	5	5	135	285	$ 68.20
MORPHINE SUL TAB 100MG ER	3	3	90	210	$ 444.66
MORPHINE SUL TAB 15MG	5	5	150	360	$ 96.75
MORPHINE SUL TAB 15MG ER	86	89	2,440	4,875	$ 2,722.59
MORPHINE SUL TAB 30MG	5	6	165	660	$ 278.27
MORPHINE SUL TAB 30MG ER	78	84	2,306	4,954	$ 4,454.54
MORPHINE SUL TAB 60MG ER	23	23	618	1,146	$ 1,645.51
NUCYNTA TAB 75MG	3	3	90	360	$ 1,755.42
OPANA ER TAB 10MG	4	4	120	150	$ 713.81
OPANA ER TAB 20MG	3	3	90	180	$ 1,507.53

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OPANA ER TAB 30MG	4	4	120	240	$ 2,824.70
OPANA ER TAB 40MG	6	6	180	360	$ 5,835.30
OXYCOD/APAP TAB 10-325MG	228	243	6,639	24,820	$ 17,982.67
OXYCOD/APAP TAB 5-325MG	11	13	370	1,110	$ 291.34
OXYCOD/APAP TAB 7.5-325	27	30	855	2,970	$ 2,081.66
OXYCODONE TAB 10MG	77	78	2,193	7,982	$ 2,435.64
OXYCODONE TAB 15MG	92	99	2,792	10,728	$ 3,413.66
OXYCODONE TAB 20MG	6	6	180	780	$ 322.16
OXYCODONE TAB 30MG	50	53	1,493	5,560	$ 2,515.85
OXYCODONE TAB 40MG ER	1	1	30	60	$ 489.89
OXYCODONE TAB 5MG	9	9	270	900	$ 199.88
OXYCONTIN TAB 15MG CR	2	2	60	120	$ 545.98
OXYCONTIN TAB 20MG CR	1	1	30	60	$ 344.94
OXYCONTIN TAB 60MG CR	2	2	60	120	$ 1,638.46
OXYMORPHONE TAB 30MG ER	7	7	210	600	$ 3,959.73
OXYMORPHONE TAB HCL 10MG	1	1	10	30	$ 81.84
OXYMORPHONE TAB HCL 5MG	2	2	60	120	$ 194.89
TRAMADOL HCL TAB 100MG ER	2	2	60	60	$ 157.54
TRAMADOL HCL TAB 50MG	33	33	867	2,388	$ 367.40
VICODIN HP TAB 10-300MG	2	2	60	240	$ 468.55
Presc 21	**854**	**881**	**4,416**	**19,704**	**$ 11,866.71**
APAP/CODEINE TAB 300-30MG	29	29	100	534	$ 335.01
HYDROCO/APAP SOL 7.5-325	4	4	24	1,200	$ 242.73
HYDROCO/APAP TAB 10-325MG	130	139	745	3,008	$ 1,869.12
HYDROCO/APAP TAB 5-325MG	158	159	834	3,293	$ 2,018.84
HYDROCO/APAP TAB 7.5-325	374	378	1,957	7,944	$ 4,849.01
OXYCOD/APAP TAB 10-325MG	42	47	232	1,098	$ 1,088.53
OXYCOD/APAP TAB 5-325MG	94	102	423	2,187	$ 1,213.61
OXYCOD/APAP TAB 7.5-325	1	1	2	12	$ 15.87
OXYCODONE TAB 10MG	3	3	15	50	$ 37.53
OXYCODONE TAB 5MG	10	10	48	194	$ 120.76
TRAMADOL HCL TAB 50MG	9	9	36	184	$ 75.70
Presc 22	**1,297**	**1,322**	**4,810**	**30,336**	**$ 18,526.80**
APAP/CODEINE SOL 120-12/5	10	10	67	2,000	$ 101.53
APAP/CODEINE TAB 300-30MG	115	119	356	1,974	$ 1,246.60
ENDOCET TAB 5-325MG	1	1	3	20	$ 13.08
ENDOCET TAB 7.5-325	6	6	26	122	$ 133.97
HYDROCO/APAP SOL 7.5-325	3	3	43	1,750	$ 233.52
HYDROCO/APAP TAB 10-325MG	73	73	297	1,694	$ 1,016.31
HYDROCO/APAP TAB 5-325MG	398	405	1,279	7,339	$ 4,983.65
HYDROCO/APAP TAB 7.5-325	237	238	890	4,978	$ 3,048.36
HYDROMORPHON TAB 2MG	10	11	37	202	$ 111.97
HYDROMORPHON TAB 4MG	15	15	65	311	$ 160.46
MEPERIDINE TAB 100MG	2	2	8	40	$ 59.88
MEPERIDINE TAB 50MG	1	1	5	30	$ 14.32
OXYCOD/APAP TAB 10-325MG	90	94	414	2,275	$ 2,193.54
OXYCOD/APAP TAB 5-325MG	208	211	773	4,299	$ 2,239.66
OXYCOD/APAP TAB 7.5-325	123	127	523	3,036	$ 2,864.80
OXYCODONE SOL 5MG/5ML	1	1	3	150	$ 44.37
OXYCODONE TAB 15MG	2	3	11	66	$ 39.30

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
TRAMADOL HCL TAB 50MG	2	2	10	50	$ 21.48
Presc 23	**2,061**	**2,139**	**61,464**	**211,748**	**$ 83,422.49**
APAP/CODEINE TAB 300-30MG	1	1	7	20	$ 13.13
BUT/APAP/CAF CAP CODEINE	1	1	17	30	$ 163.62
BUTORPHANOL SOL 10MG/ML	4	4	112	20	$ 332.17
ENDOCET TAB 10-325MG	4	5	150	810	$ 562.67
FENTANYL DIS 25MCG/HR	28	31	930	310	$ 1,467.54
FENTANYL DIS 50MCG/HR	4	6	95	32	$ 232.05
HYDROCO/APAP TAB 10-325MG	407	419	11,966	40,740	$ 11,861.42
HYDROCO/APAP TAB 5-325MG	46	46	1,229	3,192	$ 893.59
HYDROCO/APAP TAB 7.5-325	82	86	2,406	7,636	$ 2,039.89
HYDROMORPHON TAB 2MG	8	8	213	516	$ 114.88
HYDROMORPHON TAB 4MG	49	51	1,461	4,075	$ 893.59
METHADONE TAB 10MG	37	39	1,155	3,780	$ 834.74
MORPHINE SUL TAB 100MG ER	3	3	67	195	$ 415.07
MORPHINE SUL TAB 15MG	26	26	730	2,330	$ 742.42
MORPHINE SUL TAB 15MG ER	39	39	1,165	1,940	$ 1,075.12
MORPHINE SUL TAB 30MG ER	46	47	1,410	3,990	$ 2,006.12
MORPHINE SUL TAB 60MG ER	49	52	1,523	3,391	$ 4,635.11
OXYCOD/APAP TAB 10-325MG	312	321	9,271	34,900	$ 22,866.23
OXYCOD/APAP TAB 5-325MG	62	65	1,817	4,780	$ 1,208.08
OXYCOD/APAP TAB 7.5-325	35	36	1,050	3,585	$ 2,246.60
OXYCODONE CAP 5MG	3	3	90	180	$ 123.44
OXYCODONE TAB 10MG	227	237	7,022	28,570	$ 7,732.53
OXYCODONE TAB 15MG	109	112	3,297	12,021	$ 3,096.56
OXYCODONE TAB 20MG	37	39	1,170	5,880	$ 2,488.03
OXYCODONE TAB 30MG	3	4	97	300	$ 149.96
OXYCODONE TAB 5MG	131	140	3,579	11,239	$ 2,627.76
OXYCONTIN TAB 20MG CR	14	15	450	870	$ 5,219.37
OXYCONTIN TAB 30MG CR	8	8	238	476	$ 3,708.37
TRAMADOL HCL TAB 50MG	286	295	8,747	35,940	$ 3,672.43
Presc 24	**4,384**	**4,524**	**133,796**	**416,044**	**$ 399,463.07**
APAP/CODEINE TAB 300-30MG	2	2	60	300	$ 57.57
BUT/ASA/CAF/ CAP COD 30MG	16	17	510	2,040	$ 3,093.58
EMBEDA CAP 20-0.8MG	22	24	705	870	$ 5,361.10
EMBEDA CAP 30-1.2MG	50	52	1,560	2,730	$ 24,712.69
EMBEDA CAP 50-2MG	1	1	30	45	$ 549.87
EMBEDA CAP 60-2.4MG	1	1	30	60	$ 832.90
ENDOCET TAB 10-325MG	3	3	90	450	$ 288.44
FENTANYL DIS 100MCG/H	1	1	28	10	$ 244.49
FENTANYL DIS 25MCG/HR	20	20	586	195	$ 977.98
FENTANYL DIS 50MCG/HR	15	15	450	150	$ 974.09
FENTANYL DIS 75MCG/HR	11	11	330	110	$ 1,115.80
HYDROCO/APAP TAB 10-300MG	1	1	29	115	$ 196.58
HYDROCO/APAP TAB 10-325MG	645	666	19,577	78,047	$ 21,854.70
HYDROCO/APAP TAB 5-325MG	6	6	180	255	$ 96.11
HYDROCO/APAP TAB 7.5-325	93	97	2,861	9,495	$ 2,399.09
HYDROMORPHON TAB 4MG	37	37	1,073	2,620	$ 623.51
HYDROMORPHON TAB 8MG	5	5	150	600	$ 284.37
HYDROMORPHON TAB 8MG ER	2	2	60	90	$ 897.36

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
HYSINGLA ER TAB 20 MG	12	12	360	360	$ 2,746.32
LAZANDA SPR 100MCG	10	10	298	80	$ 42,656.74
METHADONE TAB 10MG	51	52	1,552	6,260	$ 1,265.55
MORPHINE SUL CAP 80MG ER	1	1	30	60	$ 464.84
MORPHINE SUL SOL 10MG/5ML	6	6	180	3,150	$ 202.66
MORPHINE SUL TAB 100MG ER	13	13	390	780	$ 1,425.98
MORPHINE SUL TAB 15MG	23	26	780	2,580	$ 688.98
MORPHINE SUL TAB 15MG ER	286	287	8,495	11,977	$ 7,151.33
MORPHINE SUL TAB 30MG	91	92	2,737	9,517	$ 3,718.89
MORPHINE SUL TAB 30MG ER	566	586	17,304	30,950	$ 25,242.59
MORPHINE SUL TAB 60MG ER	193	200	6,000	12,720	$ 16,683.74
OPANA ER TAB 10MG	4	4	120	240	$ 1,129.87
OPANA ER TAB 15MG	7	8	240	420	$ 2,736.35
OPANA ER TAB 20MG	20	20	600	1,170	$ 9,846.51
OPANA ER TAB 30MG	18	19	570	1,140	$ 13,442.91
OPANA ER TAB 40MG	11	11	330	660	$ 10,349.01
OXYCOD/APAP TAB 10-325MG	732	754	22,249	83,710	$ 55,970.04
OXYCOD/APAP TAB 5-325MG	20	20	578	2,177	$ 506.00
OXYCOD/APAP TAB 7.5-325	45	46	1,380	3,810	$ 2,571.71
OXYCODONE SOL 5MG/5ML	8	8	240	7,400	$ 1,571.44
OXYCODONE TAB 10MG	43	46	1,375	4,650	$ 1,330.75
OXYCODONE TAB 10MG ER	2	2	53	75	$ 201.74
OXYCODONE TAB 15MG	357	367	10,917	39,126	$ 11,489.93
OXYCODONE TAB 20MG	4	5	150	600	$ 237.07
OXYCODONE TAB 20MG ER	2	2	60	120	$ 561.62
OXYCODONE TAB 30MG	639	664	19,464	77,560	$ 33,708.19
OXYCODONE TAB 40MG ER	35	38	1,140	2,070	$ 16,521.44
OXYCODONE TAB 5MG	3	3	80	330	$ 65.72
OXYCODONE TAB 80MG ER	9	10	300	600	$ 8,144.50
OXYCONTIN TAB 10MG CR	13	15	440	460	$ 1,466.52
OXYCONTIN TAB 15MG CR	14	15	450	690	$ 3,002.37
OXYCONTIN TAB 20MG CR	39	39	1,170	1,905	$ 10,609.18
OXYCONTIN TAB 30MG CR	4	4	120	120	$ 964.48
OXYCONTIN TAB 40MG CR	13	13	390	780	$ 6,793.19
OXYCONTIN TAB 60MG CR	11	12	360	720	$ 10,170.41
OXYCONTIN TAB 80MG CR	9	9	270	540	$ 8,481.63
OXYMORPHONE TAB 15MG ER	12	12	360	660	$ 2,714.67
OXYMORPHONE TAB 20MG ER	2	2	60	60	$ 289.51
OXYMORPHONE TAB 30MG ER	1	1	30	60	$ 594.61
OXYMORPHONE TAB HCL 10MG	4	4	120	240	$ 509.69
PRIMLEV TAB 10-300MG	7	8	240	675	$ 12,389.56
PRIMLEV TAB 7.5-300	2	2	55	150	$ 2,532.22
TRAMADOL HCL TAB 50MG	108	112	3,360	6,240	$ 1,242.57
VICODIN HP TAB 10-300MG	3	3	90	270	$ 509.81
Presc 25	**3,302**	**3,512**	**101,402**	**390,373**	**$ 281,544.85**
APAP-CAFFEIN CAP DIHYDROC	3	3	90	360	$ 1,038.45
BUT/APAP/CAF CAP CODEINE	21	22	660	1,980	$ 10,206.10
EMBEDA CAP 20-0.8MG	1	1	30	30	$ 184.40
EMBEDA CAP 30-1.2MG	2	2	60	60	$ 534.32
EMBEDA CAP 60-2.4MG	2	2	60	120	$ 1,727.88

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
EMBEDA CAP 80-3.2MG	11	11	330	330	$ 6,277.24
FENTANYL DIS 100MCG/H	35	39	1,145	390	$ 5,172.83
FENTANYL DIS 25MCG/HR	27	27	810	270	$ 1,271.54
FENTANYL DIS 50MCG/HR	24	24	699	235	$ 1,509.98
FENTANYL DIS 75MCG/HR	10	11	259	95	$ 1,182.81
HYDROCO/APAP TAB 10-325MG	608	649	18,556	76,590	$ 21,656.79
HYDROCO/APAP TAB 5-325MG	18	19	525	1,110	$ 352.19
HYDROCO/APAP TAB 7.5-325	21	22	645	1,890	$ 509.03
HYDROMORPHON TAB 2MG	28	30	900	3,600	$ 616.79
HYDROMORPHON TAB 32MG ER	22	25	680	1,360	$ 54,740.07
HYDROMORPHON TAB 4MG	19	19	571	2,370	$ 419.58
HYDROMORPHON TAB 8MG	14	15	435	1,740	$ 798.63
HYDROMORPHON TAB 8MG ER	1	1	30	30	$ 316.90
HYSINGLA ER TAB 80 MG	8	8	240	240	$ 6,189.90
METHADONE TAB 10MG	365	390	11,317	82,011	$ 13,989.83
MORPHINE SUL TAB 100MG ER	89	94	2,790	6,210	$ 11,470.03
MORPHINE SUL TAB 15MG	41	45	1,327	3,231	$ 885.78
MORPHINE SUL TAB 15MG ER	152	157	4,619	9,808	$ 5,004.25
MORPHINE SUL TAB 200MG ER	20	21	630	1,260	$ 5,234.31
MORPHINE SUL TAB 30MG	10	11	315	1,140	$ 442.57
MORPHINE SUL TAB 30MG ER	258	271	7,847	16,761	$ 13,506.57
MORPHINE SUL TAB 60MG ER	100	111	3,180	6,360	$ 8,307.17
OPANA ER TAB 10MG	1	1	30	60	$ 289.20
OPANA ER TAB 20MG	9	9	270	540	$ 4,522.59
OPANA ER TAB 40MG	1	1	30	60	$ 915.45
OXYCOD/APAP TAB 10-325MG	502	534	15,622	64,406	$ 41,138.96
OXYCOD/APAP TAB 5-325MG	6	6	165	600	$ 144.50
OXYCOD/APAP TAB 7.5-325	12	14	345	1,155	$ 681.72
OXYCODONE TAB 10MG	64	67	1,878	7,425	$ 2,043.31
OXYCODONE TAB 15MG	429	459	13,168	55,366	$ 16,350.08
OXYCODONE TAB 20MG	88	95	2,660	10,686	$ 4,569.07
OXYCODONE TAB 30MG	153	166	4,675	19,816	$ 8,526.88
OXYCODONE TAB 40MG ER	2	2	60	120	$ 963.57
OXYCODONE TAB 5MG	5	5	150	450	$ 108.90
OXYCONTIN TAB 10MG CR	2	2	60	120	$ 375.96
OXYCONTIN TAB 15MG CR	1	1	30	90	$ 404.40
OXYCONTIN TAB 20MG CR	1	2	30	60	$ 355.10
OXYCONTIN TAB 30MG CR	10	10	300	600	$ 4,798.33
OXYMORPHONE TAB 10MG ER	6	6	180	360	$ 1,008.35
OXYMORPHONE TAB 20MG ER	2	2	60	120	$ 550.97
OXYMORPHONE TAB 30MG ER	2	2	60	120	$ 980.73
OXYMORPHONE TAB 40MG ER	10	10	300	600	$ 5,485.92
OXYMORPHONE TAB HCL 10MG	38	39	1,170	4,740	$ 10,871.23
OXYMORPHONE TAB HCL 5MG	1	1	30	60	$ 92.03
PRIMLEV TAB 10-300MG	2	2	60	150	$ 2,305.94
TRAMADOL HCL TAB 50MG	45	46	1,319	3,088	$ 515.72
Presc 3	**627**	**631**	**2,930**	**24,352**	**$ 7,949.07**
APAP/CODEINE SOL 120-12/5	59	59	372	8,244	$ 584.27
APAP/CODEINE TAB 300-30MG	79	80	262	1,960	$ 1,015.90
HYDROCO/APAP TAB 10-325MG	8	8	45	192	$ 112.21

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
HYDROCO/APAP TAB 5-325MG	76	76	297	2,009	$ 1,030.19
HYDROCO/APAP TAB 7.5-325	3	3	18	90	$ 45.87
OXYCOD/APAP TAB 10-325MG	20	20	95	532	$ 504.16
OXYCOD/APAP TAB 5-325MG	265	268	1,208	7,825	$ 3,531.54
OXYCOD/APAP TAB 7.5-325	1	1	7	30	$ 22.40
OXYCODONE TAB 10MG	1	1	10	30	$ 16.22
OXYCODONE TAB 5MG	3	3	19	80	$ 39.50
TRAMADOL HCL TAB 50MG	112	112	597	3,360	$ 1,046.81
Presc 4	**2,276**	**2,316**	**68,739**	**218,867**	**$ 192,157.35**
APAP/CODEINE TAB 300-30MG	2	2	60	300	$ 53.90
BUT/APAP/CAF CAP CODEINE	1	1	30	60	$ 73.98
BUT/ASA/CAF/ CAP COD 30MG	7	8	240	960	$ 1,432.33
EMBEDA CAP 20-0.8MG	7	7	210	270	$ 1,668.20
EMBEDA CAP 30-1.2MG	19	19	570	1,050	$ 9,621.68
EMBEDA CAP 50-2MG	1	1	30	60	$ 689.03
ENDOCET TAB 10-325MG	2	2	60	240	$ 173.21
FENTANYL DIS 100MCG/H	1	1	30	10	$ 244.49
FENTANYL DIS 12MCG/HR	1	1	30	10	$ 149.88
FENTANYL DIS 25MCG/HR	7	7	195	65	$ 327.87
FENTANYL DIS 50MCG/HR	12	12	360	120	$ 778.19
FENTANYL DIS 75MCG/HR	3	3	70	30	$ 286.16
HYDROCO/APAP TAB 10-325MG	322	331	9,954	38,530	$ 11,061.86
HYDROCO/APAP TAB 5-325MG	3	3	67	89	$ 41.56
HYDROCO/APAP TAB 7.5-325	38	38	1,130	3,765	$ 1,007.84
HYDROMORPHON TAB 2MG	1	1	10	10	$ 9.56
HYDROMORPHON TAB 4MG	22	22	635	1,690	$ 366.54
HYDROMORPHON TAB 8MG	9	9	265	1,060	$ 496.54
HYSINGLA ER TAB 20 MG	4	4	120	120	$ 935.10
METHADONE TAB 10MG	29	31	920	3,260	$ 675.26
MORPHINE SUL SOL 10MG/5ML	6	6	180	3,600	$ 222.37
MORPHINE SUL TAB 100MG ER	8	8	240	480	$ 1,003.90
MORPHINE SUL TAB 15MG	11	11	330	1,110	$ 287.78
MORPHINE SUL TAB 15MG ER	130	132	3,920	5,860	$ 3,436.78
MORPHINE SUL TAB 30MG	51	51	1,530	5,190	$ 1,896.37
MORPHINE SUL TAB 30MG ER	326	329	9,677	17,560	$ 14,567.00
MORPHINE SUL TAB 60MG ER	77	77	2,310	5,010	$ 6,674.70
OPANA ER TAB 10MG	3	3	90	180	$ 840.67
OPANA ER TAB 15MG	2	2	60	120	$ 772.47
OPANA ER TAB 20MG	7	7	210	390	$ 3,218.44
OPANA ER TAB 30MG	5	5	150	300	$ 3,505.29
OPANA ER TAB 40MG	2	2	60	120	$ 1,945.10
OXYCOD/APAP TAB 10-325MG	374	382	11,436	41,545	$ 28,065.92
OXYCOD/APAP TAB 5-325MG	8	8	240	930	$ 213.22
OXYCOD/APAP TAB 7.5-325	35	35	1,040	3,105	$ 1,979.03
OXYCODONE SOL 5MG/5ML	6	6	180	5,150	$ 1,157.39
OXYCODONE TAB 10MG	24	25	722	2,608	$ 774.89
OXYCODONE TAB 15MG	157	157	4,636	16,555	$ 5,140.84
OXYCODONE TAB 20MG	1	1	30	120	$ 50.29
OXYCODONE TAB 20MG ER	5	6	180	330	$ 1,554.28
OXYCODONE TAB 30MG	378	387	11,382	45,750	$ 19,834.52

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OXYCODONE TAB 40MG ER	10	10	300	510	$ 4,062.02
OXYCODONE TAB 5MG	6	6	160	870	$ 150.35
OXYCODONE TAB 80MG ER	9	10	300	600	$ 8,226.55
OXYCONTIN TAB 10MG CR	3	3	90	90	$ 280.85
OXYCONTIN TAB 15MG CR	1	1	30	60	$ 250.19
OXYCONTIN TAB 20MG CR	22	23	690	1,155	$ 6,346.60
OXYCONTIN TAB 30MG CR	2	2	60	90	$ 752.98
OXYCONTIN TAB 40MG CR	7	7	210	390	$ 3,560.71
OXYCONTIN TAB 60MG CR	9	10	300	600	$ 8,095.63
OXYCONTIN TAB 80MG CR	23	23	690	1,350	$ 22,834.52
OXYMORPHONE TAB 15MG ER	2	2	60	90	$ 377.92
OXYMORPHONE TAB 30MG ER	3	3	90	180	$ 1,783.83
OXYMORPHONE TAB HCL 10MG	4	4	120	240	$ 507.00
PRIMLEV TAB 10-300MG	2	2	60	195	$ 3,230.35
PRIMLEV TAB 7.5-300	2	2	60	150	$ 2,532.22
TRAMADOL HCL TAB 50MG	57	58	1,720	4,075	$ 646.94
VICODIN HP TAB 10-300MG	5	5	150	450	$ 834.91
XTAMPZA ER CAP 18MG	1	1	30	30	$ 208.24
ZOHYDRO ER CAP 20MG	1	1	30	30	$ 241.11
Presc 5	**2,443**	**2,480**	**10,647**	**43,429**	**$ 27,942.88**
APAP/CODEINE TAB 300-30MG	25	25	96	382	$ 280.36
ENDOCET TAB 5-325MG	3	3	13	50	$ 22.23
HYDROCO/APAP SOL 7.5-325	6	6	36	1,400	$ 231.98
HYDROCO/APAP TAB 10-325MG	1	1	3	15	$ 13.32
HYDROCO/APAP TAB 5-325MG	1,665	1,683	7,247	28,675	$ 19,559.78
HYDROCO/APAP TAB 7.5-325	2	2	10	40	$ 23.17
HYDROCOD/IBU TAB 7.5-200	11	11	46	170	$ 162.86
OXYCOD/APAP TAB 10-325MG	3	3	9	40	$ 48.14
OXYCOD/APAP TAB 5-325MG	722	741	3,167	12,577	$ 7,557.15
OXYCOD/APAP TAB 7.5-325	1	1	3	10	$ 14.92
TRAMADOL HCL TAB 50MG	4	4	17	70	$ 28.97
Presc 6	**493**	**512**	**14,660**	**55,640**	**$ 244,677.70**
EMBEDA CAP 60-2.4MG	2	2	45	90	$ 1,262.31
EMBEDA CAP 80-3.2MG	3	3	90	180	$ 3,303.04
FENTANYL DIS 25MCG/HR	1	1	30	10	$ 45.53
HYDROCO/APAP TAB 10-325MG	62	63	1,729	7,516	$ 2,159.63
HYDROCO/APAP TAB 7.5-325	1	1	30	90	$ 25.53
HYDROMORPHON TAB 32MG ER	24	25	750	1,500	$ 65,064.27
HYDROMORPHON TAB 8MG	27	29	606	2,860	$ 1,305.04
HYSINGLA ER TAB 80 MG	1	1	30	30	$ 819.11
KADIAN CAP 200MG ER	24	25	750	1,500	$ 97,123.30
METHADONE TAB 10MG	43	45	1,288	13,199	$ 2,131.07
MORPHINE SUL CAP 100MG ER	1	1	30	60	$ 698.45
MORPHINE SUL TAB 15MG	3	3	90	270	$ 76.56
MORPHINE SUL TAB 15MG ER	22	23	690	1,380	$ 716.74
MORPHINE SUL TAB 30MG	23	24	720	1,440	$ 648.18
MORPHINE SUL TAB 30MG ER	31	33	990	1,980	$ 1,661.36
MORPHINE SUL TAB 60MG ER	16	16	456	1,272	$ 1,449.26
NUCYNTA ER TAB 150MG	3	3	90	180	$ 1,989.59
NUCYNTA ER TAB 200MG	7	7	210	360	$ 4,947.94

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
OPANA ER TAB 20MG	4	4	120	240	$ 2,010.04
OPANA ER TAB 40MG	4	4	120	240	$ 3,731.00
OXYCOD/APAP TAB 10-325MG	63	64	1,865	7,410	$ 5,097.33
OXYCOD/APAP TAB 7.5-325	22	22	660	3,960	$ 2,374.56
OXYCODONE TAB 10MG	12	14	375	1,980	$ 564.10
OXYCODONE TAB 15MG	23	25	750	2,940	$ 832.74
OXYCODONE TAB 30MG	2	2	35	270	$ 120.72
OXYCODONE TAB 80MG ER	21	22	660	1,950	$ 26,612.57
OXYCONTIN TAB 20MG CR	1	1	12	35	$ 221.26
OXYCONTIN TAB 30MG CR	6	8	210	420	$ 3,088.73
OXYCONTIN TAB 60MG CR	11	11	329	658	$ 8,970.35
OXYCONTIN TAB 80MG CR	4	4	120	360	$ 5,348.92
TRAMADOL HCL TAB 50MG	26	26	780	1,260	$ 278.47
Presc 7	**90**	**91**	**2,266**	**12,304**	**$ 341,095.30**
APAP/CODEINE TAB 300-30MG	1	1	10	60	$ 17.03
FENTANYL DIS 25MCG/HR	4	4	120	40	$ 156.06
FENTANYL DIS 75MCG/HR	1	1	30	10	$ 95.39
HYDROCO/APAP TAB 5-325MG	5	5	92	494	$ 111.67
HYDROCO/APAP TAB 7.5-325	4	4	88	360	$ 80.69
HYDROMORPHON TAB 4MG	2	2	40	240	$ 42.91
HYDROMORPHON TAB 8MG	3	3	70	420	$ 165.37
MORPHINE SUL TAB 100MG ER	2	2	60	120	$ 257.00
MORPHINE SUL TAB 15MG ER	1	1	30	90	$ 35.52
MORPHINE SUL TAB 30MG ER	5	5	150	210	$ 151.29
MORPHINE SUL TAB 60MG ER	4	4	120	270	$ 312.01
OXYCOD/APAP TAB 10-325MG	3	3	85	360	$ 234.61
OXYCOD/APAP TAB 5-325MG	1	1	15	90	$ 22.65
OXYCODONE TAB 10MG	4	4	100	480	$ 127.68
OXYCODONE TAB 15MG	6	7	135	1,380	$ 318.89
OXYCODONE TAB 30MG	12	12	335	4,260	$ 1,588.59
OXYCONTIN TAB 30MG CR	3	3	90	180	$ 1,497.74
SUBSYS SPR 1200MCG	3	3	60	360	$ 49,095.51
SUBSYS SPR 200MCG	2	2	50	240	$ 13,454.42
SUBSYS SPR 400MCG	1	1	27	120	$ 8,918.53
SUBSYS SPR 600MCG	19	19	484	2,160	$ 264,363.43
TRAMADOL HCL TAB 50MG	4	4	75	360	$ 48.31
Presc 8	**3,381**	**3,628**	**99,944**	**351,924**	**$ 279,912.00**
APAP/CODEINE TAB 300-30MG	10	10	160	521	$ 131.38
APAP/CODEINE TAB 300-60MG	25	28	636	2,482	$ 834.30
BUPRENORPHIN DIS 20MCG/HR	1	1	28	4	$ 572.67
BUT/APAP/CAF CAP CODEINE	7	8	240	480	$ 592.26
BUTRANS DIS 10MCG/HR	12	13	372	52	$ 4,318.60
BUTRANS DIS 20MCG/HR	3	3	84	12	$ 1,910.13
EMBEDA CAP 20-0.8MG	2	2	60	120	$ 717.26
EMBEDA CAP 30-1.2MG	16	16	480	480	$ 4,408.19
ENDOCET TAB 10-325MG	1	2	60	240	$ 202.76
FENTANYL DIS 100MCG/H	3	3	90	45	$ 491.06
FENTANYL DIS 25MCG/HR	14	14	420	140	$ 620.00
FENTANYL DIS 50MCG/HR	13	13	390	130	$ 848.90
HYDROCO/APAP TAB 10-300MG	4	4	100	330	$ 529.56

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
HYDROCO/APAP TAB 10-325MG	675	719	19,745	74,906	$ 21,843.89
HYDROCO/APAP TAB 5-300MG	1	1	15	60	$ 72.00
HYDROCO/APAP TAB 5-325MG	61	63	1,667	5,746	$ 1,458.59
HYDROCO/APAP TAB 7.5-325	70	74	2,034	6,232	$ 1,734.23
HYDROCOD/IBU TAB 7.5-200	13	14	404	1,140	$ 522.03
HYDROMORPHON TAB 12MG ER	1	1	30	30	$ 507.53
HYDROMORPHON TAB 2MG	17	18	518	1,570	$ 321.88
HYDROMORPHON TAB 4MG	133	143	3,781	15,316	$ 2,872.35
HYDROMORPHON TAB 8MG	1	1	14	90	$ 43.10
HYDROMORPHON TAB 8MG ER	2	2	60	60	$ 570.21
HYSINGLA ER TAB 20 MG	3	3	90	90	$ 657.54
KADIAN CAP 40MG ER	3	3	90	180	$ 2,095.23
METHADONE TAB 10MG	132	152	4,055	15,063	$ 3,117.42
MORPHINE SUL TAB 15MG	61	67	1,814	6,959	$ 1,896.03
MORPHINE SUL TAB 15MG ER	100	102	2,990	6,280	$ 3,293.87
MORPHINE SUL TAB 30MG	3	3	84	271	$ 98.68
MORPHINE SUL TAB 30MG ER	151	158	4,604	12,040	$ 9,698.63
MORPHINE SUL TAB 60MG ER	92	96	2,849	7,050	$ 9,264.47
NUCYNTA ER TAB 100MG	11	11	315	630	$ 6,123.56
NUCYNTA ER TAB 150MG	9	10	300	570	$ 6,833.70
NUCYNTA ER TAB 200MG	12	12	360	720	$ 10,126.24
NUCYNTA ER TAB 50MG	4	4	37	240	$ 1,097.80
NUCYNTA TAB 100MG	27	32	755	2,335	$ 16,930.72
OPANA ER TAB 10MG	10	10	300	600	$ 2,842.81
OPANA ER TAB 15MG	1	1	30	60	$ 383.77
OPANA ER TAB 20MG	6	7	210	420	$ 3,509.95
OXYCOD/APAP TAB 10-325MG	581	620	17,286	73,673	$ 50,015.71
OXYCOD/APAP TAB 5-325MG	12	12	337	1,076	$ 270.63
OXYCOD/APAP TAB 7.5-325	86	88	2,565	9,554	$ 5,892.79
OXYCODONE CAP 5MG	1	1	30	60	$ 76.62
OXYCODONE TAB 10MG	241	257	6,975	24,919	$ 7,486.60
OXYCODONE TAB 10MG ER	1	1	15	30	$ 60.61
OXYCODONE TAB 15MG	334	380	10,076	41,675	$ 12,878.64
OXYCODONE TAB 20MG	1	1	30	60	$ 58.76
OXYCODONE TAB 30MG	102	104	3,050	11,410	$ 5,130.01
OXYCODONE TAB 40MG ER	19	24	555	1,140	$ 8,924.96
OXYCODONE TAB 5MG	19	19	517	1,920	$ 409.89
OXYCODONE TAB 80MG ER	1	1	30	60	$ 765.22
OXYCONTIN TAB 10MG CR	6	7	149	300	$ 845.18
OXYCONTIN TAB 15MG CR	5	6	180	450	$ 1,913.45
OXYCONTIN TAB 20MG CR	31	34	855	1,830	$ 10,258.61
OXYCONTIN TAB 30MG CR	35	37	1,100	2,240	$ 17,516.86
OXYCONTIN TAB 40MG CR	13	14	410	840	$ 7,726.85
OXYCONTIN TAB 60MG CR	7	8	220	480	$ 6,374.39
OXYMORPHONE TAB 10MG ER	10	10	300	600	$ 1,809.06
OXYMORPHONE TAB 15MG ER	6	6	180	480	$ 1,844.69
OXYMORPHONE TAB HCL 10MG	18	19	560	1,920	$ 4,436.93
TRAMADOL HCL TAB 50MG	77	84	2,333	7,198	$ 972.74
VICODIN ES TAB 7.5-300	20	23	674	1,890	$ 2,536.83
VICODIN HP TAB 10-300MG	30	32	816	3,165	$ 5,866.89

Row Labels	Sum of Count of Member	Sum of Count of Claims	Sum of Sum of Days Supply	Sum of Sum of Qty	Sum of Sum of Pd Amount
VICODIN TAB 5-300MG	14	15	400	1,200	$ 1,358.21
XTAMPZA ER CAP 18MG	1	1	30	60	$ 387.57
Presc 9	**741**	**819**	**2,281**	**12,422**	**$ 9,140.92**
APAP/CODEINE SOL 120-12/5	3	3	6	180	$ 24.03
APAP/CODEINE TAB 300-30MG	269	285	820	4,540	$ 2,988.66
HYDROCO/APAP TAB 10-325MG	1	2	4	28	$ 25.10
HYDROCO/APAP TAB 5-325MG	420	479	1,280	6,822	$ 5,531.22
HYDROCO/APAP TAB 7.5-325	35	37	108	592	$ 442.81
OXYCOD/APAP TAB 10-325MG	1	1	3	20	$ 21.76
TRAMADOL HCL TAB 50MG	12	12	60	240	$ 107.34
Grand Total	**44,414**	**47,298**	**1,157,581**	**3,970,216**	**$ 3,890,883.60**

Opioid Prescriber Trends

Top 10 Prescribers by number of Members (August 2015 – July 2017):

Prescriber Identifier	Degree	Specialty	Location	Count of Member	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
Presc 5	DDS	Oral Surgery	Reno	2135	2480	10647	43429	$ 27,942.88
Presc 22	MD/DMD	Oral Surgery	Las Vegas	1085	1322	4810	30336	$ 18,526.80
Presc 21	DDS	Oral Surgery	Las Vegas	734	881	4416	19704	$ 11,866.71
Presc 3	MD	Internal Med	Reno	550	631	2930	24352	$ 7,949.07
Presc 17	MD	Pain Management	Las Vegas	544	1898	56496	190994	$ 96,302.85
Presc 9	DMD	General Dentistry	Carson City	519	819	2281	12422	$ 9,140.92
Presc 15	ARNP	Pain Management	Las Vegas	518	1887	53830	178236	$ 87,302.00
Presc 20	ARNP	Pain Management	Las Vegas	446	1263	34401	112627	$ 74,955.05
Presc 19	MD	Pain Management	Las Vegas	442	1934	55346	165034	$ 149,635.29
Presc 11	DMD	General Dentistry	Pahrump	414	615	3040	12225	$ 7,699.67

Top 10 Prescribers by number of Claims(August 2015 – July 2017):

Prescriber Identifier	Degree	Specialty	Location	Count of Member	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
Presc 24	NP	Pain Management	Las Vegas	288	4524	133796	416044	$ 399,463.07
Presc 8	PA	Pain Management	Las Vegas	272	3628	99944	351924	$ 279,912.00
Presc 25	PA	Pain Management	Las Vegas	281	3512	101402	390373	$ 281,544.85
Presc 12	PA	Pain Management	Las Vegas	328	3131	92601	280893	$ 303,429.10
Presc 18	MD	Pain Management	Las Vegas	267	2755	76451	261697	$ 132,465.23
Presc 5	DDS	Oral Surgery	Reno	2135	2480	10647	43429	$ 27,942.88
Presc 14	MD	Physical Med/Rehab	Carson City	173	2439	64655	221892	$ 509,924.66
Presc 4	MD	Peds	Las Vegas	279	2316	68739	218867	$ 192,157.35
Presc 23	MD	Physical Med/Rehab	Truckee	210	2139	61464	211748	$ 83,422.49
Presc 10	MD	Pain Management	Reno	189	1964	46800	151922	$ 59,932.47

Top 10 Prescribers by Days Supply(August 2015 – July 2017):

Prescriber Identifier	Degree	Specialty	Location	Count of Member	Count of Claims	Sum of Days Supply	Sum of Qty		Sum of Amt Paid
Presc 24	NP	Pain Management	Las Vegas	288	4524	133796	416044	$	399,463.07
Presc 25	PA	Pain Management	Las Vegas	281	3512	101402	390373	$	281,544.85
Presc 8	PA	Pain Management	Las Vegas	272	3628	99944	351924	$	279,912.00
Presc 12	PA	Pain Management	Las Vegas	328	3131	92601	280893	$	303,429.10
Presc 18	MD	Pain Management	Las Vegas	267	2755	76451	261697	$	132,465.23
Presc 4	MD	Peds	Las Vegas	279	2316	68739	218867	$	192,157.35
Presc 14	MD	Physical Med/Rehab	Carson City	173	2439	64655	221892	$	509,924.66
Presc 23	MD	Physical Med/Rehab	Truckee	210	2139	61464	211748	$	83,422.49
Presc 1	APN	None	Reno	113	1955	57048	166119	$	105,959.72
Presc 17	MD	Pain Management	Las Vegas	544	1898	56496	190994	$	96,302.85

Top 10 Prescribers by total quantity(August 2015 – July 2017):

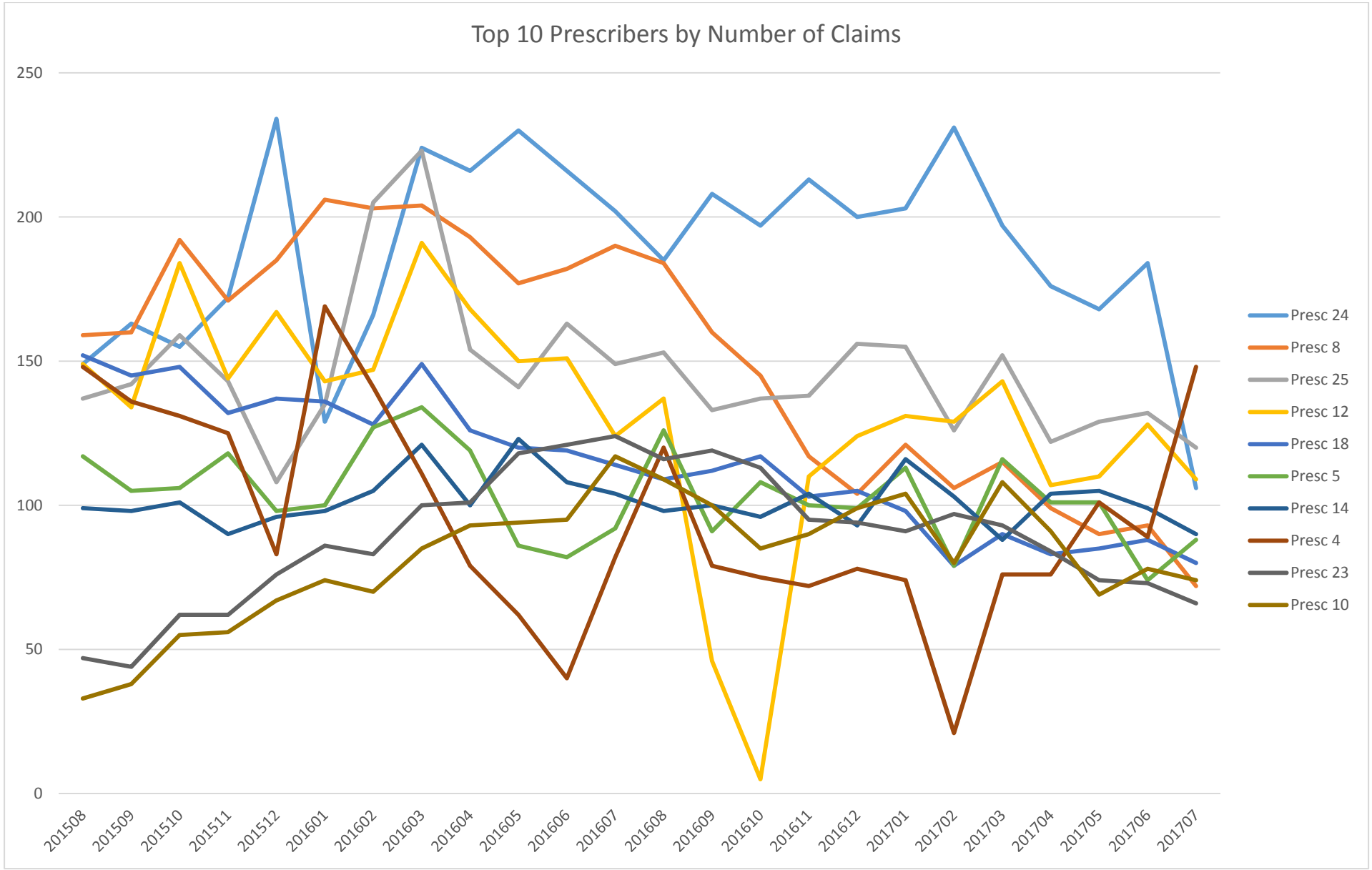
Prescriber Identifier	Degree	Specialty	Location	Count of Member	Count of Claims	Sum of Days Supply	Sum of Qty		Sum of Amt Paid
Presc 24	NP	Pain Management	Las Vegas	288	4524	133796	416044	$	399,463.07
Presc 25	PA	Pain Management	Las Vegas	281	3512	101402	390373	$	281,544.85
Presc 8	PA	Pain Management	Las Vegas	272	3628	99944	351924	$	279,912.00
Presc 12	PA	Pain Management	Las Vegas	328	3131	92601	280893	$	303,429.10
Presc 18	MD	Pain Management	Las Vegas	267	2755	76451	261697	$	132,465.23
Presc 14	MD	Physical Med/Rehab	Carson City	173	2439	64655	221892	$	509,924.66
Presc 4	MD	Peds	Las Vegas	279	2316	68739	218867	$	192,157.35
Presc 2	MD	Internal Med	Sparks	83	1417	39863	217538	$	106,836.07
Presc 23	MD	Physical Med/Rehab	Truckee	210	2139	61464	211748	$	83,422.49
Presc 17	MD	Pain Management	Las Vegas	544	1898	56496	190994	$	96,302.85

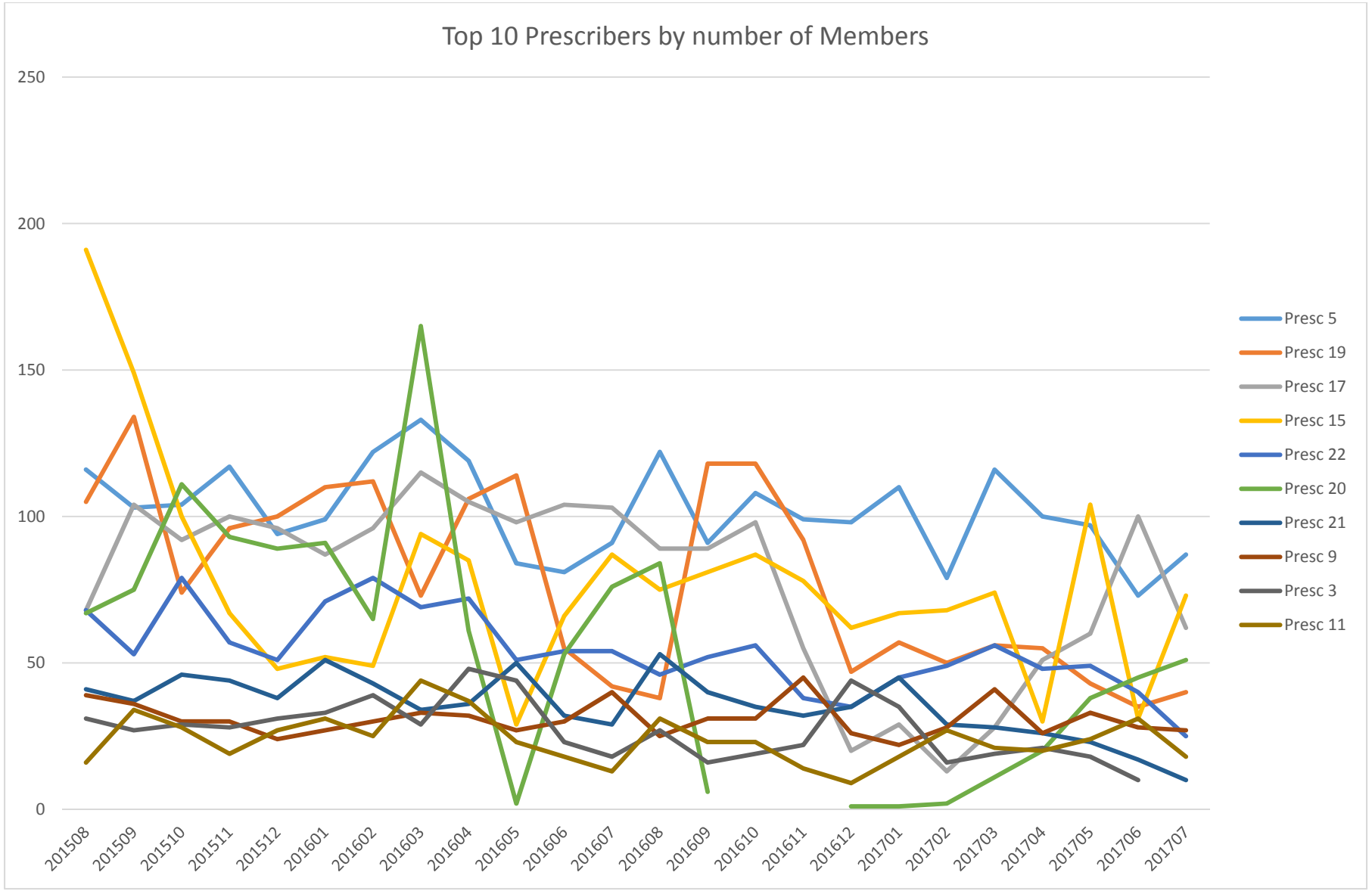
Top 10 Prescribers by Total Amount Paid(August 2015 – July 2017):

Prescriber Identifier	Degree	Specialty	Location	Count of Member	Count of Claims	Sum of Days Supply	Sum of Qty		Sum of Amt Paid
Presc 14	MD	Physical Med/Rehab	Carson City	173	2439	64655	221892	$	509,924.66
Presc 24	NP	Pain Management	Las Vegas	288	4524	133796	416044	$	399,463.07
Presc 7	MD	Internal Med	Las Vegas	13	91	2266	12304	$	341,095.30
Presc 12	PA	Pain Management	Las Vegas	328	3131	92601	280893	$	303,429.10
Presc 25	PA	Pain Management	Las Vegas	281	3512	101402	390373	$	281,544.85
Presc 8	PA	Pain Management	Las Vegas	272	3628	99944	351924	$	279,912.00
Presc 6	MD	Pain Management	Las Vegas	27	512	14660	55640	$	244,677.70
Presc 4	MD	Peds	Las Vegas	279	2316	68739	218867	$	192,157.35
Presc 16	MD	Family Medicine	Pahrump	132	1603	24425	65401	$	189,289.90
Presc 13	DO	Pain Management	Las Vegas	133	1582	45270	158495	$	169,452.45

Top Prescribers by Count of Claims by month:

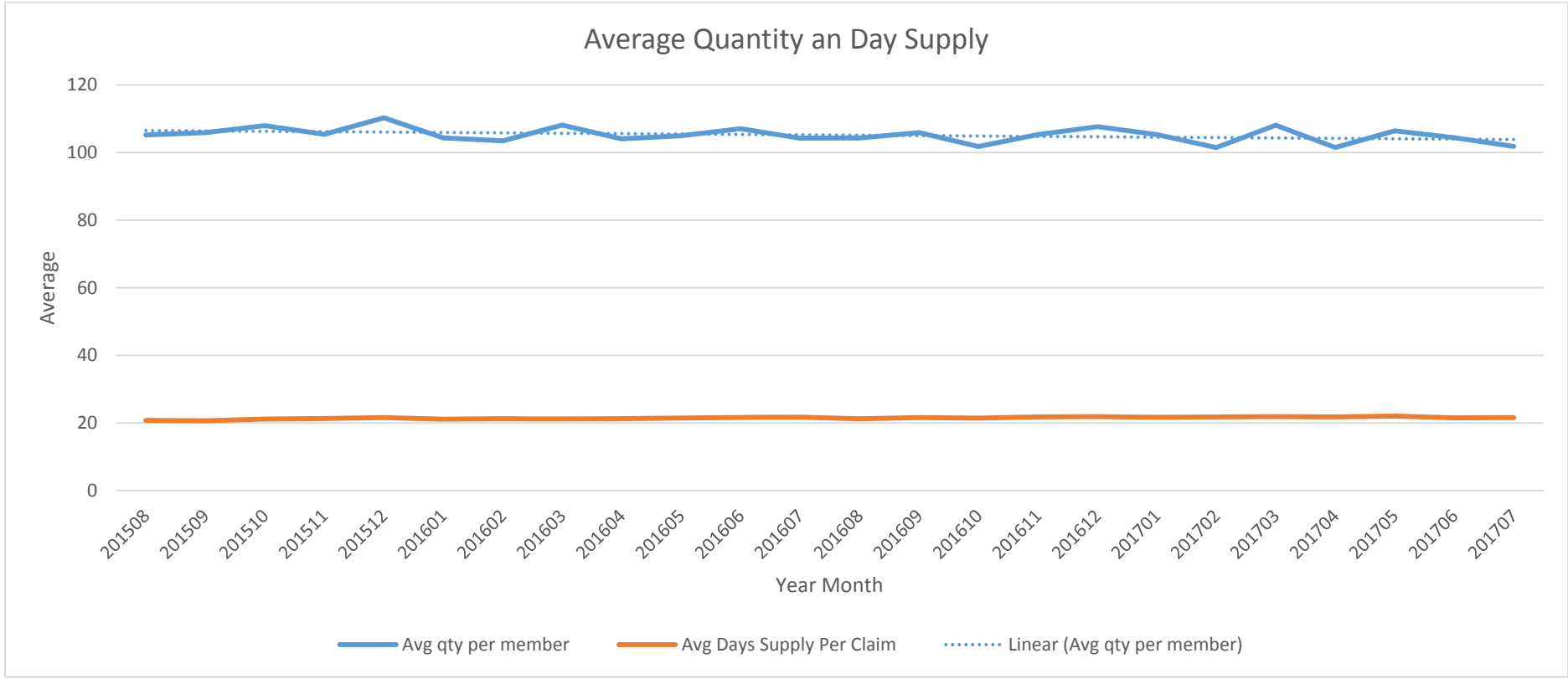
Prescriber	201508	201509	201510	201511	201512	201601	201602	201603	201604	201605	201606	201607	201608	201609	201610	201611	201612	201701	201702	201703	201704	201705	201706	201707	Gra
Presc 24	149	163	155	172	234	129	166	224	216	230	216	202	185	208	197	213	200	203	231	197	176	168	184	106	4524
Presc 8	159	160	192	171	185	206	203	204	193	177	182	190	184	160	145	117	104	121	106	115	99	90	93	72	3628
Presc 25	137	142	159	143	108	135	205	223	154	141	163	149	153	133	137	138	156	155	126	152	122	129	132	120	3512
Presc 12	149	134	184	144	167	143	147	191	168	150	151	124	137	46	5	110	124	131	129	143	107	110	128	109	3131
Presc 18	152	145	148	132	137	136	128	149	126	120	119	114	109	112	117	103	105	98	79	90	83	85	88	80	2755
Presc 5	117	105	106	118	98	100	127	134	119	86	82	92	126	91	108	100	99	113	79	116	101	101	74	88	2480
Presc 14	99	98	101	90	96	98	105	121	100	123	108	104	98	100	96	104	93	116	103	88	104	105	99	90	2439
Presc 4	148	136	131	125	83	169	141	111	79	62	40	82	120	79	75	72	78	74	21	76	76	101	89	148	2316
Presc 23	47	44	62	62	76	86	83	100	101	118	121	124	116	119	113	95	94	91	97	93	84	74	73	66	2139
Presc 10	33	38	55	56	67	74	70	85	93	94	95	117	109	100	85	90	99	104	80	108	91	69	78	74	1964
Presc 1	110	101	118	90	95	96	93	85	84	88	88	77	83	75	74	72	65	76	60	68	57	67	69	64	1955
Presc 19	106	134	78	97	103	110	112	73	110	116	55	43	38	119	119	92	49	57	56	69	59	52	37	50	1934
Presc 17	69	107	93	101	97	87	99	117	107	100	110	104	93	91	100	55	20	29	13	28	51	61	104	62	1898
Presc 15	199	158	102	67	48	52	49	96	85	30	67	89	75	82	88	80	62	67	69	78	30	109	32	73	1887
Presc 16	53	45	53	62	58	64	60	61	55	74	87	96	83	79	71	68	66	75	57	70	66	77	71	52	1603
Presc 13	75	76	76	61	71	60	64	68	72	68	64	62	65	63	57	66	69	65	62	62	67	67	64	58	1582
Presc 2	73	59	69	55	63	67	67	71	60	60	52	57	59	60	51	58	58	57	52	59	53	52	53	52	1417
Presc 22	69	53	81	57	52	74	81	69	73	52	55	55	49	52	56	38	35	45	52	57	49	52	40	26	1322
Presc 20	68	78	113	94	90	91	65	175	62	2	53	77	87	6			1	1	2	11	20	39	59	69	1263
Presc 21	41	41	48	44	40	51	43	34	37	52	33	31	54	42	37	34	36	47	30	29	27	23	17	10	881
Presc 9	39	38	31	31	25	28	33	37	35	28	30	47	28	36	40	50	31	26	35	45	27	39	30	30	819
Presc 3	31	27	29	29	31	33	39	29	49	44	24	18	27	16	20	22	44	35	16	19	21	18	10		631
Presc 11	17	35	31	21	28	32	29	48	41	25	20	13	35	23	26	15	11	19	30	21	20	26	31	18	615
Presc 6	25	22	21	25	25	25	23	29	25	26	28	21	22	19	19	18	19	19	18	16	17	15	18	17	512
Presc 7		1		2	2	1	4	2	5	3	4	3	2	2	1	4	8	6	7	8	10	6	6	4	91
Grand Total	**2165**	**2140**	**2236**	**2049**	**2079**	**2147**	**2236**	**2536**	**2249**	**2069**	**2047**	**2091**	**2137**	**1913**	**1837**	**1814**	**1726**	**1830**	**1610**	**1818**	**1617**	**1735**	**1679**	**1538**	**47298**

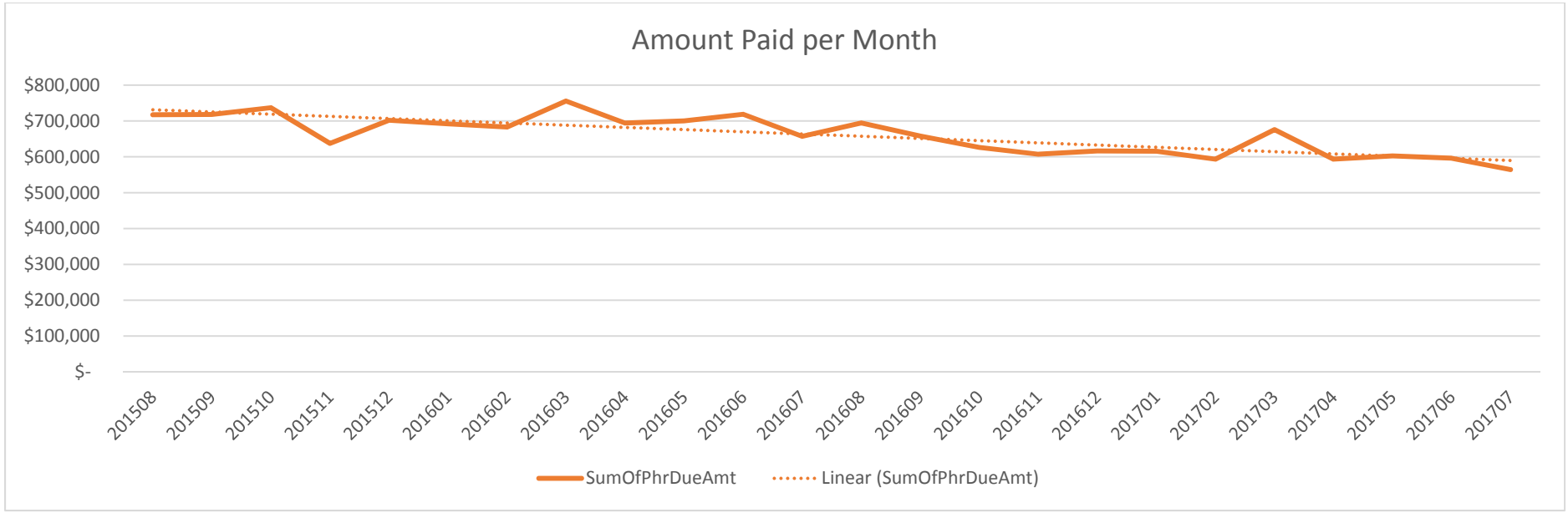

Top 10 Prescribers by Number of Claims
250
200
150
100
50
0
201508
201509
201510
201511
201512
201601
201602
201603
201604
201605
201606
201607
201608
201609
201610
201611
201612
201701
201702
201703
201704
201705
201706
201707
Presc 24
Presc 8
Presc 25
Presc 12
Presc 18
Presc 5
Presc 14
Presc 4
Presc 23
Presc 10

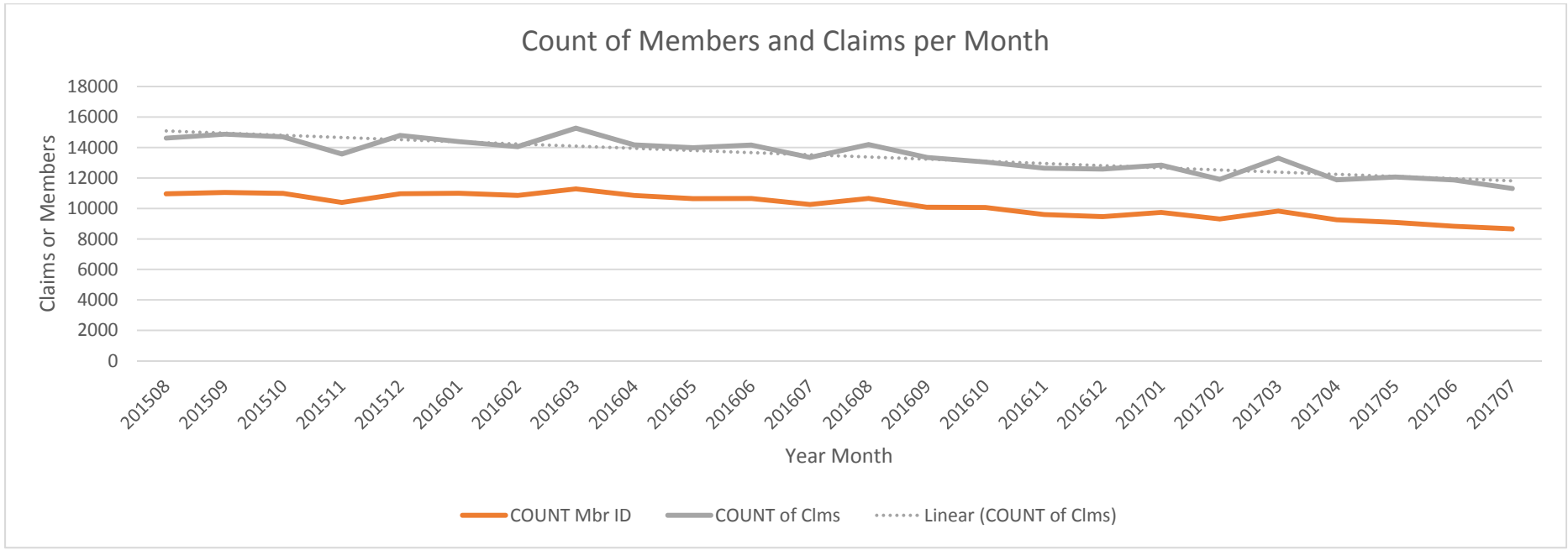

Top 10 Prescribers by number of Members
250
200
150
100
50
0
201508
201509
201510
201511
201512
201601
201602
201603
201604
201605
201606
201607
201608
201609
201610
201611
201612
201701
201702
201703
201704
201705
201706
201707
Presc 5
Presc 19
Presc 17
Presc 15
Presc 22
Presc 20
Presc 21
Presc 9
Presc 3
Presc 11

Opioid Trends

New Quantity limit effective May 15, 2017.




Amount Paid per Month
$800,000
$700,000
$600,000
$500,000
$400,000
$300,000
$200,000
$100,000
$-
201508
201509
201510
201511
201512
201601
201602
201603
201604
201605
201606
201607
201608
201609
201610
201611
201612
201701
201702
201703
201704
201705
201706
201707
SumOfPhrDueAmt
Linear (SumOfPhrDueAmt)


Count of Members and Claims per Month
Claims or Members
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
201508
201509
201510
201511
201512
201601
201602
201603
201604
201605
201606
201607
201608
201609
201610
201611
201612
201701
201702
201703
201704
201705
201706
201707
Year Month
COUNT Mbr ID
COUNT of Clms
Linear (COUNT of Clms)

Year Month	Count of Members	Count of Claims	Sum of Days Supply	Sum of qty	Sum of Pd Amt	Avg Days Supply Per Claim	Avg qty per member
201508	10,962.00	14,613.00	303,272.00	1,153,049.04	$ 717,147.17	20.75357558	105.1860099
201509	11,044.00	14,874.00	307,217.00	1,169,055.45	$ 718,185.81	20.65463224	105.8543508
201510	10,981.00	14,699.00	310,855.00	1,185,318.00	$ 737,147.22	21.14803728	107.9426282
201511	10,392.00	13,576.00	289,179.00	1,095,114.25	$ 637,398.35	21.30075133	105.380509
201512	10,964.00	14,793.00	319,460.00	1,208,781.20	$ 701,827.92	21.59534915	110.2500182
201601	10,990.00	14,385.00	303,472.00	1,146,383.80	$ 691,853.85	21.09641988	104.3115378
201602	10,854.00	14,054.00	298,998.00	1,122,566.20	$ 682,900.75	21.27493952	103.4241938
201603	11,281.00	15,272.00	324,389.00	1,219,620.85	$ 755,795.10	21.24076742	108.1128313
201604	10,853.00	14,165.00	300,912.00	1,128,820.65	$ 694,289.16	21.24334628	104.0100111
201605	10,637.00	13,982.00	299,535.00	1,116,333.88	$ 700,032.41	21.42290087	104.9481886
201606	10,652.00	14,155.00	306,539.00	1,139,992.60	$ 718,774.30	21.65588131	107.0214608
201607	10,258.00	13,344.00	289,697.00	1,069,045.95	$ 657,221.25	21.70990707	104.2158267
201608	10,658.00	14,191.00	301,514.00	1,111,192.80	$ 694,652.12	21.24684659	104.2590355
201609	10,080.00	13,350.00	288,398.00	1,067,547.40	$ 658,071.41	21.60284644	105.9074802
201610	10,058.00	13,047.00	279,813.00	1,023,649.00	$ 626,300.11	21.44653943	101.7746073
201611	9,603.00	12,639.00	275,270.00	1,011,243.10	$ 607,386.47	21.77941293	105.3049151
201612	9,461.00	12,584.00	275,275.00	1,018,394.62	$ 616,128.52	21.875	107.6413297
201701	9,745.00	12,841.00	278,303.00	1,026,048.00	$ 615,550.09	21.67300055	105.289687
201702	9,311.00	11,913.00	259,460.00	944,694.25	$ 593,640.48	21.77956854	101.4600204
201703	9,831.00	13,302.00	290,813.00	1,062,291.70	$ 676,039.89	21.86235153	108.0553046
201704	9,258.00	11,876.00	258,869.00	939,597.70	$ 593,564.85	21.79765914	101.4903543
201705	9,084.00	12,061.00	265,723.00	966,720.70	$ 602,405.47	22.03158942	106.4201563
201706	8,832.00	11,866.00	255,466.00	921,990.00	$ 596,203.08	21.52924322	104.3919837
201707	8,653.00	11,314.00	244,401.00	880,930.50	$ 564,537.51	21.60164398	101.8063677

Gastroenterology studies in recipients with extended use of proton pump inhibitors:

In 2016, a total of 4,611 Medicaid recipients received an endoscopy. Of these, 1,150 recipients were ordered at least one prescription of a proton pump inhibitor between August 2015 and July 2017. The Average duration was 217 days.

There were 7,907 recipients with at least one prescription for a proton pump inhibitor between August 2015 and July 2017 without an endoscopy in 2016. The average duration was 177 days. Of these, 4,068 recipients had a duration of more than 60 days.

Month Year Filled	Count of Members	Count of Claims	Sum of Days Supply	Sum of Qty	Sum of Amt Paid
201508	1,997	2,124	63,251	65,595	$ 319,498.18
201509	1,999	2,116	62,920	65,057	$ 306,619.08
201510	2,062	2,188	65,121	67,593	$ 318,667.51
201511	1,972	2,087	62,215	64,263	$ 282,938.48
201512	2,058	2,226	66,497	68,492	$ 290,887.08
201601	2,089	2,218	66,018	68,394	$ 299,350.33
201602	2,070	2,182	64,949	67,132	$ 296,584.30
201603	2,222	2,382	70,969	73,390	$ 316,970.14
201604	2,168	2,263	67,565	70,301	$ 293,429.07
201605	2,217	2,380	70,839	73,607	$ 302,454.26
201606	2,207	2,346	69,982	72,232	$ 295,088.43
201607	2,184	2,295	68,427	70,982	$ 289,035.40
201608	2,232	2,433	72,404	74,684	$ 307,249.78
201609	2,163	2,283	67,983	70,368	$ 287,973.11
201610	2,134	2,257	67,039	69,150	$ 281,818.25
201611	2,134	2,269	67,565	69,652	$ 283,331.51
201612	2,095	2,229	66,489	68,431	$ 277,291.27
201701	2,167	2,311	68,842	70,721	$ 279,228.24
201702	2,061	2,143	66,389	67,947	$ 268,137.03
201703	2,205	2,366	83,943	86,146	$ 325,240.74
201704	1,924	2,006	70,323	72,289	$ 282,975.81
201705	1,928	2,075	71,588	73,598	$ 286,780.57
201706	1,915	2,009	74,423	76,112	$ 287,236.05
201707	1,842	1,941	72,441	74,488	$ 281,662.92

Proton Pump Utilization

August 2015 -July 2017

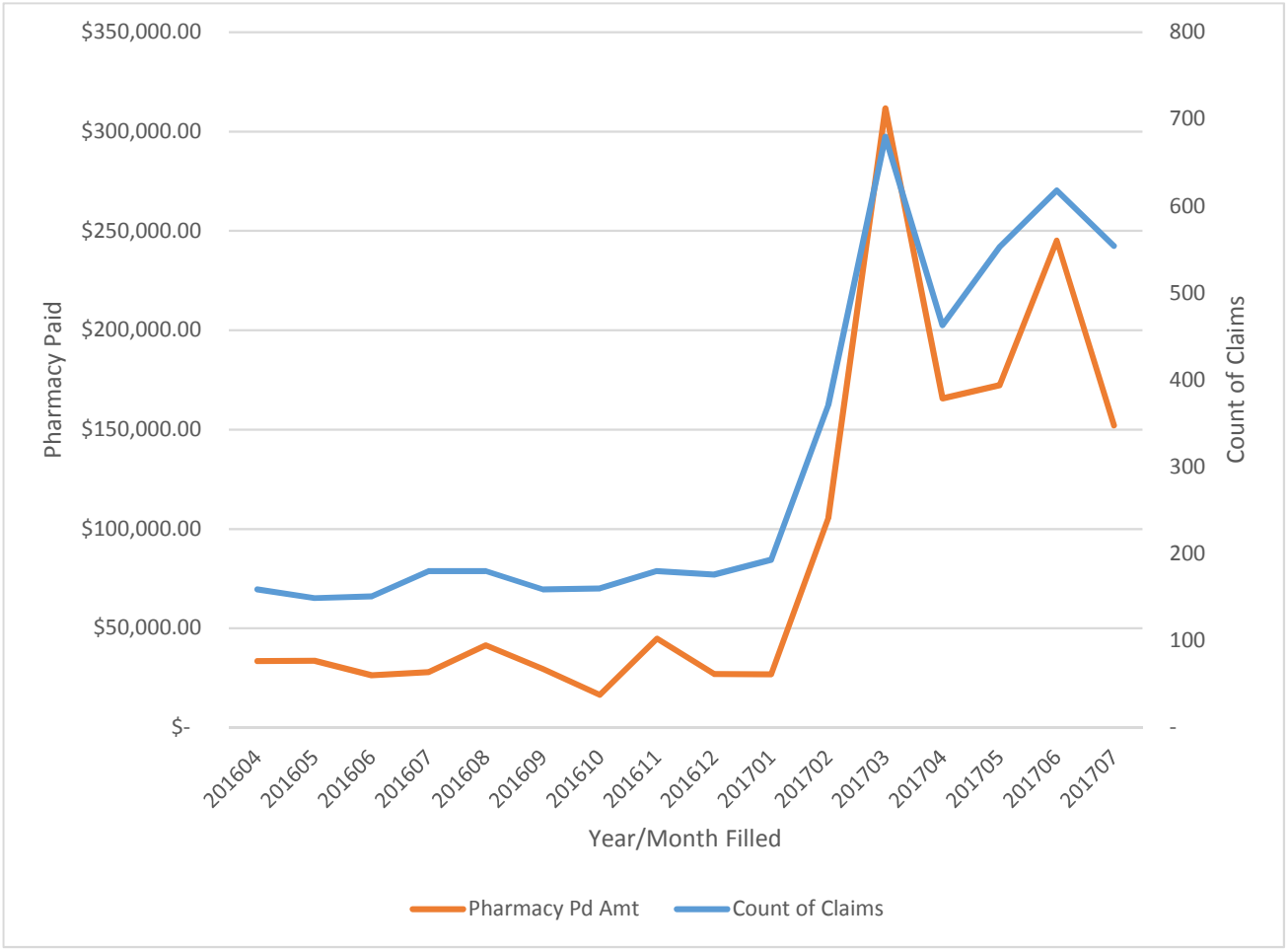
Product Name	Count of Member ID	Sum of Metric Decimal Qty	Sum of Days Supply	Sum of Phr Due Amt
DEXILANT CAP 30MG DR	49	1,470	1,470	$ 11,606.41
DEXILANT CAP 60MG DR	294	9,022	9,022	$ 72,289.38
ESOMEPRA MAG CAP 20MG DR	35	1,050	1,050	$ 2,512.40
ESOMEPRA MAG CAP 40MG DR	121	4,650	4,470	$ 5,629.57
FIRST-OMEPRA SUS 2MG/ML	4	780	120	$ 249.02
LANSOPRAZOLE CAP 15MG DR	33	1,558	988	$ 1,443.83
LANSOPRAZOLE CAP 30MG DR	116	3,539	3,479	$ 2,978.91
LANSOPRAZOLE SUS 3MG/ML	5	750	150	$ 306.07
NEXIUM CAP 20MG	4,528	144,564	141,793	$ 1,188,001.48
NEXIUM CAP 40MG	18,580	597,367	576,678	$ 5,016,756.89
NEXIUM GRA 10MG DR	466	14,475	13,938	$ 126,002.67
NEXIUM GRA 2.5MG DR	26	780	780	$ 6,942.13
NEXIUM GRA 20MG DR	274	8,398	8,368	$ 73,081.34
NEXIUM GRA 40MG DR	270	8,135	8,135	$ 71,141.17
NEXIUM GRA 5MG DR	48	1,695	1,440	$ 14,770.33
NEXIUM 24HR CAP 20MG	9	258	258	$ 169.68
OMEPRAZOLE CAP 10MG	2	60	60	$ 37.43
OMEPRAZOLE CAP 20MG	479	17,924	14,911	$ 5,764.98
OMEPRAZOLE CAP 40MG	787	25,850	24,680	$ 10,954.31
OMEPRAZOLE TAB 20MG	8	224	224	$ 158.96
PANTOPRAZOLE TAB 20MG	3,901	121,345	119,928	$ 50,133.50
PANTOPRAZOLE TAB 40MG	22,764	723,892	706,688	$ 278,264.09
PREVACID TAB 15MG STB	47	1,800	1,410	$ 23,182.47
PREVACID TAB 30MG STB	169	6,206	5,171	$ 80,271.01
PRILOSEC POW 10MG	1	30	30	$ 198.17
PROTONIX INJ 40MG	13	182	91	$ 990.08
PROTONIX PAK	6	180	180	$ 1,706.10
PROTONIX TAB 40MG	27	1,320	660	$ 12,287.56
RABEPRAZOLE TAB 20MG	69	3,180	2,070	$ 3,120.70
Grand Total	**53,131**	**1,700,684**	**1,648,242**	**$ 7,060,950.64**

90 - Day Supply Utilization

Nevada Medicaid

April 2016 - July 2017

YearMonthFilled	Member Count	Count of Claims	Days Supply	Total Qty	Disp Fee	Pharmacy Pd Amt
201604	159	159	16,315	13,059	$ 1,140.85	$ 33,566.57
201605	149	149	16,130	11,822	$ 1,186.34	$ 33,723.54
201606	151	151	16,684	12,084	$ 1,181.28	$ 26,314.79
201607	180	180	18,323	15,733	$ 1,307.74	$ 28,005.19
201608	180	180	18,779	15,042	$ 1,335.16	$ 41,493.70
201609	159	159	16,742	15,991	$ 1,209.14	$ 29,519.66
201610	160	160	16,137	13,323	$ 1,282.17	$ 16,464.21
201611	180	180	18,788	16,884	$ 1,297.74	$ 44,784.06
201612	176	176	17,477	15,664	$ 1,453.17	$ 26,994.17
201701	193	193	19,603	17,500	$ 1,291.18	$ 26,851.94
201702	371	371	38,314	33,766	$ 2,669.62	$ 105,550.60
201703	680	680	69,787	65,588	$ 5,179.13	$ 311,698.00
201704	463	463	47,806	41,837	$ 3,345.62	$ 165,673.43
201705	553	553	55,925	57,606	$ 3,812.39	$ 172,326.13
201706	618	618	63,254	56,527	$ 4,329.65	$ 245,215.22
201707	554	554	57,998	52,059	$ 3,832.36	$ 152,027.96



Top 10 Drug Group by Paid Amt

Q4 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,552	$ 8,866,116.41
85	HEMATOLOGICAL AGENTS - MISC.*	3,702	$ 8,454,118.82
12	ANTIVIRALS*	4,164	$ 7,812,360.33
27	ANTIDIABETICS*	28,313	$ 4,664,093.33
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	4,271	$ 4,243,474.24
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	40,411	$ 4,218,066.23
72	ANTICONVULSANTS*	45,497	$ 3,680,634.15
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	3,996	$ 2,671,373.75
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	4,990	$ 2,272,638.36
65	ANALGESICS - OPIOID*	62,601	$ 2,234,328.62

Q1 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
85	HEMATOLOGICAL AGENTS - MISC.*	3,662	$ 9,325,628.04
12	ANTIVIRALS*	5,203	$ 7,266,435.97
27	ANTIDIABETICS*	27,611	$ 6,425,317.42
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	32,411	$ 5,892,304.25
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	44,908	$ 4,796,359.79
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	4,068	$ 3,991,362.58
72	ANTICONVULSANTS*	46,753	$ 3,945,512.52
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	4,017	$ 2,759,685.73
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	5,400	$ 2,322,888.21
61	ADHD/ANTI-NARCOLEPSY/ANTI-OBESITY/ANOREX	10,959	$ 2,284,652.13

Q2 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
85	HEMATOLOGICAL AGENTS - MISC.*	3,457	$ 10,924,453.46
12	ANTIVIRALS*	4,246	$ 7,675,577.73
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	31,299	$ 5,609,573.39
27	ANTIDIABETICS*	20,020	$ 5,235,915.50
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	4,240	$ 5,147,044.39
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	41,941	$ 4,762,202.79
72	ANTICONVULSANTS*	45,627	$ 3,982,719.66
74	NEUROMUSCULAR AGENTS*	337	$ 2,794,526.15
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	3,899	$ 2,601,347.46
62	PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	5,248	$ 2,268,181.85

Top 10 Drug Group by Claim Count

Q4 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	56,599	$ 2,051,814.21
58	ANTIDEPRESSANTS*	43,569	$ 844,724.12
72	ANTICONVULSANTS*	43,293	$ 3,612,420.84
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	41,376	$ 4,323,625.98
36	ANTIHYPERTENSIVES*	33,634	$ 474,958.24
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	29,443	$ 8,542,669.89
27	ANTIDIABETICS*	25,956	$ 4,562,842.00
39	ANTIHYPERLIPIDEMICS*	25,544	$ 750,890.68
57	ANTIANXIETY AGENTS*	24,325	$ 283,154.70
66	ANALGESICS - ANTI-INFLAMMATORY*	24,105	$ 1,716,848.76

Q1 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	59,662	$ 2,086,447.21
72	ANTICONVULSANTS*	46,753	$ 3,945,512.52
58	ANTIDEPRESSANTS*	46,102	$ 901,813.95
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	44,908	$ 4,796,359.79
36	ANTIHYPERTENSIVES*	33,497	$ 535,039.24
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	32,411	$ 5,892,304.25
27	ANTIDIABETICS*	27,611	$ 6,425,317.42
39	ANTIHYPERLIPIDEMICS*	27,327	$ 773,511.80
57	ANTIANXIETY AGENTS*	26,161	$ 291,756.42
49	ULCER DRUGS*	25,806	$ 1,240,036.94

Q2 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	57,647	$ 1,960,118.79
72	ANTICONVULSANTS*	45,627	$ 3,982,719.66
58	ANTIDEPRESSANTS*	43,789	$ 846,962.47
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	41,941	$ 4,762,202.79
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	31,299	$ 5,609,573.39
57	ANTIANXIETY AGENTS*	25,761	$ 283,662.72
49	ULCER DRUGS*	24,549	$ 1,176,384.46
36	ANTIHYPERTENSIVES*	24,325	$ 359,353.24
39	ANTIHYPERLIPIDEMICS*	24,318	$ 722,355.35
66	ANALGESICS - ANTI-INFLAMMATORY*	23,771	$ 1,871,181.95

Top 10 Drug Classes by Paid Amt

Q4 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	94	$ 8,922,391.95
1235	HEPATITIS AGENTS**	297	$ 4,317,718.35
5925	QUINOLINONE DERIVATIVES**	4,496	$ 3,935,124.04
1210	ANTIRETROVIRALS**	2,219	$ 3,092,747.28
2710	INSULIN**	8,116	$ 3,045,841.66
4420	SYMPATHOMIMETICS**	28,338	$ 2,792,919.73
7260	ANTICONVULSANTS - MISC.**	31,667	$ 2,447,446.65
5907	BENZISOXAZOLES**	6,963	$ 2,020,701.71
6240	MULTIPLE SCLEROSIS AGENTS**	379	$ 1,591,092.89
5940	ANTIPSYCHOTICS - MISC.**	2,789	$ 1,383,181.37

Q1 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	118	$ 8,909,353.08
2710	INSULIN**	8,943	$ 4,283,103.71
1235	HEPATITIS AGENTS**	328	$ 3,929,771.33
4420	SYMPATHOMIMETICS**	30,551	$ 3,170,155.87
1210	ANTIRETROVIRALS**	2,535	$ 3,157,821.11
7260	ANTICONVULSANTS - MISC.**	34,315	$ 2,705,834.35
5907	BENZISOXAZOLES**	7,659	$ 2,163,906.94
6240	MULTIPLE SCLEROSIS AGENTS**	324	$ 1,751,131.75
5940	ANTIPSYCHOTICS - MISC.**	3,090	$ 1,472,868.59
2153	ANTINEOPLASTIC ENZYME INHIBITORS**	174	$ 1,366,624.72

Q2 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	95	$ 10,279,220.11
1235	HEPATITIS AGENTS**	343	$ 4,431,089.27
2710	INSULIN**	6,311	$ 3,446,189.72
4420	SYMPATHOMIMETICS**	28,438	$ 3,166,342.54
1210	ANTIRETROVIRALS**	2,196	$ 3,128,703.60
7260	ANTICONVULSANTS - MISC.**	33,660	$ 2,706,848.12
5907	BENZISOXAZOLES**	7,364	$ 2,091,603.88
7470	SPINAL MUSCULAR ATROPHY AGENTS (SMA)**	13	$ 2,000,132.21
2135	ANTINEOPLASTIC - ANTIBODIES**	333	$ 1,799,186.78
6240	MULTIPLE SCLEROSIS AGENTS**	304	$ 1,671,342.11

Top 10 Drug Classes by Claim Count

Q4 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
6599	OPIOID COMBINATIONS**	31,931	$ 863,099.94
7260	ANTICONVULSANTS - MISC.**	31,667	$ 2,447,446.65
4420	SYMPATHOMIMETICS**	28,338	$ 2,792,919.73
6510	OPIOID AGONISTS**	23,801	$ 1,016,722.41
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	23,636	$ 310,226.82
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	21,287	$ 270,181.48
3940	HMG COA REDUCTASE INHIBITORS**	21,156	$ 395,673.72
5710	BENZODIAZEPINES**	17,507	$ 182,854.92
7510	CENTRAL MUSCLE RELAXANTS**	15,661	$ 287,458.13
3610	ACE INHIBITORS**	14,335	$ 140,103.07

Q1 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
7260	ANTICONVULSANTS - MISC.**	34,315	$ 2,705,834.35
6599	OPIOID COMBINATIONS**	33,578	$ 810,834.57
4420	SYMPATHOMIMETICS**	30,551	$ 3,170,155.87
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	25,202	$ 321,555.13
6510	OPIOID AGONISTS**	25,168	$ 1,063,262.89
3940	HMG COA REDUCTASE INHIBITORS**	22,722	$ 428,842.94
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	22,212	$ 270,607.46
5710	BENZODIAZEPINES**	18,734	$ 189,624.66
7510	CENTRAL MUSCLE RELAXANTS**	16,795	$ 290,601.35
2210	GLUCOCORTICOSTEROIDS**	14,370	$ 180,288.84

Q2 2017

Class	Drug Class Name	Count of Claims	Pharmacy Paid
7260	ANTICONVULSANTS - MISC.**	45,637	$ 3,667,824.50
6599	OPIOID COMBINATIONS**	43,574	$ 998,712.92
4420	SYMPATHOMIMETICS**	39,281	$ 4,329,537.64
6510	OPIOID AGONISTS**	34,049	$ 1,406,192.97
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	32,205	$ 408,779.15
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	28,866	$ 360,187.39
3940	HMG COA REDUCTASE INHIBITORS**	28,068	$ 543,311.48
5710	BENZODIAZEPINES**	25,010	$ 249,237.17
7510	CENTRAL MUSCLE RELAXANTS**	21,710	$ 372,188.71
2210	GLUCOCORTICOSTEROIDS**	18,266	$ 355,741.10

Top 50 Drugs by Amount - Q4 2016

Drug Code	Drug Name	Claim Count		Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	16.00	$	3,830,078.78	114,532	16
5925001500	ARIPIPRAZOLE	4,288.00	$	3,736,132.19	17	15
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	6.00	$	2,520,061.02	210,000	30
1235990240	LEDIPASVIR-SOFOSBUVIR	143.00	$	2,330,403.27	12	12
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	15.00	$	1,646,384.77	56,593	20
5907005010	PALIPERIDONE PALMITATE	657.00	$	1,432,521.34	1	21
5940002310	LURASIDONE HCL	1,092.00	$	1,160,264.16	17	15
2710400300	INSULIN GLARGINE	3,240.00	$	1,105,835.88	12	25
1950206000	PALIVIZUMAB	409.00	$	1,086,912.38	1	20
9410003000	GLUCOSE BLOOD	7,091.00	$	950,744.77	73	22
4420101010	ALBUTEROL SULFATE	19,301.00	$	950,467.96	39	15
4420990270	FLUTICASONE-SALMETEROL	2,950.00	$	882,791.36	42	22
7260005700	PREGABALIN	2,594.00	$	833,824.70	48	20
4927002510	ESOMEPRAZOLE MAGNESIUM	3,734.00	$	829,043.22	21	20
3010002000	SOMATROPIN	219.00	$	813,914.39	2	10
5915307010	QUETIAPINE FUMARATE	7,895.00	$	747,871.32	28	19
6627001500	ADALIMUMAB	175.00	$	737,241.66	1	11
1235308000	SOFOSBUVIR	29.00	$	710,313.33	9	9
1235990265	SOFOSBUVIR-VELPATASVIR	46.00	$	691,074.97	10	10
2710400500	INSULIN LISPRO	1,450.00	$	632,595.93	10	20
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	256.00	$	593,770.89	20	20
4530402000	DORNASE ALFA	169.00	$	552,055.44	53	17
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	1,994.00	$	525,987.92	22	24
6629003000	ETANERCEPT	127.00	$	510,570.23	2	14
2710400200	INSULIN ASPART	1,200.00	$	505,962.40	11	20
2153253000	EVEROLIMUS	29.00	$	502,226.40	17	12
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2,358.00	$	494,814.93	8	24
6135303010	GUANFACINE HCL (ADHD)	1,796.00	$	486,986.45	19	18
6240552500	DIMETHYL FUMARATE	73.00	$	461,737.41	16	8
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	347.00	$	458,269.72	20	20
1235302510	DACLATASVIR DIHYDROCHLORIDE	27.00	$	448,243.09	9	9
7210000700	CLOBAZAM	347.00	$	441,138.25	62	14
6599000220	OXYCODONE W/ ACETAMINOPHEN	9,986.00	$	438,852.33	58	15
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,866.00	$	438,045.68	22	21
7260003600	LACOSAMIDE	800.00	$	430,259.25	61	15
6140002010	METHYLPHENIDATE HCL	2,347.00	$	405,406.70	35	19
8240157000	PEGFILGRASTIM	84.00	$	405,347.56	1	3
9310002500	DEFERASIROX	65.00	$	403,717.03	23	11
6510007510	OXYCODONE HCL	8,249.00	$	401,081.87	73	18
3090685000	IDURSULFASE	18.00	$	395,054.84	20	9
9340002010	NALOXONE HCL	169.00	$	379,844.11	0	7
7460003500	ETEPLIRSEN	4.00	$	377,640.68	14	3
0700007000	TOBRAMYCIN	118.00	$	377,466.68	111	11
2710400600	INSULIN DETEMIR	1,141.00	$	373,242.54	11	22
8580005000	ECULIZUMAB	18.00	$	372,012.00	97	1
6599170210	HYDROCODONE-ACETAMINOPHEN	20,021.00	$	367,433.47	61	16
9085006000	LIDOCAINE	1,582.00	$	353,261.05	53	13
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	21.00	$	344,384.57	6,092	11
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	2,806.00	$	340,917.45	28	20
1910002010	IMMUNE GLOBULIN (HUMAN) IV	78.00	$	331,920.18	506	3

Top 50 Drugs by Amount - Q1 2017

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	18	$ 3,839,329.14	84,192	12
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	26	$ 2,342,506.36	54,693	23
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	4	$ 1,747,240.68	70,000	10
1235990240	LEDIPASVIR-SOFOSBUVIR	110	$ 1,667,082.78	14	14
5907005010	PALIPERIDONE PALMITATE	870	$ 1,540,505.35	1	21
2710400300	INSULIN GLARGINE	3562	$ 1,500,640.34	14	30
1235990265	SOFOSBUVIR-VELPATASVIR	110	$ 1,369,292.39	10	10
7460003500	ETEPLIRSEN	15	$ 1,304,152.55	24	5
1950206000	PALIVIZUMAB	476	$ 1,279,326.33	1	23
5940002310	LURASIDONE HCL	1297	$ 1,254,908.36	19	16
4420101010	ALBUTEROL SULFATE	20177	$ 1,134,441.48	36	14
9410003000	GLUCOSE BLOOD	7239	$ 984,523.11	75	23
7260005700	PREGABALIN	2943	$ 940,770.95	49	21
4420990270	FLUTICASONE-SALMETEROL	3098	$ 940,038.25	42	23
6627001500	ADALIMUMAB	216	$ 901,309.53	1	10
2710400500	INSULIN LISPRO	1515	$ 885,555.96	13	25
4927002510	ESOMEPRAZOLE MAGNESIUM	3726	$ 855,958.62	22	21
5925001500	ARIPIPRAZOLE	4802	$ 807,374.79	16	15
3010002000	SOMATROPIN	196	$ 759,977.48	2	11
2710400200	INSULIN ASPART	1351	$ 724,327.84	14	26
5915307010	QUETIAPINE FUMARATE	8615	$ 721,499.51	30	20
1910002010	IMMUNE GLOBULIN (HUMAN) IV	114	$ 629,454.96	530	4
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	276	$ 590,289.02	20	20
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	2313	$ 581,000.18	23	25
2710400600	INSULIN DETEMIR	1285	$ 549,479.14	13	25
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2721	$ 540,719.19	8	24
4530402000	DORNASE ALFA	160	$ 527,980.89	49	17
7260003600	LACOSAMIDE	992	$ 522,831.76	55	14
2153253000	EVEROLIMUS	28	$ 508,688.67	14	9
6135303010	GUANFACINE HCL (ADHD)	1861	$ 507,517.53	20	19
7470005000	NUSINERSEN	3	$ 500,030.51	1	3
9310002500	DEFERASIROX	68	$ 494,704.90	21	10
6110002510	LISDEXAMFETAMINE DIMESYLATE	1953	$ 491,320.59	22	22
6240552500	DIMETHYL FUMARATE	73	$ 483,939.47	14	7
7210000700	CLOBAZAM	390	$ 467,317.24	67	15
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	364	$ 450,240.89	21	20
8240157000	PEGFILGRASTIM	83	$ 447,135.96	0	4
6629003000	ETANERCEPT	113	$ 446,375.49	2	12
3090685000	IDURSULFASE	24	$ 432,964.43	14	6
6140002010	METHYLPHENIDATE HCL	2404	$ 427,317.93	34	19
6599000220	OXYCODONE W/ ACETAMINOPHEN	10650	$ 405,381.61	58	15
3090404500	NITISINONE	6	$ 397,514.34	51	13
6510007510	OXYCODONE HCL	8937	$ 393,651.50	72	18
9085006000	LIDOCAINE	1887	$ 386,563.39	65	15
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	23	$ 382,498.53	5,552	11
2755007010	SITAGLIPTIN PHOSPHATE	1190	$ 379,463.48	29	29
1235308000	SOFOSBUVIR	17	$ 368,836.29	8	8
3030001000	CORTICOTROPIN	6	$ 363,881.02	2	2
6599170210	HYDROCODONE-ACETAMINOPHEN	21026	$ 352,175.15	60	15
0700007000	TOBRAMYCIN	102	$ 347,845.19	119	13

Top 50 Drugs by Amount - Q2 2017

Drug Code	Drug Name	Claim Count		Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	19	$	4,369,916.59	99,132	14
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	6	$	2,620,861.02	210,000	30
1235990240	LEDIPASVIR-SOFOSBUVIR	116	$	2,048,837.39	8	8
7470005000	NUSINERSEN	13	$	2,000,132.21	5	21
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	12	$	1,977,028.26	105,864	25
1235990265	SOFOSBUVIR-VELPATASVIR	118	$	1,786,388.20	7	7
5907005010	PALIPERIDONE PALMITATE	763	$	1,518,854.65	1	24
5940002310	LURASIDONE HCL	1,109	$	1,186,130.47	17	15
2710400300	INSULIN GLARGINE	2,384	$	1,115,309.42	15	34
4420101010	ALBUTEROL SULFATE	18,298	$	1,086,491.30	36	15
9410003000	GLUCOSE BLOOD	6,959	$	982,791.69	75	24
7260005700	PREGABALIN	2,793	$	929,163.42	44	19
4420990270	FLUTICASONE-SALMETEROL	2,867	$	918,205.04	43	23
6627001500	ADALIMUMAB	191	$	881,404.72	1	9
4927002510	ESOMEPRAZOLE MAGNESIUM	3,293	$	840,872.98	22	22
3010002000	SOMATROPIN	206	$	765,718.19	2	10
2710400500	INSULIN LISPRO	1,029	$	747,245.48	15	27
5925001500	ARIPIPRAZOLE	4,750	$	733,191.61	18	17
1910002010	IMMUNE GLOBULIN (HUMAN) IV	108	$	675,973.90	515	3
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	259	$	633,591.95	19	19
5915307010	QUETIAPINE FUMARATE	8,209	$	589,994.06	28	20
7460003500	ETEPLIRSEN	8	$	582,481.36	19	6
2153253000	EVEROLIMUS	35	$	578,474.20	12	9
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	2,113	$	570,614.56	24	25
2710400200	INSULIN ASPART	969	$	567,788.62	15	29
1235990230	ELBASVIR-GRAZOPREVIR	48	$	545,144.71	14	14
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2,541	$	540,079.03	8	24
4530402000	DORNASE ALFA	163	$	536,405.25	47	16
7260003600	LACOSAMIDE	1,027	$	534,377.91	51	13
8580005000	ECULIZUMAB	23	$	525,948.00	107	1
6135303010	GUANFACINE HCL (ADHD)	1,810	$	513,496.77	20	19
7210000700	CLOBAZAM	401	$	498,776.01	61	14
9310002500	DEFERASIROX	67	$	496,752.14	24	11
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,872	$	478,678.04	22	21
6240552500	DIMETHYL FUMARATE	70	$	463,542.76	15	7
9085006000	LIDOCAINE	2,129	$	459,717.09	85	16
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	22	$	452,702.31	8,886	12
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	317	$	442,135.71	21	21
6140002010	METHYLPHENIDATE HCL	2,391	$	436,009.44	34	19
8240157000	PEGFILGRASTIM	79	$	433,288.68	0	3
3090685000	IDURSULFASE	40	$	423,739.34	8	3
6629003000	ETANERCEPT	97	$	419,174.40	2	12
2710400600	INSULIN DETEMIR	951	$	405,721.20	16	30
3030001000	CORTICOTROPIN	6	$	400,263.02	2	5
9037403530	DICLOFENAC SODIUM (ACTINIC KERATOSES)	457	$	398,615.67	217	20
2135303200	IPILIMUMAB	7	$	376,015.51	118	1
2133502000	BEVACIZUMAB	326	$	358,038.97	6	1
6599000220	OXYCODONE W/ ACETAMINOPHEN	10,154	$	350,216.66	56	15
6510007510	OXYCODONE HCL	8,512	$	347,380.03	71	18
2135304100	NIVOLUMAB	83	$	334,212.12	138	1

Top 50 Drugs by Claim Count - Q4 2016

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
6599170210	HYDROCODONE-ACETAMINOPHEN	20021	$ 367,433.47	61	16
4420101010	ALBUTEROL SULFATE	19301	$ 950,467.96	39	15
3610003000	LISINOPRIL	12793	$ 102,955.51	32	29
7260003000	GABAPENTIN	12769	$ 186,635.62	70	22
6610002000	IBUPROFEN	11339	$ 107,259.48	47	13
3940001010	ATORVASTATIN CALCIUM	10703	$ 112,201.25	26	26
3400000310	AMLODIPINE BESYLATE	10082	$ 78,325.14	27	26
6599000220	OXYCODONE W/ ACETAMINOPHEN	9986	$ 438,852.33	58	15
5710001000	ALPRAZOLAM	9796	$ 105,865.78	50	22
2810001010	LEVOTHYROXINE SODIUM	9724	$ 148,347.60	30	29
2725005000	METFORMIN HCL	9702	$ 231,185.78	56	28
6510007510	OXYCODONE HCL	8249	$ 401,081.87	73	18
5812008010	TRAZODONE HCL	8101	$ 88,664.55	29	21
5915307010	QUETIAPINE FUMARATE	7895	$ 747,871.32	28	19
9410003000	GLUCOSE BLOOD	7091	$ 950,744.77	73	22
4450505010	MONTELUKAST SODIUM	6778	$ 113,460.24	21	21
5816007010	SERTRALINE HCL	6740	$ 73,828.41	27	22
0120001010	AMOXICILLIN	6670	$ 70,952.42	58	6
4220003230	FLUTICASONE PROPIONATE (NASAL)	6539	$ 78,146.84	13	24
3320003010	METOPROLOL TARTRATE	6424	$ 50,657.51	45	24
6410001000	ASPIRIN	6240	$ 34,429.09	24	23
6510005510	MORPHINE SULFATE	6184	$ 178,619.54	29	12
5025006505	ONDANSETRON HCL	6083	$ 35,887.99	5	2
7720203200	CHOLECALCIFEROL	5842	$ 43,455.74	24	22
5907007000	RISPERIDONE	5660	$ 91,465.09	35	20
3940007500	SIMVASTATIN	5575	$ 43,960.27	29	29
4927007010	PANTOPRAZOLE SODIUM	5573	$ 55,318.11	21	20
4920002010	RANITIDINE HCL	5479	$ 69,692.48	44	22
0340001000	AZITHROMYCIN	5450	$ 75,873.83	7	4
6510009510	TRAMADOL HCL	5227	$ 49,991.91	58	16
5816004000	FLUOXETINE HCL	5222	$ 94,505.77	26	20
2210004500	PREDNISONE	5099	$ 44,127.46	16	9
7510005010	CYCLOBENZAPRINE HCL	5058	$ 53,623.28	37	16
4155003000	LORATADINE	4965	$ 53,111.15	32	21
7210001000	CLONAZEPAM	4943	$ 52,514.14	45	22
3620101010	CLONIDINE HCL	4883	$ 68,442.96	38	22
3720003000	FUROSEMIDE	4873	$ 36,222.10	30	24
5025006500	ONDANSETRON	4844	$ 57,500.27	6	3
3615004020	LOSARTAN POTASSIUM	4631	$ 39,176.46	28	26
5816002010	CITALOPRAM HYDROBROMIDE	4431	$ 40,609.31	25	24
7250001010	DIVALPROEX SODIUM	4427	$ 217,346.48	58	20
7720203000	ERGOCALCIFEROL	4317	$ 46,102.27	4	23
5925001500	ARIPIPRAZOLE	4288	$ 3,736,132.19	17	15
6610005200	MELOXICAM	4252	$ 36,331.68	26	23
7975001000	SODIUM CHLORIDE	4211	$ 10,448.88	484	1
7510009010	TIZANIDINE HCL	4204	$ 109,194.06	51	21
4155002010	CETIRIZINE HCL	4127	$ 45,664.10	42	20
7260004000	LAMOTRIGINE	4120	$ 246,319.29	43	21
3330000700	CARVEDILOL	4103	$ 33,323.89	49	25
5710006000	LORAZEPAM	3962	$ 39,018.92	23	10

Top 50 Drugs by Claim Count - Q1 2017

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
6599170210	HYDROCODONE-ACETAMINOPHEN	21026	$ 352,175.15	60	15
4420101010	ALBUTEROL SULFATE	20177	$ 1,134,441.48	36	14
7260003000	GABAPENTIN	13926	$ 194,129.29	71	23
3610003000	LISINOPRIL	12603	$ 100,453.99	40	36
6610002000	IBUPROFEN	12049	$ 110,434.50	47	13
3940001010	ATORVASTATIN CALCIUM	11798	$ 122,816.93	27	27
6599000220	OXYCODONE W/ ACETAMINOPHEN	10650	$ 405,381.61	58	15
5710001000	ALPRAZOLAM	10585	$ 109,483.61	50	22
2810001010	LEVOTHYROXINE SODIUM	10274	$ 151,489.65	29	30
3400000310	AMLODIPINE BESYLATE	10098	$ 73,020.04	36	35
2725005000	METFORMIN HCL	9709	$ 290,240.42	68	33
6510007510	OXYCODONE HCL	8937	$ 393,651.50	72	18
5915307010	QUETIAPINE FUMARATE	8615	$ 721,499.51	30	20
5812008010	TRAZODONE HCL	8561	$ 93,315.60	30	22
0120001010	AMOXICILLIN	7821	$ 83,475.39	63	6
4220003230	FLUTICASONE PROPIONATE (NASAL)	7490	$ 86,066.49	12	23
4450505010	MONTELUKAST SODIUM	7416	$ 119,008.11	22	22
9410003000	GLUCOSE BLOOD	7239	$ 984,523.11	75	23
5816007010	SERTRALINE HCL	7109	$ 76,036.66	27	22
6510005510	MORPHINE SULFATE	6640	$ 160,160.00	26	11
0340001000	AZITHROMYCIN	6555	$ 86,352.66	7	4
5025006505	ONDANSETRON HCL	6455	$ 37,693.16	5	2
6410001000	ASPIRIN	6434	$ 34,570.31	23	22
3320003010	METOPROLOL TARTRATE	6414	$ 52,266.28	59	32
7720203200	CHOLECALCIFEROL	6181	$ 46,380.73	24	22
4927007010	PANTOPRAZOLE SODIUM	6149	$ 57,699.94	21	21
5907007000	RISPERIDONE	5968	$ 101,042.46	37	21
2210004500	PREDNISONE	5749	$ 48,602.15	16	9
3940007500	SIMVASTATIN	5730	$ 42,726.75	31	31
4920002010	RANITIDINE HCL	5625	$ 70,155.71	46	23
5816004000	FLUOXETINE HCL	5563	$ 93,185.41	30	23
4155003000	LORATADINE	5408	$ 58,871.07	34	21
7510005010	CYCLOBENZAPRINE HCL	5388	$ 54,584.87	39	17
6510009510	TRAMADOL HCL	5315	$ 48,457.17	58	16
7210001000	CLONAZEPAM	5280	$ 52,585.02	44	21
5025006500	ONDANSETRON	5073	$ 55,526.12	7	3
7250001010	DIVALPROEX SODIUM	4875	$ 211,227.34	56	20
3720003000	FUROSEMIDE	4852	$ 35,588.32	38	30
3615004020	LOSARTAN POTASSIUM	4826	$ 39,490.01	37	35
5925001500	ARIPIPRAZOLE	4802	$ 807,374.79	16	15
6610005200	MELOXICAM	4669	$ 39,791.60	27	24
3620101010	CLONIDINE HCL	4634	$ 67,221.11	50	29
7510009010	TIZANIDINE HCL	4537	$ 103,551.25	51	21
7720203000	ERGOCALCIFEROL	4535	$ 47,908.25	4	25
7975001000	SODIUM CHLORIDE	4469	$ 11,103.14	454	1
5816002010	CITALOPRAM HYDROBROMIDE	4469	$ 39,656.51	26	25
4155002010	CETIRIZINE HCL	4459	$ 49,592.44	42	20
7260004000	LAMOTRIGINE	4356	$ 226,335.99	42	21
5710006000	LORAZEPAM	4213	$ 39,458.32	22	10
6020408010	ZOLPIDEM TARTRATE	4186	$ 38,016.79	24	24

Top 50 Drugs by Claim Count - Q2 2017

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
6599170210	HYDROCODONE-ACETAMINOPHEN	19967	$ 317,947.99	58	15
4420101010	ALBUTEROL SULFATE	18298	$ 1,086,491.30	36	15
7260003000	GABAPENTIN	13551	$ 181,760.42	72	23
3940001010	ATORVASTATIN CALCIUM	10892	$ 112,588.26	27	26
6610002000	IBUPROFEN	10837	$ 97,499.04	43	13
5710001000	ALPRAZOLAM	10250	$ 105,012.40	50	21
6599000220	OXYCODONE W/ ACETAMINOPHEN	10154	$ 350,216.66	56	15
2810001010	LEVOTHYROXINE SODIUM	9441	$ 145,862.61	30	30
3610003000	LISINOPRIL	8945	$ 66,304.67	41	37
6510007510	OXYCODONE HCL	8512	$ 347,380.03	71	18
5915307010	QUETIAPINE FUMARATE	8209	$ 589,994.06	28	20
5812008010	TRAZODONE HCL	8131	$ 89,113.53	30	22
5025006505	ONDANSETRON HCL	7412	$ 36,721.93	4	2
4220003230	FLUTICASONE PROPIONATE (NASAL)	7377	$ 83,623.08	12	24
3400000310	AMLODIPINE BESYLATE	7273	$ 42,720.36	40	38
4450505010	MONTELUKAST SODIUM	7212	$ 110,790.63	23	22
6510005510	MORPHINE SULFATE	7026	$ 137,661.23	21	9
9410003000	GLUCOSE BLOOD	6959	$ 982,791.69	75	24
2725005000	METFORMIN HCL	6886	$ 232,635.80	77	38
5816007010	SERTRALINE HCL	6866	$ 73,542.78	28	23
6410001000	ASPIRIN	6475	$ 34,222.78	23	22
7720203200	CHOLECALCIFEROL	6183	$ 47,835.76	26	24
0120001010	AMOXICILLIN	6010	$ 62,758.77	56	6
5907007000	RISPERIDONE	5870	$ 95,601.79	36	21
4927007010	PANTOPRAZOLE SODIUM	5799	$ 53,914.30	21	20
7975001000	SODIUM CHLORIDE	5677	$ 14,969.13	469	1
4155003000	LORATADINE	5449	$ 60,149.79	32	20
5025006500	ONDANSETRON	5291	$ 56,766.01	7	3
4920002010	RANITIDINE HCL	5256	$ 67,650.17	49	24
5816004000	FLUOXETINE HCL	5207	$ 92,346.65	30	23
7510005010	CYCLOBENZAPRINE HCL	5011	$ 51,405.23	42	19
7210001000	CLONAZEPAM	4996	$ 50,998.40	44	22
6510009510	TRAMADOL HCL	4995	$ 44,401.99	56	16
2210004500	PREDNISONE	4877	$ 42,034.53	16	9
3940007500	SIMVASTATIN	4848	$ 35,080.47	33	33
5925001500	ARIPIPRAZOLE	4750	$ 733,191.61	18	17
4155002010	CETIRIZINE HCL	4716	$ 51,359.83	41	20
7250001010	DIVALPROEX SODIUM	4689	$ 182,064.27	56	20
3320003010	METOPROLOL TARTRATE	4443	$ 33,076.91	56	30
7260004000	LAMOTRIGINE	4381	$ 216,349.22	44	22
0340001000	AZITHROMYCIN	4365	$ 56,749.34	7	3
5710006000	LORAZEPAM	4293	$ 38,248.63	20	10
7720203000	ERGOCALCIFEROL	4265	$ 45,392.53	4	26
7510009010	TIZANIDINE HCL	4252	$ 94,135.97	50	20
6610005200	MELOXICAM	4235	$ 35,246.25	27	24
5816002010	CITALOPRAM HYDROBROMIDE	4146	$ 37,724.15	27	26
4920003000	FAMOTIDINE	4012	$ 32,014.24	25	15
7260004300	LEVETIRACETAM	4008	$ 176,681.52	127	20
5830004010	BUPROPION HCL	3938	$ 84,795.78	32	23
6020408010	ZOLPIDEM TARTRATE	3869	$ 37,015.76	24	24

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2016-10-01 and 2016-12-31

Client Totals:

Total Rxs	Plan Paid	Member Paid
735,135	$75,586,654	$0

DUR Information as a percent of total:

DUR Type	Total Rxs	Percent of Total Rxs - Paid	Cases	Rejected Rxs	Percent of Total Rxs - Rejects
Total Claims Paid	735,135	0.0%	0	0	0.0%
Cases / Rxs	355,263	48.3%	307,190	240,497	32.7%
TD - Therapeutic Duplication	102,700	14.0%	83,887	104,733	14.2%
LR - Underuse Precaution	66,289	9.0%	66,544	7,852	1.1%
ID - Ingredient Duplication	54,619	7.4%	19,621	54,524	7.4%
DD - Drug-Drug Interaction	47,058	6.4%	53,213	61,192	8.3%
LD - Low Dose Alert	34,959	4.8%	34,780	4,775	0.6%
MN - Insufficnt Duration Alert	21,182	2.9%	20,731	1,280	0.2%
HD - High Dose Alert	19,468	2.6%	19,192	3,743	0.5%
MX - Excessive Duration Alert	8,930	1.2%	9,158	2,396	0.3%
PA - Drug-Age Precaution	50	0.0%	56	2	0.0%
SX - Drug Gender Alert	8	0.0%	8	0	0.0%

* More than one DUR message per paid, rejected or reversed claim(Cases > Rxs)
* Same claims could have multiple DUR messages. And there could multiple of the same DUR message on a claim
* This report does not include reversals.

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2016-10-01 and 2016-12-31

DD

Curr Rank	Top Drug Drug Interaction	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	TRAZODONE HCL - QUETIAPINE	Message Only	997	248	$11,369.75	$11.40	$0.00	26.67	36.37
2	TRAZODONE - QUETIAPINE FUMARATE	Message Only	944	233	$14,315.81	$15.17	$0.00	25.93	40.53
3	SPIRONOLACTONE - LISINOPRIL	Message Only	619	168	$6,701.43	$10.83	$0.00	35.01	38.75
4	SPIRONOLACT - LISINOPRIL	Message Only	568	140	$4,633.55	$8.16	$0.00	33.55	39.35
5	TRAZODONE HCL - CITALOPRAM	Message Only	534	180	$5,428.43	$10.17	$0.00	29.50	37.98
6	TRAZODONE - CITALOPRAM HYDROBROMIDE	Message Only	526	148	$4,588.39	$8.72	$0.00	28.93	29.49
7	DIVALPROEX - CLONAZEPAM	Message Only	462	186	$4,359.02	$9.44	$0.00	26.29	55.54
8	SIMVASTATIN - FENOFIBRATE	Message Only	452	129	$7,386.65	$16.34	$0.00	35.00	34.92
9	FENOFIBRATE - ATORVASTATIN CALCIUM	Message Only	439	120	$4,876.97	$11.11	$0.00	31.28	31.35
10	QUETIAPINE - ONDANSETRON HCL	Message Only	432	3	$180.49	$0.42	$0.00	1.00	1.69
10	TRAZODONE - ONDANSETRON HCL	Message Only	432	24	$182.52	$0.42	$0.00	1.00	2.05
All Others			46,808	59,613	$4,932,892.68	$105.39	$0.00	23.41	44.65
Summary			53,213	61,192	$4,996,915.69	$93.90	$0.00	23.70	43.29

HD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	KETOROLAC TROMETHAMINE	GERIATRIC MAX DLY = 2.00UN	Message Only	521	41	$7,640.63	$14.67	$0.00	1.00	6.11
2	HYDROCODONE/ ACETAMINOPHEN	ADULT MAX DLY = 6.00 UN	Message Only	433	54	$12,277.73	$28.36	$0.00	14.57	111.47
3	GRANISETRON HCL	GERIATRIC MAX DLY = .85UN	Message Only	278	20	$3,368.99	$12.12	$0.00	1.00	1.00
4	ZOLPIDEM TARTRATE	GERIATRIC MAX DLY = .50UN	Message Only	276	20	$847.06	$3.07	$0.00	30.34	30.34
5	MIDAZOLAM HCL	GERIATRIC MAX DLY = 3.50UN	Message Only	259	7	$746.48	$2.88	$0.00	1.00	8.43
6	MIDAZOLAM HCL	GERIATRIC MAX DLY = .70UN	Message Only	244	6	$287.63	$1.18	$0.00	1.00	1.39
7	IBUPROFEN	ADULT MAX DLY = 4.00 UN	Message Only	190	30	$2,055.12	$10.82	$0.00	7.89	37.52
8	BETAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 1.50UN	Message Only	186	13	$4,901.49	$26.35	$0.00	1.00	5.26
9	INVEGA SUSTENNA	ADULT MAX DLY = .05 UN	Message Only	182	115	$368,399.64	$2,024.17	$0.00	27.31	1.50
10	CEFTRIAXONE SODIUM	GERIATRIC MAX DLY = 4.00UN	Message Only	179	2	$6,574.05	$36.73	$0.00	1.00	51.31
All Others				16,444	3,435	$6,992,866.61	$425.25	$0.00	15.47	258.08
HD				19,192	3,743	$7,399,965.43	$385.58	$0.00	14.44	225.31

ID

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	PROAIR HFA	PROAIR HFA AER	Message Only	270	17	$18,440.80	$68.30	$0.00	24.14	9.76
2	GABAPENTIN	GABAPENTIN CAP 300MG	Message Only	254	7	$3,357.39	$13.22	$0.00	34.17	100.24
3	ONDANSETRON ODT	ONDANSETRON TAB 4MG ODT	Message Only	203	0	$85.17	$0.42	$0.00	1.00	1.07
4	CLONIDINE HCL	CLONIDINE TAB 0.1MG	Message Only	189	12	$2,007.15	$10.62	$0.00	30.28	52.55
5	TRAZODONE HCL	TRAZODONE TAB 100MG	Message Only	168	16	$2,037.58	$12.13	$0.00	29.47	43.48
6	TRAZODONE HCL	TRAZODONE TAB 50MG	Message Only	154	6	$1,612.18	$10.47	$0.00	28.79	37.11
7	AMLODIPINE BESYLATE	AMLODIPINE TAB 10MG	Message Only	150	7	$1,476.02	$9.84	$0.00	31.37	31.57
8	PANTOPRAZOLE SODIUM	PANTOPRAZOLE TAB 40MG	Message Only	147	9	$1,650.99	$11.23	$0.00	29.65	30.54
8	ONETOUCH ULTRA BLUE	ONETOUCH TES ULTRA BL	Message Only	147	0	$17,121.24	$116.47	$0.00	28.08	86.43
10	HYDROCODONE/ ACETAMINOPHEN	HYDROCO/APAP TAB 5-325MG	Message Only	146	0	$34.58	$0.24	$0.00	1.00	1.78
All Others				17,793	54,450	$2,833,999.47	$159.28	$0.00	27.44	93.95
ID				19,621	54,524	$2,881,822.57	$146.87	$0.00	27.12	88.94

LD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	ONDANSETRON HCL	GERIATRIC MIN DLY = 2.00UN	Message Only	2,445	57	$595.43	$0.24	$0.00	1.13	1.13
2	ONDANSETRON ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	1,306	16	$596.42	$0.46	$0.00	1.22	1.12
3	IPRATROPIUM BROMIDE/ ALBUT	GERIATRIC MIN DLY = 9.00UN	Message Only	1,006	23	$480.42	$0.48	$0.00	1.59	6.74
4	ALBUTEROL SULFATE	GERIATRIC MIN DLY = 9.00UN	Message Only	637	22	$749.12	$1.18	$0.00	2.96	14.86
5	HEPARIN SODIUM	GERIATRIC MIN DLY = 4.00UN	Message Only	569	13	$1,358.21	$2.39	$0.00	1.16	1.87
6	VITAMIN D	ADULT MIN DLY = .14 UN	Message Only	534	63	$5,142.83	$9.63	$0.00	31.21	3.23
7	METFORMIN HCL	ADULT MIN DLY = 1.70 UN	Message Only	487	107	$4,334.04	$8.90	$0.00	36.00	35.17
8	GABAPENTIN	ADULT MIN DLY = 3.00 UN	Message Only	442	87	$4,665.93	$10.56	$0.00	32.82	52.86
9	PROPRANOLOL HCL	ADULT MIN DLY = 3.00 UN	Message Only	371	68	$6,114.94	$16.48	$0.00	29.75	52.53
10	ZOFRAN ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	334	3	$6,896.20	$20.65	$0.00	1.00	1.00
All Others				26,649	4,316	$3,744,584.18	$140.51	$0.00	24.37	45.54
LD				34,780	4,775	$3,775,517.72	$108.55	$0.00	20.64	37.30

LR

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	LISINOPRIL	7 DAYS LATE REFILLING	Message Only	91	13	$779.36	$8.56	$0.00	29.00	32.30
2	ATORVASTATIN CALCIUM	7 DAYS LATE REFILLING	Message Only	86	18	$978.15	$11.37	$0.00	30.00	30.00
3	METFORMIN HCL	7 DAYS LATE REFILLING	Message Only	82	5	$676.40	$8.25	$0.00	30.73	62.01
4	GABAPENTIN	7 DAYS LATE REFILLING	Message Only	74	3	$1,254.11	$16.95	$0.00	29.58	99.53
5	LISINOPRIL	8 DAYS LATE REFILLING	Message Only	73	9	$592.56	$8.12	$0.00	29.66	31.51
6	AMLODIPINE BESYLATE	7 DAYS LATE REFILLING	Message Only	70	2	$590.80	$8.44	$0.00	30.20	30.73
6	ATORVASTATIN CALCIUM	8 DAYS LATE REFILLING	Message Only	70	7	$789.15	$11.27	$0.00	29.70	29.49
8	LEVOTHYROXINE SODIUM	8 DAYS LATE REFILLING	Message Only	66	5	$803.32	$12.17	$0.00	29.98	29.53
9	LISINOPRIL	9 DAYS LATE REFILLING	Message Only	65	5	$515.19	$7.93	$0.00	30.02	30.94
10	AMLODIPINE BESYLATE	8 DAYS LATE REFILLING	Message Only	64	5	$501.37	$7.83	$0.00	28.73	29.44
All Others				65,803	7,780	$7,414,496.61	$112.68	$0.00	28.72	52.09
LR				66,544	7,852	$7,421,977.02	$111.53	$0.00	28.73	51.96

MN

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	IPRATROPIUM BROMIDE/ALBUT	MIN. DAYS THERAPY = 30	Message Only	1,880	201	$13,187.60	$7.01	$0.00	4.88	62.10
2	PANTOPRAZOLE SODIUM	MIN. DAYS THERAPY = 7	Message Only	754	14	$161.86	$0.21	$0.00	1.05	1.12
3	LISINOPRIL	MIN. DAYS THERAPY = 7	Message Only	730	19	$153.22	$0.21	$0.00	1.07	1.44
4	AMLODIPINE BESYLATE	MIN. DAYS THERAPY = 7	Message Only	563	8	$89.86	$0.16	$0.00	1.04	1.15
5	METOPROLOL TARTRATE	MIN. DAYS THERAPY = 7	Message Only	518	27	$149.56	$0.29	$0.00	1.09	1.62
6	CLONIDINE HCL	MIN. DAYS THERAPY = 7	Message Only	469	27	$656.49	$1.40	$0.00	1.31	3.41
7	ATORVASTATIN CALCIUM	MIN. DAYS THERAPY = 7	Message Only	462	1	$261.84	$0.57	$0.00	1.13	1.29
8	QUETIAPINE FUMARATE	MIN. DAYS THERAPY = 7	Message Only	440	50	$339.15	$0.77	$0.00	1.12	2.43
9	LEVETIRACETAM	MIN. DAYS THERAPY = 14	Message Only	392	27	$2,898.08	$7.39	$0.00	3.41	33.39
10	CARVEDILOL	MIN. DAYS THERAPY = 7	Message Only	386	12	$44.28	$0.11	$0.00	1.02	1.93
All Others				14,137	894	$1,243,665.75	$87.97	$0.00	2.38	21.67
MN				20,731	1,280	$1,261,607.69	$60.86	$0.00	2.36	21.40

MX

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	2,692	1,746	$28,601.84	$10.62	$0.00	30.19	66.31
2	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	1,585	1	$17,235.39	$10.87	$0.00	30.16	68.62
3	FLUCONAZOLE	MAX DAYS THERAPY = 1	Message Only	505	123	$6,561.90	$12.99	$0.00	6.41	3.00
4	AZITHROMYCIN	MAX DAYS THERAPY = 5	Message Only	297	54	$6,688.89	$22.52	$0.00	11.64	19.84
5	EPIPEN 2-PAK	MAX DAYS THERAPY = 1	Message Only	241	11	$156,702.17	$650.22	$0.00	11.26	2.42
6	MAPAP	MAX DAYS THERAPY = 10	Message Only	235	6	$2,170.12	$9.23	$0.00	25.26	120.57
7	SENEXON-S	MAX DAYS THERAPY = 14	Message Only	172	13	$1,622.71	$9.43	$0.00	31.40	59.16
8	DIPHENOXYLATE/ ATROPINE	MAX DAYS THERAPY = 14	Message Only	163	9	$5,393.33	$33.09	$0.00	27.83	99.12
9	PHENAZOPYRIDINE HCL	MAX DAYS THERAPY = 2	Message Only	151	1	$6,202.94	$41.08	$0.00	5.61	15.01
10	EVZIO	MAX DAYS THERAPY = 1	Message Only	147	2	$470,871.75	$3,203.21	$0.00	22.31	0.78
All Others				2,970	430	$709,868.39	$239.01	$0.00	24.74	70.02
MX				9,158	2,396	$1,411,919.43	$154.17	$0.00	25.33	61.18

PA

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	PROMETHAZINE-DM	AGE LESS THAN 4	Message Only	16	0	$106.22	$6.64	$0.00	10.06	84.12
2	NITROFURANTOIN	AGE LESS THAN 4	Message Only	12	2	$2,637.69	$219.81	$0.00	16.50	162.50
3	PROMETHAZINE HCL	AGE LESS THAN 4	Message Only	10	0	$186.74	$18.67	$0.00	9.20	91.80
4	PROMETHAZINE/ DEXTROMETHOR	AGE LESS THAN 4	Message Only	8	0	$88.65	$11.08	$0.00	9.75	97.00
5	NITROFURANTOIN MACROCRYST	AGE LESS THAN 4	Message Only	3	0	$68.05	$22.68	$0.00	30.00	20.00
5	PROMETHAZINE HCL PLAIN	AGE LESS THAN 4	Message Only	3	0	$15.98	$5.33	$0.00	4.33	73.33
7	PROMETHAZINE/ CODEINE	AGE LESS THAN 4	Message Only	2	0	$20.80	$10.40	$0.00	9.50	180.00
8	INFANRIX	AGE GREATER THAN 64	Message Only	1	0	$22.40	$22.40	$0.00	1.00	0.50
8	NITROFURANTOIN MONOHYDRAT	AGE LESS THAN 4	Message Only	1	0	$20.56	$20.56	$0.00	5.00	10.00
PA				56	2	$3,167.09	$56.56	$0.00	11.73	100.72

SX

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	BICALUTAMIDE	GENERAL CONTRAINDICATION	Message Only	8	0	$102.45	$12.81	$0.00	9.62	9.62
SX				8	0	$102.45	$12.81	$0.00	9.62	9.62

TD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx
1	QUETIAPINE FUMARATE	ORAL ANTIPSYCHOTICS	Message Only	2,268	0	$40,462.54	$17.84	$0.00	28.53
2	RISPERIDONE	ORAL ANTIPSYCHOTICS	Message Only	1,537	0	$19,976.33	$13.00	$0.00	28.43
3	MORPHINE SULFATE	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,420	140	$3,968.55	$2.79	$0.00	1.00
4	GABAPENTIN	GABAPENTIN AND RELATED	Message Only	1,147	0	$19,514.19	$17.01	$0.00	32.60
5	HYDROMORPHONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	995	73	$4,299.59	$4.32	$0.00	1.00
6	LISINOPRIL	ANGIOTENSIN BLOCKERS	Message Only	965	0	$8,713.92	$9.03	$0.00	41.02
7	LEVOTHYROXINE SODIUM	THYROID HORMONES	Message Only	853	0	$13,846.55	$16.23	$0.00	41.31
8	HYDROCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	829	114	$16,086.68	$19.40	$0.00	19.38
9	OXYCODONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	801	68	$24,681.28	$30.81	$0.00	25.04
10	ABILIFY	ORAL ANTIPSYCHOTICS	Message Only	786	0	$833,973.02	$1,061.03	$0.00	28.40
All Others				72,286	104,338	$10,925,863.58	$151.15	$0.00	22.94
TD				83,887	104,733	$11,911,386.23	$141.99	$0.00	23.12

TD

Quantity Per Rx
41.63
48.68
1.71
102.75
2.84
44.96
40.83
77.69
107.91
32.93
64.68
62.26

Selected Filters

Client(s): Nevada Medicaid - HPES

Carrier(s): NVM-NEVADA MEDICAID

Account(s): ALL

Group(s): ALL

Date Type:	Date Filled Submitted
Start Date:	2016-10-01
End Date:	2016-12-31
Relative Description:	Select Date Range
Display Report Description:	No
Top Values to Display:	10

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2017-01-01 and 2017-03-31

Client Totals:

Total Rxs	Plan Paid	Member Paid
769,702	$78,090,741	$0

DUR Information as a percent of total:

DUR Type	Total Rxs	Percent of Total Rxs - Paid	Cases	Rejected Rxs	Percent of Total Rxs - Rejects
Total Claims Paid	769,702	0.0%	0	0	0.0%
Cases / Rxs	367,423	47.7%	323,381	254,287	33.0%
TD - Therapeutic Duplication	107,656	14.0%	90,863	109,640	14.2%
LR - Underuse Precaution	64,369	8.4%	64,769	8,063	1.0%
ID - Ingredient Duplication	55,795	7.2%	21,111	55,727	7.2%
DD - Drug-Drug Interaction	51,923	6.7%	59,733	67,948	8.8%
LD - Low Dose Alert	35,131	4.6%	34,893	4,874	0.6%
MN - Insufficnt Duration Alert	22,759	3.0%	22,388	1,316	0.2%
HD - High Dose Alert	20,176	2.6%	19,883	4,041	0.5%
MX - Excessive Duration Alert	9,550	1.2%	9,669	2,674	0.3%
PA - Drug-Age Precaution	58	0.0%	66	3	0.0%
SX - Drug Gender Alert	6	0.0%	6	1	0.0%

* More than one DUR message per paid, rejected or reversed claim(Cases > Rxs)
* Same claims could have multiple DUR messages. And there could multiple of the same DUR message on a claim
* This report does not include reversals.

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2017-01-01 and 2017-03-31

DD

Curr Rank	Top Drug Drug Interaction	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	TRAZODONE HCL - QUETIAPINE	Message Only	1,092	301	$13,009.86	$11.91	$0.00	28.15	38.76
2	TRAZODONE - QUETIAPINE FUMARATE	Message Only	1,044	267	$16,036.62	$15.36	$0.00	28.35	44.80
3	SPIRONOLACTONE - LISINOPRIL	Message Only	648	155	$6,959.49	$10.74	$0.00	43.02	46.98
4	TRAZODONE - CITALOPRAM HYDROBROMIDE	Message Only	622	181	$5,341.86	$8.59	$0.00	30.57	31.72
5	TRAZODONE HCL - CITALOPRAM	Message Only	612	203	$6,682.12	$10.92	$0.00	31.08	41.68
6	SPIRONOLACT - LISINOPRIL	Message Only	611	146	$4,516.55	$7.39	$0.00	40.91	47.89
7	DIVALPROEX - CLONAZEPAM	Message Only	605	260	$4,979.97	$8.23	$0.00	24.24	49.45
8	TRAZODONE - ONDANSETRON HCL	Message Only	548	20	$303.07	$0.55	$0.00	1.11	2.29
9	QUETIAPINE - CITALOPRAM HYDROBROMIDE	Message Only	516	156	$4,892.47	$9.48	$0.00	30.09	32.38
10	SIMVASTATIN - FENOFIBRATE	Message Only	515	152	$6,870.56	$13.34	$0.00	35.81	36.00
All Others			52,920	66,107	$6,030,125.51	$113.95	$0.00	25.13	45.69
Summary			59,733	67,948	$6,099,718.08	$102.12	$0.00	25.62	44.84

HD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	ZOLPIDEM TARTRATE	GERIATRIC MAX DLY = .50UN	Message Only	478	40	$1,086.50	$2.27	$0.00	29.63	29.63
2	KETOROLAC TROMETHAMINE	GERIATRIC MAX DLY = 2.00UN	Message Only	451	14	$6,505.72	$14.43	$0.00	1.00	7.60
3	HYDROCODONE/ ACETAMINOPHEN	ADULT MAX DLY = 6.00 UN	Message Only	400	64	$10,833.97	$27.08	$0.00	14.90	115.22
4	GRANISETRON HCL	GERIATRIC MAX DLY = .85UN	Message Only	288	8	$4,416.62	$15.34	$0.00	1.00	1.16
5	INVEGA SUSTENNA	ADULT MAX DLY = .05 UN	Message Only	226	0	$561,235.30	$2,483.34	$0.00	23.92	1.85
5	MIDAZOLAM HCL	GERIATRIC MAX DLY = 3.50UN	Message Only	226	5	$692.64	$3.06	$0.00	1.00	9.15
7	MIDAZOLAM HCL	GERIATRIC MAX DLY = .70UN	Message Only	219	3	$268.94	$1.23	$0.00	1.00	1.42
8	IBUPROFEN	ADULT MAX DLY = 4.00 UN	Message Only	216	13	$2,273.41	$10.53	$0.00	7.67	34.57
9	BETAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 1.50UN	Message Only	202	2	$5,033.42	$24.92	$0.00	1.00	5.03
10	DEXAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 4.00UN	Message Only	199	8	$3,558.34	$17.88	$0.00	1.00	36.81
All Others				16,978	3,884	$9,186,884.10	$541.11	$0.00	16.63	145.47
HD				19,883	4,041	$9,782,788.96	$492.02	$0.00	15.65	128.38

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2017-01-01 and 2017-03-31

ID

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	PROVENTIL HFA	PROVENTIL AER HFA	Message Only	346	20	$31,780.04	$91.85	$0.00	25.68	7.82
2	GABAPENTIN	GABAPENTIN CAP 300MG	Message Only	291	17	$4,081.99	$14.03	$0.00	37.98	118.51
3	TRAZODONE HCL	TRAZODONE TAB 100MG	Message Only	195	7	$2,197.53	$11.27	$0.00	31.67	43.48
4	HYDROCODONE/ ACETAMINOPHEN	HYDROCO/APAP TAB 5-325MG	Message Only	180	0	$46.65	$0.26	$0.00	1.00	2.00
5	AMLODIPINE BESYLATE	AMLODIPINE TAB 10MG	Message Only	176	12	$1,803.88	$10.25	$0.00	50.64	51.59
6	ONDANSETRON ODT	ONDANSETRON TAB 4MG ODT	Message Only	168	0	$61.57	$0.37	$0.00	1.00	1.01
7	SERTRALINE HCL	SERTRALINE TAB 100MG	Message Only	163	4	$2,048.41	$12.57	$0.00	33.42	47.62
8	FLUTICASONE PROPIONATE	FLUTICASONE SPR 50MCG	Message Only	157	12	$2,043.45	$13.02	$0.00	33.50	16.61
9	TRAZODONE HCL	TRAZODONE TAB 50MG	Message Only	156	9	$1,683.18	$10.79	$0.00	33.15	42.60
10	CLONIDINE HCL	CLONIDINE TAB 0.1MG	Message Only	152	13	$1,784.89	$11.74	$0.00	46.82	84.66
10	PREDNISONE	PREDNISONE TAB 20MG	Message Only	152	0	$52.73	$0.35	$0.00	1.00	2.49
All Others				18,975	55,633	$2,983,942.04	$157.26	$0.00	33.23	91.23
ID				21,111	55,727	$3,031,526.36	$143.60	$0.00	32.64	86.05

LD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	ONDANSETRON ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	1,343	26	$602.77	$0.45	$0.00	1.39	1.32
2	ONDANSETRON HCL	GERIATRIC MIN DLY = 2.00UN	Message Only	1,222	73	$322.07	$0.26	$0.00	1.82	1.89
3	IPRATROPIUM BROMIDE/ ALBUT	GERIATRIC MIN DLY = 9.00UN	Message Only	1,042	17	$624.67	$0.60	$0.00	1.68	7.34
4	HEPARIN SODIUM	GERIATRIC MIN DLY = 4.00UN	Message Only	728	4	$2,206.55	$3.03	$0.00	1.36	2.47
5	ALBUTEROL SULFATE	GERIATRIC MIN DLY = 9.00UN	Message Only	705	27	$908.89	$1.29	$0.00	3.07	14.89
6	METFORMIN HCL	ADULT MIN DLY = 1.70 UN	Message Only	547	99	$4,811.65	$8.80	$0.00	50.44	49.70
7	VITAMIN D	ADULT MIN DLY = .14 UN	Message Only	527	54	$5,296.75	$10.05	$0.00	35.10	3.72
8	GABAPENTIN	ADULT MIN DLY = 3.00 UN	Message Only	467	76	$4,616.89	$9.89	$0.00	33.30	54.74
9	PROPRANOLOL HCL	ADULT MIN DLY = 3.00 UN	Message Only	372	63	$6,567.33	$17.65	$0.00	38.73	64.34
10	ALBUTEROL SULFATE	PEDIATRIC MIN DLY = 9.00UN	Message Only	369	16	$5,857.51	$15.87	$0.00	24.66	121.50
All Others				27,571	4,419	$4,046,737.32	$146.78	$0.00	26.45	45.32
LD				34,893	4,874	$4,078,552.40	$116.89	$0.00	23.60	40.03

LR

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	ATORVASTATIN CALCIUM	8 DAYS LATE REFILLING	Message Only	85	9	$935.42	$11.00	$0.00	30.42	30.60
2	LISINOPRIL	7 DAYS LATE REFILLING	Message Only	83	7	$709.45	$8.55	$0.00	41.59	44.69
3	ATORVASTATIN CALCIUM	7 DAYS LATE REFILLING	Message Only	82	10	$842.71	$10.28	$0.00	29.50	29.50
4	LEVOTHYROXINE SODIUM	7 DAYS LATE REFILLING	Message Only	73	4	$859.20	$11.77	$0.00	30.40	30.05
4	GABAPENTIN	7 DAYS LATE REFILLING	Message Only	73	5	$886.59	$12.15	$0.00	28.97	99.97
6	AMLODIPINE BESYLATE	7 DAYS LATE REFILLING	Message Only	68	7	$507.25	$7.46	$0.00	41.13	44.66
7	PROVENTIL HFA	11 DAYS LATE REFILLING	Message Only	61	3	$5,167.66	$84.72	$0.00	19.21	6.92
7	GABAPENTIN	8 DAYS LATE REFILLING	Message Only	61	7	$822.04	$13.48	$0.00	29.16	92.10
9	LISINOPRIL	8 DAYS LATE REFILLING	Message Only	60	7	$509.28	$8.49	$0.00	44.00	49.50
10	PROVENTIL HFA	12 DAYS LATE REFILLING	Message Only	57	6	$4,775.29	$83.78	$0.00	19.63	6.94
10	AMLODIPINE BESYLATE	9 DAYS LATE REFILLING	Message Only	57	0	$440.86	$7.73	$0.00	41.30	44.70
10	AMLODIPINE BESYLATE	8 DAYS LATE REFILLING	Message Only	57	5	$485.92	$8.52	$0.00	40.25	40.25
10	LEVOTHYROXINE SODIUM	8 DAYS LATE REFILLING	Message Only	57	4	$811.47	$14.24	$0.00	31.00	30.12
All Others				63,895	7,989	$7,595,022.23	$118.87	$0.00	32.18	58.81
LR				64,769	8,063	$7,612,775.37	$117.54	$0.00	32.19	58.59

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2017-01-01 and 2017-03-31

MN

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	IPRATROPIUM BROMIDE/ALBUT	MIN. DAYS THERAPY = 30	Message Only	2,065	204	$15,062.53	$7.29	$0.00	4.71	61.94
2	LISINOPRIL	MIN. DAYS THERAPY = 7	Message Only	844	11	$70.61	$0.08	$0.00	1.03	1.24
3	PANTOPRAZOLE SODIUM	MIN. DAYS THERAPY = 7	Message Only	768	8	$111.15	$0.14	$0.00	1.02	1.07
4	METOPROLOL TARTRATE	MIN. DAYS THERAPY = 7	Message Only	622	20	$132.34	$0.21	$0.00	1.06	1.40
5	AMLODIPINE BESYLATE	MIN. DAYS THERAPY = 7	Message Only	500	2	$79.50	$0.16	$0.00	1.05	1.19
6	LEVETIRACETAM	MIN. DAYS THERAPY = 14	Message Only	486	30	$2,955.71	$6.08	$0.00	2.61	31.60
7	ATORVASTATIN CALCIUM	MIN. DAYS THERAPY = 7	Message Only	442	11	$172.71	$0.39	$0.00	1.08	1.19
8	QUETIAPINE FUMARATE	MIN. DAYS THERAPY = 7	Message Only	414	34	$422.46	$1.02	$0.00	1.24	3.28
9	CARVEDILOL	MIN. DAYS THERAPY = 7	Message Only	403	7	$99.24	$0.25	$0.00	1.04	1.53
10	KLOR-CON M20	MIN. DAYS THERAPY = 7	Message Only	394	3	$181.43	$0.46	$0.00	1.00	1.90
All Others				15,450	986	$1,256,149.08	$81.30	$0.00	2.27	20.00
MN				22,388	1,316	$1,275,436.76	$56.97	$0.00	2.26	20.50

MX

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	2,796	1,889	$28,144.65	$10.07	$0.00	30.81	66.08
2	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	1,634	0	$17,086.26	$10.46	$0.00	30.98	71.12
3	FLUCONAZOLE	MAX DAYS THERAPY = 1	Message Only	527	178	$6,516.00	$12.36	$0.00	6.69	2.84
4	AZITHROMYCIN	MAX DAYS THERAPY = 5	Message Only	313	68	$6,471.38	$20.68	$0.00	12.22	19.33
5	MAPAP	MAX DAYS THERAPY = 10	Message Only	274	17	$2,504.74	$9.14	$0.00	26.06	114.49
6	DIPHENOXYLATE/ ATROPINE	MAX DAYS THERAPY = 14	Message Only	233	20	$7,227.86	$31.02	$0.00	28.63	110.45
7	EPIPEN 2-PAK	MAX DAYS THERAPY = 1	Message Only	231	13	$145,369.87	$629.31	$0.00	11.22	2.43
8	CEFDINIR	MAX DAYS THERAPY = 10	Message Only	178	15	$6,857.96	$38.53	$0.00	16.66	87.08
9	POLYETHYLENE GLYCOL 3350	MAX DAYS THERAPY = 14	Message Only	177	7	$6,292.04	$35.55	$0.00	31.08	33.60
10	SENEXON-S	MAX DAYS THERAPY = 14	Message Only	175	25	$1,679.81	$9.60	$0.00	31.58	57.60
All Others				3,131	442	$992,229.98	$316.91	$0.00	25.34	60.91
MX				9,669	2,674	$1,220,380.55	$126.22	$0.00	26.25	60.86

PA

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	PROMETHAZINE-DM	AGE LESS THAN 4	Message Only	19	2	$150.40	$7.92	$0.00	9.00	70.53
2	PROMETHAZINE HCL PLAIN	AGE LESS THAN 4	Message Only	11	0	$53.63	$4.88	$0.00	6.91	99.36
3	NITROFURANTOIN	AGE LESS THAN 4	Message Only	10	0	$867.13	$86.71	$0.00	27.10	155.00
4	PROMETHAZINE HCL	AGE LESS THAN 4	Message Only	8	0	$67.13	$8.39	$0.00	10.50	111.62
5	PROMETHAZINE/ DEXTROMETHOR	AGE LESS THAN 4	Message Only	7	1	$77.93	$11.13	$0.00	9.29	86.43
6	NITROFURANTOIN MACROCRYST	AGE LESS THAN 4	Message Only	4	0	$381.55	$95.39	$0.00	25.00	21.25
7	PHENYLEPHRINE HCL	AGE LESS THAN 4	Message Only	3	0	$241.63	$80.54	$0.00	49.67	11.67
8	INFANRIX	AGE GREATER THAN 64	Message Only	2	0	$44.80	$22.40	$0.00	1.00	0.50
9	PROMETHAZINE/ CODEINE	AGE LESS THAN 4	Message Only	1	0	$8.95	$8.95	$0.00	8.00	120.00
9	PROMETHAZINE VC PLAIN	AGE LESS THAN 4	Message Only	1	0	$15.70	$15.70	$0.00	3.00	50.00
PA				66	3	$1,908.85	$28.92	$0.00	14.08	87.45

SX

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	BICALUTAMIDE	GENERAL CONTRAINDICATION	Message Only	6	1	$115.74	$19.29	$0.00	12.67	33.33
SX				6	1	$115.74	$19.29	$0.00	12.67	33.33

TD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx
1	QUETIAPINE FUMARATE	ORAL ANTIPSYCHOTICS	Message Only	2,551	0	$39,253.86	$15.39	$0.00	29.34
2	RISPERIDONE	ORAL ANTIPSYCHOTICS	Message Only	1,605	0	$20,786.34	$12.95	$0.00	28.86
3	MORPHINE SULFATE	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,524	92	$4,107.74	$2.70	$0.00	1.00
4	GABAPENTIN	GABAPENTIN AND RELATED	Message Only	1,237	0	$20,174.02	$16.31	$0.00	34.38
5	ARIPIPRAZOLE	ORAL ANTIPSYCHOTICS	Message Only	1,086	0	$85,522.23	$78.75	$0.00	29.42
6	LISINOPRIL	ANGIOTENSIN BLOCKERS	Message Only	967	0	$9,076.75	$9.39	$0.00	53.66
7	HYDROMORPHONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	930	132	$4,696.61	$5.05	$0.00	1.00
8	OLANZAPINE	ORAL ANTIPSYCHOTICS	Message Only	905	0	$14,995.26	$16.57	$0.00	29.00
9	LEVOTHYROXINE SODIUM	THYROID HORMONES	Message Only	901	0	$14,245.09	$15.81	$0.00	42.83
10	HYDROCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	845	107	$15,220.05	$18.01	$0.00	19.24
All Others				78,312	109,309	$12,753,581.20	$162.86	$0.00	25.59
TD				90,863	109,640	$12,981,659.15	$142.87	$0.00	25.70

TD

Quantity Per Rx
42.81
48.80
1.58
110.92
35.26
58.59
2.81
36.46
41.28
76.65
70.23
66.69

Selected Filters

Client(s): Nevada Medicaid - HPES

Carrier(s): NVM-NEVADA MEDICAID

Account(s): ALL

Group(s): ALL

Date Type:	Date Filled Submitted
Start Date:	2017-01-01
End Date:	2017-03-31
Relative Description:	Previous Quarter
Display Report Description:	No
Top Values to Display:	10

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2017-04-01 and 2017-06-30

Client Totals:

Total Rxs	Plan Paid	Member Paid
702,122	$78,464,924	$0

DUR Information as a percent of total:

DUR Type	Total Rxs	Percent of Total Rxs - Paid	Cases	Rejected Rxs	Percent of Total Rxs - Rejects
Total Claims Paid	702,122	0.0%	0	0	0.0%
Cases / Rxs	508,986	72.5%	621,766	339,014	48.3%
DD - Drug-Drug Interaction	198,957	28.3%	367,009	145,228	20.7%
TD - Therapeutic Duplication	111,783	15.9%	93,854	114,296	16.3%
ID - Ingredient Duplication	58,493	8.3%	22,795	58,893	8.4%
LR - Underuse Precaution	56,332	8.0%	56,600	7,339	1.0%
LD - Low Dose Alert	33,782	4.8%	32,539	5,958	0.8%
MN - Insufficnt Duration Alert	22,872	3.3%	22,410	1,319	0.2%
HD - High Dose Alert	17,849	2.5%	17,603	3,531	0.5%
MX - Excessive Duration Alert	8,872	1.3%	8,906	2,448	0.3%
PA - Drug-Age Precaution	46	0.0%	50	2	0.0%

* More than one DUR message per paid, rejected or reversed claim(Cases > Rxs)
* Same claims could have multiple DUR messages. And there could multiple of the same DUR message on a claim
* This report does not include reversals.

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2017-04-01 and 2017-06-30

DD

Curr Rank	Top Drug Drug Interaction	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	HYDROCODONE/ ACETAMINOPHEN - ALPRAZOLAM	Message Only	3,513	611	$61,411.85	$17.48	$0.00	21.73	84.35
2	SIMVASTATIN - LISINOPRIL	Message Only	2,837	684	$20,158.26	$7.11	$0.00	48.64	51.32
3	LISINOPRIL - FUROSEMIDE	Message Only	2,783	905	$19,503.44	$7.01	$0.00	50.96	60.86
4	HYDROCO/APAP - ALPRAZOLAM	Message Only	2,691	579	$24,485.03	$9.10	$0.00	25.88	60.42
5	ONDANSETRON HCL - HYDROCO/APAP	Message Only	2,325	61	$6,525.06	$2.81	$0.00	2.46	5.48
6	OXYCODONE HCL - ALPRAZOLAM	Message Only	1,995	445	$51,418.62	$25.77	$0.00	25.49	102.66
7	LISINOPRIL - IBUPROFEN	Message Only	1,926	497	$17,198.32	$8.93	$0.00	35.53	67.73
8	OXYCODONE - ALPRAZOLAM	Message Only	1,816	488	$18,172.11	$10.01	$0.00	26.26	65.85
9	OXYCODONE/ ACETAMINOPHEN - ALPRAZOLAM	Message Only	1,710	329	$57,714.91	$33.75	$0.00	21.94	86.76
10	MORPHINE SULFATE ER - GABAPENTIN	Message Only	1,604	335	$42,901.66	$26.75	$0.00	24.79	52.90
All Others			343,809	140,294	$19,623,050.59	$57.08	$0.00	29.90	56.53
Summary			**367,009**	**145,228**	**$19,942,539.85**	**$54.34**	**$0.00**	**29.85**	**56.97**

HD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	ZOLPIDEM TARTRATE	GERIATRIC MAX DLY = .50UN	Message Only	453	41	$841.74	$1.86	$0.00	29.21	29.21
2	KETOROLAC TROMETHAMINE	GERIATRIC MAX DLY = 2.00UN	Message Only	395	12	$5,789.34	$14.66	$0.00	1.00	7.08
3	HYDROCODONE/ ACETAMINOPHEN	ADULT MAX DLY = 6.00 UN	Message Only	298	30	$8,002.90	$26.86	$0.00	14.99	117.91
4	MIDAZOLAM HCL	GERIATRIC MAX DLY = 3.50UN	Message Only	240	11	$645.98	$2.69	$0.00	1.00	7.92
5	GRANISETRON HCL	GERIATRIC MAX DLY = .85UN	Message Only	239	6	$4,349.48	$18.20	$0.00	1.00	1.38
6	BETAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 1.50UN	Message Only	202	1	$5,534.64	$27.40	$0.00	1.00	5.44
7	CEFTRIAXONE SODIUM	GERIATRIC MAX DLY = 4.00UN	Message Only	200	4	$9,935.91	$49.68	$0.00	1.00	172.52
8	DEXAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 4.00UN	Message Only	191	3	$3,365.64	$17.62	$0.00	1.00	290.86
9	INVEGA SUSTENNA	ADULT MAX DLY = .05 UN	Message Only	184	129	$379,876.69	$2,064.55	$0.00	27.35	1.50
10	IBUPROFEN	ADULT MAX DLY = 4.00 UN	Message Only	174	21	$1,875.61	$10.78	$0.00	8.22	37.97
All Others				15,027	3,273	$9,186,466.36	$611.33	$0.00	16.65	376.16
HD				**17,603**	**3,531**	**$9,606,684.29**	**$545.74**	**$0.00**	**15.67**	**329.71**

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between 2017-04-01 and 2017-06-30

ID

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	PROVENTIL HFA	PROVENTIL AER HFA	Message Only	409	23	$39,307.30	$96.11	$0.00	27.62	8.08
2	GABAPENTIN	GABAPENTIN CAP 300MG	Message Only	247	21	$3,239.56	$13.12	$0.00	36.45	110.97
3	CLONIDINE HCL	CLONIDINE TAB 0.1MG	Message Only	204	22	$2,646.82	$12.97	$0.00	75.65	130.24
3	SERTRALINE HCL	SERTRALINE TAB 100MG	Message Only	204	12	$2,483.96	$12.18	$0.00	34.72	47.91
5	LISINOPRIL	LISINOPRIL TAB 20MG	Message Only	195	9	$2,239.60	$11.49	$0.00	78.74	90.56
6	AMLODIPINE BESYLATE	AMLODIPINE TAB 10MG	Message Only	175	17	$1,815.75	$10.38	$0.00	74.33	73.65
7	ONDANSETRON ODT	ONDANSETRON TAB 4MG ODT	Message Only	174	0	$63.13	$0.36	$0.00	1.00	1.06
7	TRAZODONE HCL	TRAZODONE TAB 50MG	Message Only	174	4	$1,936.33	$11.13	$0.00	33.84	46.23
9	METFORMIN HCL	METFORMIN TAB 500MG	Message Only	173	10	$1,909.31	$11.04	$0.00	78.01	155.55
10	TRAZODONE HCL	TRAZODONE TAB 100MG	Message Only	167	8	$1,899.19	$11.37	$0.00	36.38	50.54
All Others				20,673	58,767	$5,060,240.43	$244.78	$0.00	39.29	122.65
ID				**22,795**	**58,893**	**$5,117,781.38**	**$224.51**	**$0.00**	**39.88**	**117.43**

LD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	ONDANSETRON ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	1,285	18	$628.73	$0.49	$0.00	1.30	1.24
2	IPRATROPIUM BROMIDE/ ALBUT	GERIATRIC MIN DLY = 9.00UN	Message Only	935	7	$709.63	$0.76	$0.00	1.98	8.83
3	HEPARIN SODIUM	GERIATRIC MIN DLY = 4.00UN	Message Only	815	13	$2,041.66	$2.51	$0.00	1.40	2.41
4	HEPARIN SODIUM	GERIATRIC MIN DLY = 20.00UN	Message Only	751	891	$3,424.07	$4.56	$0.00	1.00	3.01
5	ALBUTEROL SULFATE	GERIATRIC MIN DLY = 9.00UN	Message Only	533	23	$1,187.65	$2.23	$0.00	5.23	26.53
6	ONDANSETRON HCL	GERIATRIC MIN DLY = 2.00UN	Message Only	529	57	$290.79	$0.55	$0.00	2.79	2.79
7	VITAMIN D	ADULT MIN DLY = .14 UN	Message Only	524	56	$5,321.45	$10.16	$0.00	37.87	4.12
8	GABAPENTIN	ADULT MIN DLY = 3.00 UN	Message Only	482	85	$4,897.75	$10.16	$0.00	33.44	55.30
9	METFORMIN HCL	ADULT MIN DLY = 1.70 UN	Message Only	379	114	$3,145.47	$8.30	$0.00	59.60	59.02
10	METFORMIN HCL	GERIATRIC MIN DLY = 1.70UN	Message Only	353	40	$624.54	$1.77	$0.00	40.10	39.11
All Others				25,953	4,654	$3,563,066.08	$137.29	$0.00	28.18	49.00
LD				**32,539**	**5,958**	**$3,585,337.82**	**$110.19**	**$0.00**	**25.01**	**41.99**

LR

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	ATORVASTATIN CALCIUM	7 DAYS LATE REFILLING	Message Only	67	5	$676.96	$10.10	$0.00	30.87	30.87
1	LEVOTHYROXINE SODIUM	7 DAYS LATE REFILLING	Message Only	67	6	$747.78	$11.16	$0.00	29.97	29.97
3	PROVENTIL HFA	12 DAYS LATE REFILLING	Message Only	65	6	$5,871.68	$90.33	$0.00	20.42	7.52
4	GABAPENTIN	7 DAYS LATE REFILLING	Message Only	61	5	$817.48	$13.40	$0.00	29.39	92.49
5	TRAZODONE HCL	7 DAYS LATE REFILLING	Message Only	60	21	$588.95	$9.82	$0.00	29.17	41.65
6	ATORVASTATIN CALCIUM	8 DAYS LATE REFILLING	Message Only	58	7	$615.40	$10.61	$0.00	32.10	32.10
6	GABAPENTIN	9 DAYS LATE REFILLING	Message Only	58	3	$637.86	$11.00	$0.00	28.93	91.76
8	ATORVASTATIN CALCIUM	9 DAYS LATE REFILLING	Message Only	56	10	$607.08	$10.84	$0.00	30.79	30.79
9	PROVENTIL HFA	11 DAYS LATE REFILLING	Message Only	55	4	$4,457.41	$81.04	$0.00	20.16	6.70
10	MONTELUKAST SODIUM	7 DAYS LATE REFILLING	Message Only	54	2	$1,174.12	$21.74	$0.00	30.00	30.56
10	LEVOTHYROXINE SODIUM	8 DAYS LATE REFILLING	Message Only	54	4	$692.71	$12.83	$0.00	30.02	30.02
All Others				55,945	7,266	$6,968,670.60	$124.56	$0.00	31.71	59.18
LR				**56,600**	**7,339**	**$6,985,558.03**	**$123.42**	**$0.00**	**31.67**	**58.94**

MN

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	IPRATROPIUM BROMIDE/ALBUT	MIN. DAYS THERAPY = 30	Message Only	1,854	240	$14,385.58	$7.76	$0.00	5.22	65.94
2	LISINOPRIL	MIN. DAYS THERAPY = 7	Message Only	940	10	$84.20	$0.09	$0.00	1.03	1.35
3	PANTOPRAZOLE SODIUM	MIN. DAYS THERAPY = 7	Message Only	808	5	$127.82	$0.16	$0.00	1.02	1.07
4	METOPROLOL TARTRATE	MIN. DAYS THERAPY = 7	Message Only	713	7	$120.75	$0.17	$0.00	1.06	1.48
5	AMLODIPINE BESYLATE	MIN. DAYS THERAPY = 7	Message Only	636	11	$73.21	$0.12	$0.00	1.04	1.16
6	LEVETIRACETAM	MIN. DAYS THERAPY = 14	Message Only	612	27	$3,268.50	$5.34	$0.00	2.60	30.25
7	KLOR-CON M20	MIN. DAYS THERAPY = 7	Message Only	586	7	$343.25	$0.59	$0.00	1.06	2.13
8	ATORVASTATIN CALCIUM	MIN. DAYS THERAPY = 7	Message Only	551	4	$157.18	$0.29	$0.00	1.06	1.16
9	CARVEDILOL	MIN. DAYS THERAPY = 7	Message Only	470	16	$27.97	$0.06	$0.00	1.01	1.37
10	CLONIDINE HCL	MIN. DAYS THERAPY = 7	Message Only	436	37	$497.64	$1.14	$0.00	1.26	3.48
All Others				14,804	955	$1,187,349.13	$80.20	$0.00	2.02	35.87
MN				**22,410**	**1,319**	**$1,206,435.23**	**$53.83**	**$0.00**	**2.08**	**30.33**

MX

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	2,421	1,766	$25,011.69	$10.33	$0.00	31.54	66.38
2	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	1,461	0	$15,094.83	$10.33	$0.00	32.20	72.54
3	FLUCONAZOLE	MAX DAYS THERAPY = 1	Message Only	500	159	$6,442.39	$12.88	$0.00	7.69	3.05
4	EPIPEN 2-PAK	MAX DAYS THERAPY = 1	Message Only	365	8	$232,394.92	$636.70	$0.00	10.83	2.27
5	AZITHROMYCIN	MAX DAYS THERAPY = 5	Message Only	265	70	$5,814.26	$21.94	$0.00	11.47	20.98
6	EPINEPHRINE	MAX DAYS THERAPY = 1	Message Only	251	10	$77,655.31	$309.38	$0.00	14.49	2.46
7	DIPHENOXYLATE/ ATROPINE	MAX DAYS THERAPY = 14	Message Only	197	7	$5,903.85	$29.97	$0.00	27.97	95.22
7	POLYETHYLENE GLYCOL 3350	MAX DAYS THERAPY = 14	Message Only	197	14	$5,836.07	$29.62	$0.00	31.45	32.09
9	SENEXON-S	MAX DAYS THERAPY = 14	Message Only	182	14	$1,717.78	$9.44	$0.00	32.14	62.90
10	MAPAP	MAX DAYS THERAPY = 10	Message Only	164	8	$1,582.96	$9.65	$0.00	26.52	135.23
All Others				2,903	392	$748,210.60	$257.74	$0.00	29.47	68.13
MX				**8,906**	**2,448**	**$1,125,664.66**	**$126.39**	**$0.00**	**27.55**	**59.70**

PA

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx
1	PROMETHAZINE HCL	AGE LESS THAN 4	Message Only	16	0	$183.15	$11.45	$0.00	8.12	177.75
2	PROMETHAZINE HCL PLAIN	AGE LESS THAN 4	Message Only	10	0	$57.37	$5.74	$0.00	9.60	105.00
2	NITROFURANTOIN	AGE LESS THAN 4	Message Only	10	2	$1,613.65	$161.36	$0.00	24.80	154.50
4	PROMETHAZINE/ DEXTROMETHOR	AGE LESS THAN 4	Message Only	5	0	$54.41	$10.88	$0.00	11.20	78.80
4	PROMETHAZINE-DM	AGE LESS THAN 4	Message Only	5	0	$57.57	$11.51	$0.00	11.60	126.00
6	PROMETHEGAN	AGE LESS THAN 4	Message Only	2	0	$157.63	$78.82	$0.00	3.00	8.50
7	PHENYLEPHRINE HCL	AGE LESS THAN 4	Message Only	1	0	$100.17	$100.17	$0.00	30.00	15.00
7	BENZTROPINE MESYLATE	AGE LESS THAN 4	Message Only	1	0	$13.69	$13.69	$0.00	30.00	60.00
PA				**50**	**2**	**$2,237.64**	**$44.75**	**$0.00**	**13.08**	**131.10**

TD

Curr Rank	Top Drug	Therapy / Reason	DUR Response	Paid Rxs	Rejected Rxs	Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx
1	QUETIAPINE FUMARATE	ORAL ANTIPSYCHOTICS	Message Only	2,700	1	$41,363.12	$15.32	$0.00	29.31
2	RISPERIDONE	ORAL ANTIPSYCHOTICS	Message Only	1,653	0	$20,443.59	$12.37	$0.00	29.85
3	MORPHINE SULFATE	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,577	49	$4,344.98	$2.76	$0.00	1.00
4	LISINOPRIL	ANGIOTENSIN BLOCKERS	Message Only	1,153	0	$11,780.89	$10.22	$0.00	69.99
5	GABAPENTIN	GABAPENTIN AND RELATED	Message Only	1,148	0	$18,455.19	$16.08	$0.00	35.02
6	ARIPIPRAZOLE	ORAL ANTIPSYCHOTICS	Message Only	1,079	0	$59,319.66	$54.98	$0.00	30.68
7	LEVOTHYROXINE SODIUM	THYROID HORMONES	Message Only	932	0	$16,731.01	$17.95	$0.00	49.28
8	OLANZAPINE	ORAL ANTIPSYCHOTICS	Message Only	878	0	$14,087.72	$16.05	$0.00	28.60
9	HYDROMORPHONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	871	48	$3,914.04	$4.49	$0.00	1.00
10	SERTRALINE HCL	SSRIS AND SNRIS	Message Only	808	0	$9,785.66	$12.11	$0.00	34.27
All Others				81,055	114,198	$14,680,252.55	$181.11	$0.00	29.45
TD				**93,854**	**114,296**	**$14,880,478.41**	**$158.55**	**$0.00**	**29.52**

TD

Quantity Per Rx
41.78
49.40
1.70
75.67
112.64
35.33
47.82
37.16
2.44
42.18
75.92
71.59

RXT6050D - Summarized DUR Activity Report

Between 2017-04-01 and 2017-06-30

Selected Filters

Client(s): Nevada Medicaid - HPES

Carrier(s): NVM-NEVADA MEDICAID

Account(s): ALL

Group(s): ALL

Date Type:	Date Filled Submitted
Start Date:	2017-04-01
End Date:	2017-06-30
Relative Description:	Select Date Range
Display Report Description:	No
Top Values to Display:	10

Dear Dr. _____

A RetroDUR initiative was recently conducted on patients who required a visit to the emergency room due to uncontrolled asthma or COPD and were not receiving a long-term control medication.

Emergency room visits between MM/DD/20YY - MM/DD/20YY were reviewed to determine those patients that met the criteria above. Your patient, _____ was seen in the emergency room and it was determined that there was not a current claim for a long-term control medication.

According to guidelines provided by the National Institutes of Health Heart, Lung, and Blood Institute, it is recommended that patients receive daily long-term control medications on a long-term basis to achieve and maintain control of persistent asthma. Long-term control medications include inhaled corticosteroid, long-acting bronchodilators, leukotriene modifiers, cromolyn, theophylline, and immunomodulators.

The 2017 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines state that the management strategy for stable COPD should be based on an assessment of the patient's symptoms and future risk of exacerbations.

Assessment of symptoms and risk of exacerbations to determine GOLD patient group

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

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

Group	Recommendations
A (low risk, less symptoms)	Start short- or long-acting bronchodilator treatment
B (low risk, more symptoms)	Initial therapy - long-acting bronchodilator (LAMA or LABA) For persistent breathlessness on monotherapy - two bronchodilators recommended (LAMA + LABA)

	For patients with severe breathlessness - initial therapy with two bronchodilators may be considered
C (high risk, less symptoms)	Initial therapy - LAMA For persistent exacerbations Add a second long-acting bronchodilator (LAMA + LABA, preferred) OR ICS + LABA
D (high risk, more symptoms)	Start therapy with a LAMA + LABA combination History and/or findings suggestive of asthma-COPD overlap - Initial therapy with an ICS + LABA Further exacerbations on LAMA + LABA therapy, alternative pathways include escalation to a LAMA + LABA + ICS (preferred) or a switch to an ICS + LABA.

We realize that there are clinical variables influencing individual patient treatment that are not apparent in claims data or that a patient may have been inadvertently identified as being under your care. However, we believe this information to be useful in caring for your patient(s) with asthma or COPD. We thank you for reviewing this information and for your support in caring for Nevada Medicaid's patients

References

1. National Heart, Lung, and Blood Institute. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma NHLBI 2007. Available from http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines. Accessed March 17, 2017

2. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention 2016. Available from: www.ginasthma.org. Accessed March 20, 2017.

3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2017 Report. Available at: http://goldcopd.org/. Accessed March 20, 2017

RefNbr	Usefullness	Patient not seen in Office	Therapy adjusted	Therapy Adequate	Will address at next appt.	Letter Returned	Notes
6261701						7/8/2017	Not deliverable as addressed.
6261702						7/2/2017	Not deliverable as addressed.
6261703							
6261704						7/6/2017	Not deliverable as addressed.
6261705							
6261706	1	-	-	-	-	-	This Quideline for PCP,not ED. Stable COPD not managed thru ED.
6261707						7/6/2017	Attempted - Not known
6261708						7/20/2017	Attempted - Not known
6261709						7/1/2017	Insufficient address.
6261710						7/1/2017	Insufficient address.
6261711						7/6/2017	Attempted - Not known.
6261712							
6261713							
6261714	8		X				
6261715							
6261716							
6261717							
6261718							
6261719							
6261720							
6261721						7/8/2017	Attempted - Not known.
6261722						6/30/2017	Not deliverable as addressed.
6261723							
6261724						7/1/2017	Not deliverable as addressed.
6261725							
6261726							
6261727							
6261728	7				X		
6261729	7				X		
6261730							
6261731							
6261732							
6261733						7/17/2017	Not deliverable as addressed.
6261734						7/15/2017	Not deliverable as addressed.
6261735						7/7/2017	Attempted - Not known.
6261736							
6261737							
6261738							
6261739							
6261740							
6261741							
6261742						7/2/2017	Attempted - Not known
6261743						7/7/2017	Attempted - Not known
6261744						7/17/2017	No longer at this location.
6261745							
6261746						6/30/2017	Attempted - Not known.
6261747						7/7/2017	Unclaimed.
6261748							

6261749						6/29/2017	Not deliverable as addressed.
6261750							
6261751							
6261752							
6261753							
6261754							
6261755						7/6/2017	Insufficient address.

Dear Dr. _____

A RetroDUR initiative was recently conducted on patients less than 18 years of age who received a codeine and/or tramadol prescription in the last 3 months.

The Food and Drug Administration (FDA) recently issued a safety announcement restricting the use of codeine and tramadol in children. These medications have caused life-threatening respiratory depression and death, with the risk greater in those younger than 12 years. The use of these medications in some older children should also be limited.

The following new restrictions were added by the FDA to the warning labels of codeine and tramadol:

- For children under 12 years, codeine is contraindicated for the treatment of pain or cough and tramadol is contraindicated in the treatment of pain.
- Tramadol is contraindicated in the treatment of pain after surgery to remove tonsils and/or adenoids for children under 18.
- For adolescents between 12 and 18 years, codeine and tramadol are not recommended for use in those who are obese or have conditions such as obstructive sleep apnea or severe lung disease.
- Codeine or tramadol are not recommended for mothers who are breastfeeding.

We understand that there is patient information that is not apparent in claims data or that a patient may have been inadvertently identified as being under your care. However, we believe this information to be useful in caring for your pediatric patient(s) receiving codeine and/ or tramadol. We thank you for reviewing this information and for your support in caring for Nevada Medicaid's patients

References

1. Food and Drug Administration. FDA Drug Safety Communication: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women. FDA website. https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm. Accessed July 12, 2017.

2. American Academy of Pediatrics. AAP News. Do not use codeine, tramadol in children: FDA. http://www.aappublications.org/news/2017/04/20/Codeine042017. Accessed July 12, 2017.