BRIAN SANDOVAL
Governor

RICHARD WHITLEY, MS
Director
MARTA JENSEN
Acting 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

REVISED

Date of Posting:	**June 17, 2016**
Date of Meeting:	**Thursday, July 28, 2016 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**
Webinar Registration:	**Go to:** **https://catamaranrx.webex.com/catamaranrx/onstage/g.php?MTID=e7600cb1feb29ee4e0a1de879858d6df8** **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:	**746 330 261** **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.

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 28, 2016.

b. Status Update by DHCFP:
CMS final rule on covered outpatient drugs update.
Update on DUR Board policy changes from January and April.

4. Clinical Presentations

a. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for pediatric use of gonadotropin-releasing hormone (GnRH) analogs.

i. Public comment on adoption of policy.
ii. Presentation of utilization and clinical information.
iii. Discussion by the Board and review of utilization data.
iv. Possible adoption of prior authorization criteria/policy.

b. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for medications used to treat Irritable-Bowel Syndrome.

i. Public comment on adoption of policy.
ii. Presentation of utilization and clinical information.
iii. Discussion by the Board and review of utilization data.
iv. Possible adoption of prior authorization criteria/policy.

c. **For Possible Action:** Discussion and possible removal of prior authorization criteria for duloxetine.

i. Public comment on proposed clinical prior authorization criteria.
ii. Presentation of utilization and clinical information.
iii. Discussion by the 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 for the medication class Antiasthmatic Monoclonal Antibodies.

i. Public Comment on proposed clinical prior authorization criteria.
ii. Presentation of utilization and clinical information.
iii. Discussion by the 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 for the medication class Hepatitis C Direct-acting antivirals.

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 prior authorization criteria and/or quantity limits for the medication class short-acting opioids and opioid agonists used for the treatment of pain.

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. Hepatitis C – 14 day trial compliance.
i. Discussion by the Board and review of utilization data.

b. Long-acting steroid inhaler combination utilization correlated with emergency department visits and short-acting rescue medication utilization.
i. Discussion by the Board and review of utilization data.

c. Utilization of short-acting insulin without long-acting/basal insulin.
i. Discussion by the Board and review of utilization data.

d. Proton pump inhibitors and complications/adverse effects.
i. Discussion by the Board and review of utilization data.

e. Long and short-acting opioid utilization.
i. Discussion by the Board and review of utilization data.

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 2015, Q1 2016 and Q2 2016 (by Payment and by Claims).
ii. Top 50 Drugs of Q4 2015, Q1 2016 and Q2 2016 (by Payment and by Claims).

b. Concurrent Drug Utilization Review (ProDUR)

i. Review of Q4 2015, Q1 2016 and Q2 2016.
ii. Review of Top Encounters by Problem Type.

c. Retrospective Drug Utilization Review (RetroDUR)

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

9. Closing Discussion

a. Public comments on any subject.

b. Date and location of the next meeting.

i. Discussion of the time of the next meeting.

c. Adjournment.

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

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

If requested in writing, a copy of the meeting materials will be mailed to you. Requests and/or written comments may be sent to Ellen Felsing at the Division of Health Care Financing and

Policy, 1100 E. William Street, Suite 101, Carson City, NV 89701, at least 3 days before the public hearing.

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

Note: We are pleased to make accommodations for members of the public who have disabilities and wish to attend the meeting. If special arrangements are necessary, notify the Division of Health Care Financing and Policy as soon as possible and at least ten days in advance of the meeting, by e-mail at ellen.felsing@dhcfp.nv.gov in writing, at 1100 East William Street, Suite 101, Carson City, Nevada 89701 or call Ellen Felsing at (775) 684-3684.

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
Acting Administrator

NEVADA MEDICAID
DRUG USE REVIEW BOARD
DRAFT MEETING MINUTES

Date of Meeting: **Thursday, April 28, 2016 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; Michael Owens, MD; Paul Oesterman, Pharm.D.; David England, Pharm.D.

Non-voting Members via Teleconference: Chris Shea, Pharm.D.

Committee Members Absent: Jeffrey Zollinger, DO

Others Present:
DHCFP: Shannon Sprout, Chief, Program Services; Mary Griffith, RN, Pharmacy Services Specialist; Darrell Faircloth, Deputy Attorney General

HPES: Beth Slamowitz, Pharm.D.

OptumRx: Carl Jeffery, Pharm.D.; Kevin Whittington, RPh

Others: Shane Hall, Purdue; Krystal Joy, Otsuka; Chris Adams, Lundbeck; Karen Miller, Lundbeck; Karen Campbell, Pharm.D., Allergan; Sean McGarr, Allergan; Kerry Kostman, Astra Zeneca; Jin Yun, Astra Zeneca; William Mullen, Indivior; Charissa Anne, J&J; Laura Litzenberger, Janssen; James Kotusky, Gilead; Janet Osalvo, DHCFP; Sandy Sierawski, Pfizer; Bonnie Romero, Alkermes; Brian Evans; Jeanette Belz, NV Psychiatric Association; Brooke Maylath, TAG;

Others On Line: Shannon Groppenbacher, J&J; Jill Sugg, UCB; Georgette Dzwilewski, Indivior; Christopher Anstead, Amgen; Ray Kong, Amgen; Michael Faithe, Amgen; Risa Reuscher, Amgen; Joanna Jacob, Ferrari Public Affairs

1. Call to Order and Roll Call

Meeting called to order at 5:15PM

Roll Call:

Carl Jeffery – Optum Rx

Kevin Whittington

David England

Michael Owens

Paul Oesterman, Chair

Darrell Faircloth

James Marx

Beth Slamowitz

Mary Griffith

2. Public Comment on Any Matter on the Agenda

Paul Oesterman, Chair: Is there any public comment to start? Please limit comments to 5 minutes.

3. Administrative

a. **For Possible Action:** Review and Approve Meeting Minutes from January 28, 2016.

Paul Oesterman, Chair: Seeing no comments, we will start with review of the meeting minutes.

James Marx: I move to approve.

David England: Second.

Voting: Ayes across the board, the motion carries.

b. Status Update by DHCFP

Paul Oesterman, Chair: We will get an update from the Department.

Mary Griffith: Shannon Sprout is our new Chief. Chapter 1200 changes, the presented criteria in April were approved, that included the psychotropic changes for children. That policy now requires a PA for every child under the age of 6, for 6-18 years it only requires a PA for more than one drug within a class or four or more different classes. Also we approved some new criteria for Corlanor, Praluent, Invega Trinza. The other change is not requiring a diagnosis for diabetic supplies unless they are new to getting diabetic supplies. We have received several new rules from CMS. Pharmacy got off pretty easy. Right now, our department is in crunch time for the budget.

Paul Oesterman, Chair: What was the one significant change for pharmacy from CMS?

Mary Griffith: All the states are going to have to use the NADAC or acquisition cost and a 340B ceiling price, but now that has been moved to 2017.

James Marx: There was an announcement that all recipients are being moved to MCO, is that true?

Mary Griffith: No, I don't know about that.

4. Board Action

a. **For Possible Adoption**: Discussion and possible adoption of coverage policy on medications used for the hormonal transition treatment for transgender individuals

Paul Oesterman, Chair: Now we will move to the Board items. Our first is discussion and possible adoption of coverage policy on medications used for the hormonal transition treatment for transgender individuals.

Carl Jeffery: This has come up recently and is coming down from the Director, I have the Chapter 1200 limitations on hormones limited to females and males. We need some discussion from the Board for coverage of these to override the restrictions.

Mary Griffith: Right now we have gender edits. We were proposing to require a diagnosis of gender dysphoria that would override the gender requirement. But this is something that will come up again.

Paul Oesterman, Chair: Do we have any public comment?

Brook Maylath: My name is Brook Maylath, I am the president of the Transgender Allies Group in Reno. The treatment has been established in the 1930's. The guidelines have a clinical

pathway for the use of hormones for the treatment of gender dysphoria. The dysphoric feelings can be eliminated with treatment. Monitoring pathways are online by UCSF and are very useful for diagnosis, signs, and proper pathways. This can be done in a safe manner for each patient. Without this, 41% suicide attempt rate and 60% suicide ideation in transgender individuals. Access to appropriate care is difficult especially in rural areas. In the Affordable Care Act, if a payer is providing a hormone therapy for one person, they cannot deny it for another person. If estrogen is approved for post-menopausal women, you will have to pay for a transgender woman. If we fail to provide this, potential civil rights cases could be brought.

Paul Oesterman, Chair: Any other public comment? So we have restrictions in place by gender, and we are proposing to eliminate those.

Mary Griffith: Right, we want to allow for gender dysphoria.

Paul Oesterman, Chair: If we had a diagnosis of gender dysphoria for a PA?

Carl Jeffery: What we talked about doing is adding some criteria to allow bypassing the limitation at the point of sale if the diagnosis of gender dysphoria is transmitted on the claim. I think that was the simplest of the ideas.

Paul Oesterman, Chair: What do we need to do?

Carl Jeffery: Does the Board need to take any action?

Beth Slamowitz: What we are looking for is any additional input and discussion about putting the diagnosis override code on to allow to pay. I don't think we need anything else from the Board.

Mary Griffith: Unless Darryl thinks so.

James Marx: I think the crux of the situation is who can make a diagnosis of gender dysphoria? Is it self-proclaimed diagnosis? Or prescribed by a certain specialty of physicians? Who is qualified to make a diagnosis of gender dysphoria?

Beth Slamowitz: I don't think we discussed the type of provider, it just needed to be on the prescription. We didn't want to restrict access of care.

Carl Jeffery: Especially in the rural areas, we don't want to limit who can make the diagnosis.

Paul Oesterman, Chair: I think as long as it is someone that is licensed to prescribe in the State, it should be ok. I don't think there is anything we need to vote on, it is just something part of the criteria. Brook, would that meet what you are looking for?

Brook Maylath: Yes. A diagnosis is often made with careful review with the provider and many times with a behavioral health therapist. These are not easily written, so just being able to pay for the medication as prescribed is a wonderful advance forward.

Paul Oesterman, Chair: Any further discussion? No.

b. **For Possible Action**: Discussion and adoption of coverage policy on allowance of pharmacist submitted prior authorizations.

Paul Oesterman, Chair: We will move to the next agenda item which is discussion and adoption of coverage policy on allowance of pharmacist submitted prior authorizations. Carl?

Carl Jeffery: I was hoping Chris would be able to send some information in. It is more of a prompt for discussion from the Board. Right now, we have a limited number of pharmacists that are allowed to submit a prior authorization in the name of the physician, acting as the agent of the physician. These pharmacists have access to the medical record, and can make sure all the information is listed.

David England: This would only be available to those with access to the medical information?

Carl Jeffery: We talked about some proposed criteria of the pharmacist needs to be in a clinical setting, with access to the medical record.

David England: Would the physician still need to give permission for the pharmacist to submit these PAs like a collaborative practice agreement?

Carl Jeffery: I think this is an opportunity for pharmacists to act as an agent of the physician. The criteria we talked about are: No in-patient pharmacist, have access to the clinical record, they work in a clinical setting. But we need to figure out a way for the call center to identify these pharmacists. We don't want every retail pharmacist submitting PAs.

David England: What if a retail pharmacist does have access through an EHR or something else?

Beth Slamowitz: From a system perspective, we list pharmacies as provider type. If we open up pharmacies through the portal to submit PAs, that would mean anyone listed as a pharmacy would be able to submit a PA. Picking up the phone and calling the call center or faxing something, that would be different to define who is submitting the PA request. From a system point, it will be difficult to define who we are getting PAs from.

Paul Oesterman, Chair: Can you do a subset, using NPI number?

Beth Slamowitz: The only way we could do it that way is to give pharmacist provider types, and that would take a lot of work.

David England: that is what I was leaning toward. In some cases, a retail outlet could have that same relationship. But we need to identify that pharmacist and how they have access to the records.

Beth Slamowitz: Until we can get the state to recognize pharmacists as a provider, that may be difficult.

David England: I'm not sold that you can't practice clinically without being in a clinical setting, but we need some way to identify these individuals so we know they have access to the clinical setting.

Mary Griffith: Could you do it by a location code, like place of service?

Carl Jeffery: There is place of service on the claim, but that is something the pharmacy decides on their own. It is not attached to the provider ID.

Beth Slamowitz: I think whatever you decide, we'll need to figure out the system.

Paul Oesterman, Chair: I think we are looking at two different things. One is the criteria to allow a pharmacist to submit a PA and second is how the system is going to work to do it. We are only concerned with the first part right now. I'll ask for any public comment at this point. How is it that Chris is allowed to submit and others can't?

Carl Jeffery: The call center knows his name.

James Marx: This is amusing because we have a hard time getting information from the retail pharmacies when there is a reject in the first place. I don't think there will be many pharmacies wanting to do this anyway.

Paul Oesterman, Chair: I don't think there is going to be a large number of pharmacies getting on board.

Michael Owens: I wish pharmacists had the ability to change for formulary.

Beth Slamowitz: When you're talking about Medicaid, it is pretty easy, but commercial insurances can change all the time. But many pharmacists aren't going to have time to look it up.

Chris Shea: We have been successful from the institutional side in submitting PAs. Most Med D plans allow anyone to submit a PA if the patient is in an institutional setting like skilled nursing. It takes a lot of time to get the paperwork to the physician for PAs.

David England: He is able to do that is because he is identified with the facility rather than as an individual.

Carl Jeffery: Maybe we create a list of pharmacists to pre-register and we maintain that list at the call center.

Beth Slamowitz: As long as those facilities have all their pharmacists registered or one with a backup.

Paul Oesterman, Chair: I think at this point, for updating policy, we want to say pharmacists who work in a clinical setting or who have access to clinical records have the ability to submit Prior Authorization requests, having once registered with Medicaid for that capability.

David England: I'll move that.

James Marx: Second.

Paul Oesterman, Chair: Any further discussion?

Voting: Ayes across the board, the motion carries.

c. **For Possible Action**: Discussion and adoption of coverage policy on use of brand name products when a generic is available and Dispense As Written requirements

Paul Oesterman, Chair: The next topic on the agenda is the discussion and adoption of coverage policy on the use of brand name products when a generic is available and dispense as written requirements. Is there any public comment? No. Right now a physician has to write in their own hand writing, "Dispense As Written." That is the background, Carl can you give us more details?

Carl Jeffery: Your binder has the Chapter 1200 criteria. I included proposed changes. Right now, it still requires prior authorization as well as other requirements. The binder also has a report of brand products. The first several are all preferred brand on our PDL.

James Marx: The requirement that the physician hand write, "Dispense As Written," on the prescription seems like a punitive measure.

Carl Jeffery: My proposed criteria do not include that. The drugs we are concerned with are a little further down the list, Ativan is about half-way down the page. There are cases as a pharmacist, it is difficult to justify the use of the brand over the generic. There is no reason brands need to be dispensed. The proposed criterion says, two different manufacturers must be tried, an FDA Medwatch form must be submitted. If they truly are having a reaction to the generic, the FDA should know about it. An exception would be allowed for the narrow therapeutic index drugs, like warfarin, digoxin, lithium, thyroid medication and others and if the generic is not available, it would bypass the requirement.

Michael Owens: The most frustrating thing is formulary changes and I wish pharmacists would be allowed to substitute per formulary. Or if there was a note from the pharmacist that suggests what is formulary.

David England: This makes sense too but how cumbersome is this going to be for prescribers. But we do need something documented of why it can't be given.

Paul Oesterman, Chair: I used to work in a call center for Medco when Prilosec went generic. The pill said omeprazole but it was the same as the brand. Patients would call claiming the generic is ineffective even though it was exactly the same. I think these differences should be submitted to the FDA if it really isn't effective. I like this proposed criteria.

James Marx: There is one difference, the manufacturer variation and manufacturing differences. I have seen patients with some opioids where the generic doesn't work as well.

Paul Oesterman, Chair: Where they AB rated?

James Marx: Well, they were AB rated on the day the FDA was there, but how do you know they are still manufacturing it the same way now?

David England: I was reviewing the Orange Book the other day and there are several different codes available now. So there is some confusion about what can be substituted. So I think it is good to alert the FDA so they know and maybe there is something to it.

Paul Oesterman, Chair: Do we have a motion to approve the criteria as submitted?

David England: So moved.

James Marx: Second.

Voting: Ayes across the board.

5. Clinical Presentations

a. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria for colony stimulating factors.

Paul Oesterman, Chair: Our next topic is the clinical presentation and the discussion and possible adoption of updated prior authorization criteria for colony stimulating factors. We have the proposed criteria here. Do we have any public comment?

Ray Kong: My name is Ray Kong, I am the medical science liaison for Amgen. We do not have any prepared comments but we are available for questions from the Board.

Paul Oesterman, Chair: Thank you.

Carl Jeffery: The current criteria is listed by agent, we consolidated it to simpler criteria. The utilization is shown in your binder with both regular pharmacy claims and physician administered drug claims. Utilization is all identified there, I don't think anything is out of the ordinary. Page 40 has the new guidelines rolled into a single category rather than different medications. The criteria are the same, only consolidated.

Paul Oesterman, Chair: On the new criteria, there is a quantity limit for Neulasta, but not the others.

Carl Jeffery: I'm not sure why the others didn't get on there; they have been on past criteria.

Mary Griffith: Should the others have quantity limits?

Carl Jeffery: Yes, they should.

Paul Oesterman, Chair: So if we were to approve these criteria, we would want the quantity limit for all products.

David England: Does it make a difference on page 40 it mentions Neulasta, but not as the generic. But there is not a generic available yet. So on page 40, these restrictions would cover all the products.

Carl Jeffery: Right, and keep in mind these only apply to fee for service, not the physician administered drug. It is only the few pharmacies that dispense on an outpatient basis.

Paul Oesterman, Chair: It looks like this simplifies the process. We have the proposed criteria here, do we have a motion?

James Marx: So moved.

David England: Second.

Voting: Ayes across the board, the motion carries.

b. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for eluxadoline (Viberzi®)

Paul Oesterman, Chair: Our next agenda item is the discussion and possible adoption of prior authorization criteria for eluxadoline or Viberzi. Do we have any public comment?

Karen Campbell: I'm Karen Campbell, a Pharm.D. and a scientific liaison with Allergan. I am here to provide comments on Viberzi, indications, background of Irritable Bowel Syndrome (IBS-D), previously available treatments, review of evidence, study results for efficacy, mechanism of action, side effects and safety data. We request Nevada Medicaid make eluxadoline available for IBS-D patients.

James Marx: Do we need the ICD-10 diagnosis in there?

Carl Jeffery: We can, but there are some other step therapy proposed in the criteria. Something that isn't on here is the response rate was about 24-25% vs. placebo. It was more effective than placebo, but really pretty low. Getting in to some of the secondary endpoints, it gets a little better. For the people who respond to this, great, but if only ¼ of the population is going to respond, maybe not everyone needs to get it.

David England: So the criteria do state they need to have treatment failure with something else before getting this.

James Marx: Are we going to have some temporary approval to see if it is effective?

Carl Jeffery: We didn't include that step in the proposed criteria, but maybe not a bad idea. We added some trial of the other treatments.

David England: Karen, does the use of another product before this medication result in any decreased efficacy or aggravate the disease state?

Karen Campbell: Prior to the availability, that is all there was. Most patients will have already tried these.

David England: I just want to make sure there won't be any significant drawbacks to having patients try other agents first.

Carl Jeffery: We rely on physician testimony regarding previous failed therapy.

Michael Owens: This is not a medication used as a PRN for symptoms, you're on this medication long term.

Karen Campbell: Right, it is for patients with the more severe and persistent symptoms.

Carl Jeffery: For the next meeting, we will get the whole class for the IBS category.

Paul Oesterman, Chair: One of my concerns is the 25% efficacy. We should do a trial short period before approving a long-term.

Carl Jeffery: In the trial, the initial run-in was 12 weeks. So a 12 week PA.

Paul Oesterman, Chair: Since it is schedule 4, the PA should only be 6 months.

Beth Slamowitz: Is this something that they see a response right away?

Karen Campbell: Most patients respond within 4 weeks. The symptoms do get more progressive if they are not treated properly.

Paul Oesterman, Chair: So then a 4 week trial run to see if they will respond.

David England: Do we want to add that in and if approved, then they could get it approved for a year.

Carl Jeffery: Can this just be a phone call from the patient to the prescriber's office or will this be something the patient needs to make an appointment.

Michael Owens: I think it would just be a phone call. That is usually how it is anyway.

Carl Jeffery: So they wouldn't have to make another office visit.

Paul Oesterman, Chair: We have the proposed criteria with the addition of a 12 week initial treatment and then change to a 6 month PA after the initial treatment.

David England: So moved.

James Marx: Second.

Voting: Ayes across the board, the motion carries.

c. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for doxylamine succinate/pyridoxine hydrochloride (Diclegis®).

Paul Oesterman, Chair: Our next item is the discussion and possible adoption of prior athorization criteria for doxylamine succinate and pyridoxine hydrochloride or Diclegis. Any public comment?

Carl Jeffery: The utilization is in the binder, you may remember this as Bendectine. There were a number of lawsuits claiming birth defects. This is not approved for hyperemesis gravidarum, so it has not been studied.

David England: In the studies, were they able to use this in combination?

Carl Jeffery: I'm not sure if it was used in combination. It looks like it was all either/or compared with ondansetron or placebo.

Paul Oesterman, Chair: Did they do any comparisons with H1 blockers?

Carl Jeffery: No, I don't see anything. We don't have a huge number of claims for this. The chart is broken down by regular fee for service, pregnancy category and PAD claims. About 15-20 claims per month. The criteria are if they are pregnant.

Paul Oesterman, Chair: Do we need the female requirement if they are pregnant?

David England: I say leave it as-is.

Michael Owens: Why the age limit?

Carl Jeffery: That is just what it was studied for.

Paul Oesterman, Chair: They can always take the separate components, but they are not long acting.

Michael Owens: How much less expensive are the separate components?

Beth Slamowitz: Used to give out Benadryl and Vitamin B6 in the pharmacy for this.

Paul Oesterman, Chair: As a reminder, price is not a factor for step therapy. We have the proposed criteria. We need a motion to approve.

David England: So moved.

James Marx: Second.

Paul Oesterman, Chair: Has the P&T Committee reviewed this yet?

Carl Jeffery: They did and they made it preferred.

Paul Oesterman, Chair: Can we send this back to them and have them re-think it? Consider adding the separate ingredients.

Carl Jeffery: Sure, we can bring it back.

James Marx: I retract my second.

David England: I'll retract my motion.

Paul Oesterman, Chair: So can we send this back to the P&T, looking at ondansetron and the separate components.

d. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for Neurokinin-1 (NK1) Receptor Antagonists and Combinations

Paul Oesterman, Chair: Our next agenda item is the discussion and possible adoption of prior authorization criteria for neurokinin-1 receptor antagonists and combinations. Any public comment?

Theresa Beckert: My name is Theresa Beckert, I'm a medical science liaison with Eisai and speaking on Akynzeo for the prevention of chemo-induced nausea and vomiting, background of CINV, guidelines, dosing recommendations, packaging, efficacy, safety, and common adverse events. I request open access when prescribed by an oncologist for patients undergoing chemotherapy.

Carl Jeffery: We have the criteria in the binder. We don't have any utilization of the Akynzeo or Varubi. Just a reminder, the PAD claims are not subject to the clinical criteria and that is really where you are going to see this. Adding these criteria is just going to make sure a retail pharmacy is dispensing it for something other than chemo-induced nausea and vomiting.

Paul Oesterman, Chair: Do we want anything in here that it is being prescribed by an oncology or in consultation with an oncologist?

Carl Jeffery: It wouldn't hurt.

David England: So we would have, B: ordered by oncologist or in consultation with an oncologist.

Michael Owens: Is this used for post-operative treatment?

Carl Jeffery: It isn't indicated.

Michael Owens: For Emend, it is listed below.

David England: So this isn't used for PONV, it doesn't look like it should be

Carl Jeffery: The way the criteria are written, they shouldn't be allowed to use it for PONV.

Paul Oesterman, Chair: We have the proposed criteria here, with the addition that it is ordered by an oncologist or in consultation with an oncologist. Do we have a motion to approve?

James Marx: I'll move.

David England: Second.

Voting: Ayes across the board, the motion carries.

e. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria for medications used for opioid dependence.

Paul Oesterman, Chair: Our next item is the discussion and possible adoption of updated prior authorization criteria for medications used for opioid dependence. We have the existing prior authorization criteria here, we have some proposed changes. Do we have any public comment?

William Mullen: My name is Will Mullen, I'm a clinical advisor for the medical affairs team for the manufacturer of Suboxone. We agree with the proposals on the PA criteria with some additions. Section F, other states require a drug monitoring program, the PMP as one of the criteria. Section G, the one thing about the mono product, it is recommended that anyone dependent on a long-acting opioid, that the induction phase be done on the mono product. After three days moving to stabilization, they move to the combo product. With G, with pregnancy, we are not contraindicated in pregnancy, if the benefits outweigh the risk, they can remain on the combo product. We are fine with the two units per day, but a standardization of the brands, the Zubsolv says 17.1mg is the top strength allowed in the label.

James Marx: What is the DEA limit for the Suboxone per day, it isn't two is it?

William Mullen: We have 2, 4, 8 and 12 mg, you can get to 24 mg. We don't recommend people maintained at 24 mg, but should be just the first part of treatment.

James Marx: I do all the time. I see a lot of failed patients from other programs, especially those coming from heroin. We start a fair number on 36mg per day and have had good results.

William Mullen: If you are taking on the worst of the worst, then 36mg may be appropriate. It is off label and we can't recommend that.

James Marx: I'm afraid this is becoming a big problem.

William Mullen: Other states are opening up access, but we support clinical authorizations to make sure it is used appropriately.

James Marx: Can the pharmacies dispense a three day supply without a prior authorization.

Carl Jeffery: I'm not sure, if it is a new PA with a new prescription, they can dispense up to a 96 hour override, and only works for new prescriptions.

Paul Oesterman, Chair: Your comment regarding checking the PMP is now mandatory in Nevada.

Carl Jeffery: We were prompted to bring this back because of high dose requests. The call center doesn't have any criteria to exceed the dose. And we are seeing requests to treat chronic pain, which probably isn't appropriate.

James Marx: I actually have a lot of patients using it for chronic pain. It is particularly appropriate for patients with a prior history of abuse. We have converted many from oxycodone and Belbuca seems to be effective for this.

Carl Jeffery: Ok, we can discuss these criteria, but the proposed criteria has that it can't be used for chronic pain. We also have that they are not on concurrent opioids.

James Marx: Should we address the issue of the quantity limit first?

Carl Jeffery: Yes, it is in the criteria proposed here. It is approved for up to 24 mg, we had it set a little lower.

Michael Owens: Does this medication have a street value.

James Marx: Yes, and it is abusable too. It is not a total solution.

Michael Owens: Does it show on a lab?

William Mullen: It doesn't show on a standard lab, but the metabolite can be tested

Paul Oesterman, Chair: Are we considering elimination of C on here which is the request for chronic pain.

Carl Jeffery: This drug itself is limited to the X DEA, is this something any prescriber with an X DEA number can write for this?

James Marx: When you write it for chronic pain, you don't use the X DEA. You use your regular DEA and mark it is for chronic pain. Any prescriber can do it and it is off label. It is a very good product.

Beth Slamowitz: I think that is why we are going to need that C on the criteria.

James Marx: There is peer-reviewed literature supporting the use of it.

Beth Slamowitz: Then that could be added to the criteria or the PA request.

Carl Jeffery: I don't want to see every prescriber writing for this. If we limit so it can't be used for chronic pain, then they have to use their X DEA number.

James Marx: You're inducing someone to write a fraudulent script if they are using for chronic pain because they are saying they are using it for addiction treatment.

Paul Oesterman, Chair: We could put something like chronic pain…

William Mullen: I think this would be more under analgesia criteria.

Paul Oesterman, Chair: I think that may be appropriate to have under an opioid analgesic.

Carl Jeffery: We would have to bring those criteria to the next meeting. It certainly shouldn't be first line.

James Marx: There are some that do support using as first line, as the primary analgesic.

Paul Oesterman, Chair: Let's bring that part back to the next meeting. We have the proposed PA criteria. Quantity limits set. Do we have a motion to approve as presented?

David England: So moved.

James Marx: Second.

Voting: Ayes across the board.

Paul Oesterman, Chair: So the next meeting we will discuss this being used for the opiate analgesics.

Paul Oesterman, Chair: So the next meeting we will discuss this being used for the opiate analgesics.

f. **For Possible Action:** Discussion and possible adoption of prior authorization criteria for medications used for opioid induced constipation.

Paul Oesterman, Chair: The next topic is the discussion and possible adoption of prior authorization criteria for medications used for opioid induced constipation. Any public omment?

Carl Jeffery: This is another class that has been out for a while with a couple new products on the market. The utilization is in the binder. The proposed criteria are also included. These are very effective and have their place in therapy, but we want to make sure they are being used judiciously.

James Marx: There is going to be a step therapy edit.

Carl Jeffery: Right, they need to show they have tried one of the three traditional therapies.

James Marx: That's good because a lot of people do respond to the osmotic laxatives.

Paul Oesterman, Chair: On the Section D, the methylnaltrexone, if the patient's weight is over 140kg…

Carl Jeffery: That is just for those that exceed the quantity limit.

Paul Oesterman, Chair: In my practice setting, we have a lot of elderly opiate users, using methylnaltrexone, but they only need it about once a week. The one per day limit seems pretty high.

James Marx: We prescribe it daily, but patients come in and only use half of what they are prescribed.

Paul Oesterman, Chair: Can we look at the data in six months again to see how it is being utilized. We need a motion.

David England: So moved.

James Marx: Second.

Voting: Ayes across the board, the motion carries.

Paul Oesterman, Chair: In six months, let's look at the utilization again.

g. **For Possible Action:** Discussion and possible adoption of updated prior authorization criteria for long-acting opioids.

Paul Oesterman, Chair: Our next agenda item is discussion and possible adoption of updated prior authorization criteria for long-acting opioids. We have the prior criteria and usage data.

Carl Jeffery: This was brought up because we have no criteria to exceed the quantity outside cancer pain. This will add criteria so the call center can evaluate consistently.

David England: Is this the new CDC guidelines.

Carl Jeffery: My understanding it was more of a recommendation.

James Marx: It supported the use of alternative agents before getting to opioids. The other option is SNRI's, but we are going to end up pushing the dose of acetaminophen to treat the pain.

David England: I don't want to go against the CDC guidelines.

James Marx: The CDC was more focused on acute pain rather than chronic pain.

David England: And this is for chronic pain here, so that is ok. I feel better about this if that is the case.

James Marx: 1B does allow for opiate exceeding the quantity as long as they meet the three criteria.

Carl Jeffery: Right, I think the bulk of the people will meet these criteria. They will only need a PA if they exceed the quantity limits. Before, all we had was A, the only time we could approve was if they had terminal cancer.

Paul Oesterman, Chair: Let's call for public comment.

Sandy Sierawski: Sandy Sierawski, I'm a pharmacist with Pfizer. I don't have a formal presentation, but I noticed on the criteria for Embeda is set for one per day and the package insert says one every 24 hours or every 12 hours.

Paul Oesterman, Chair: We have the proposed criteria. Do we want to revise the quantity limit for Embeda to up to 2 per day? I will call for a motion.

David England: So moved.

James Marx: Second.

Voting: Ayes across the board, the motion carries.

6. Public Comment on any DUR Board Requested Report

Paul Oesterman, Chair: Any public comment on the DUR Board requested reports? No, then let's look at the reports.

7. DUR Board Requested Reports

a. Cumulative acetaminophen report

Carl Jeffery: Starting on page 97 is the cumulative acetaminophen dose. The numbers on the left is an encrypted Medicaid ID. So our highest utilizer is 3500mg a day. We don't have any hard edits to stop the different ingredients. I think our pharmacists are doing a pretty good job.

Paul Oesterman, Chair: One of my concerns, are the patients taking any over the counter products that we don't know about. We won't know that. Next report?

b. Long-acting steroid inhaler combination utilization

Carl Jeffery: Starting on page 102, the long-acting steroid combination products. Advair by far, but Symbicort is coming up pretty fast. Symbicort has been made preferred.

Paul Oesterman, Chair: One of the things coming up is Breo Ellipta has been added to the hospital formulary, so that may drive some of the utilization coming up.

Carl Jeffery: Yeah, it is a good product, we have it non-preferred right now, but it will be reviewed at an upcoming P&T meeting.

Paul Oesterman, Chair: It is interesting to see the last three time periods, respiratory products are on an increase. Can we correlate this to an increase or decrease in visits to the ED. If we are using more medication and reducing ED visits, I think that is good.

David England: Would we also want to look at beta agonist use? Are we seeing more or less beta agonists?

Beth Slamowitz: I think you could look at a certain time period with a diagnosis set, and then look at what medications they are on. Look at asthma and COPD.

Carl Jeffery: It also appears to be seasonal.

c. Utilization of short-acting insulin without long-acting/basal insulin

Paul Oesterman, Chair: Basal insulin, what do we have?

Carl Jeffery: This shows the number of members on fast acting insulin without a long acting agent. For comparison, the two charts below show the total number getting long and short-acting insulin.

Paul Oesterman, Chair: the numbers in both columns are the same. Is it the count of members or count of claims? Can you redo this and bring it back next time?

Carl Jeffery: Sure.

d. Narcotic cough suppressants utilization

Paul Oesterman, Chair: Narcotic cough suppressants.

Carl Jeffery: We ran this looking for all opioid antitussive agents. On average we're doing pretty well with utilization.

Paul Oesterman, Chair: Interesting, the physician administered, the promethazine with codeine and Pennkinetic, is that coming from a rural area? It is not a lot, but I can't envision a physician's office administering cough syrup.

Carl Jeffery: I'm not sure, we can drill down on that if needed.

Paul Oesterman, Chair: It seems like we have been able to impact the quantities, it worked. Any of the Board have questions?

8. Public Comment on any Standard DUR Report

Paul Oesterman, Chair: Our standard reports now, any public comment?

9. Standard DUR Reports

Carl Jeffery: These are the standard reports and the trends are holding as from previous versions.

Paul Oesterman, Chair: What about the Abilify, it is generic now.

Carl Jeffery: We still have the brand preferred

Paul Oesterman, Chair: It would be nice to know which brand name products we have preferred so we know what we need to address.

Carl Jeffery: I'll have to look at that and see if there is an easy way to identify that. The Abilify is listed on a later report so you can see how it stands up to the other agents. Pages 106 and 107 are sorted at a different level and gets into the specific class types. We have seen the hepatitis agents level off a little. Starting page 110, we have the specific drugs by paid amount. Nothing jumps out to me. Hemophilia certainly fluctuates quite a bit from quarter to quarter. ProDUR edits start on page 116. The last quarter starts on page 142.

Paul Oesterman, Chair: Total paid claims from third quarter to first quarter took a jump. The ProDUR report fairly consistent. What has transpired from total membership?

Carl Jeffery: Fee for service has held pretty steady.

Beth Slamowitz: It has held steady around the 160,000 mark.

Paul Oesterman, Chair: Do we have any additional topics for next time?

James Marx: I want to look at proton pump inhibitors and cardiovascular complications. That is such a ubiquitous drug now.

Paul Oesterman, Chair: Anything else?

David England: With the changes with the CDC, do we want to look at NSAID use or changes in the opioid use and could we differentiate between chronic or acute pain.

James Marx: But we are not going to be able to see if patients are getting OTC medications.

Beth Slamowitz: I think looking at opioids will be a benefit and track the changes.

James Marx: I wouldn't NOT look at the NSAIDS, but I think the numbers are going to be a little skewed.

David England: Maybe look at antiepileptics with the NSAIDS too.

Carl Jeffery: Does the CDC letters have an impact on the prescribing trends?

Michael Owens: I'm not a pain specialist and we have an opioid cap at our practice, but we get a lot of chronic pain patients that are in withdrawal. We still have the focus that pain is the fifth vital sign and our practice is the only group that will prescribe opioids.

David England: You have to treat these patients, but then these guidelines don't give any real alternatives.

James Marx: The problem is these patients are going back to the street if they can't get what they need from their prescriber. We are seeing more counterfeit opioids like fentanyl.

Michael Owens: When you talk about Suboxone for pain management, but it does not have the pull of the very abusive narcotic user.

James Marx: I like it when patients feel comfortable with me and tell me they prefer some medications over others, we try to accommodate them and they do much better.

6. Closing Discussion

Paul Oesterman, Chair: Next meeting is July 28th, same time, same place.

Meeting adjourned at 7:50pm.

Gonadotropin-Releasing Hormone Utilization

Count of Members

July 2015 - June 2016

Count of Member ID	Age																
Sex/Drug Name	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Grand Total
F			1	1	2	1	1	2	7	12	7	3	1	1	1	2	42
ANASTROZOLE TAB 1MG									1	1							2
LETROZOLE TAB 2.5MG										1	1						2
LUPR DEP-PED INJ 11.25MG									1								1
LUPR DEP-PED INJ 30MG							1	1	5	8	5	3	1				24
LUPRON DEPOT INJ 11.25MG																1	1
MEGESTROL AC SUS 40MG/ML			1	1	1	1				2	1			1	1	1	10
SUPPRELIN LA KIT 50MG					1			1									2
M	2	1		2	2	1	3	2	1	1	2	1			2	2	22
LETROZOLE TAB 2.5MG									1	1					1		3
MEGESTROL AC SUS 40MG/ML	2	1		2	2	1	3	2			1	1			1	1	17
SUPPRELIN LA KIT 50MG											1					1	2
Grand Total	**2**	**1**	**1**	**3**	**4**	**2**	**4**	**4**	**8**	**13**	**9**	**4**	**1**	**1**	**3**	**4**	**64**

DIVISION OF HEALTH CARE FINANCING AND POLICY
NEVADA MEDICAID
DRUG USE REVIEW (DUR) BOARD
PROPOSED PRIOR AUTHORIZATION CRITERIA

Therapeutic Class: GnRH Analogs
Last Reviewed by the DUR Board: N/A

1. **Coverage and limitations:**

   Approval of Lupron® (leuprolide) will be given if the following criteria are met.

   A. The recipient has a diagnosis of idiopathic or neurogenic central precocious puberty (CPP) and all of the following:
      1) Requested dose and frequency is appropriate
      2) Prescriber is a pediatric endocrinologist or provides documentation of a consultation with a pediatric endocrinologist
      3) Onset of secondary sex characteristics before age 8 years (females) or 9 years (males)
      4) Member is currently less than 11 years old (females) or 12 years old (males)

   B. The recipient has a diagnosis of endometriosis and all of the following:
      1) Requested dose and frequency is appropriate
      2) Inadequate response, adverse reaction, or contraindication to an NSAID
      3) Inadequate response, adverse reaction, or contraindication to a hormonal contraceptive

   C. The recipient has a diagnosis of Uterine leiomyomata (Fibroids) and all of the following:
      1) Requested dose and frequency is appropriate
      2) Must be symptomatic
      3) Anticipated surgery date (or notation that surgery is planned once fibroids shrink) or clinical rational why surgical intervention is not required

   D. The recipient has a diagnosis of Prostate Cancer and all of the following:
      1) Requested dose and frequency is appropriate

2. **Prior Authorization Guidelines:**
   A. Prior authorization will be given for an appropriate length of therapy based on the diagnosis, unless the prescriber indicates a shorter duration of approval:
      1) CPP: 1 year, or until the member reaches the age of 11 years (female) or 12 years (male)
      2) Endometriosis: 1 year
      3) Uterine Leiomyomata (fibroids): 1 month or until time of surgery documented (max 3 months)
      4) Prostate Cancer: 3 year

3. **Quantity Limitations**:
   A. Lupron DEPOT 1-Month (7.5 mg): 1 injection/4 weeks
   B. Lupron DEPOT 3-Month (22.5 mg): 1 injection/12 weeks
   C. Lupron DEPOT 4-Month (30 mg): 1 injection/16 weeks
   D. Lupron DEPOT 6-Month (45 mg): 1 injection/24 weeks
   E. Lupron DEPOT-PED 1-month (7.5 mg, 11.25 mg and 15 mg): 1 injection/4 weeks
   F. Lupron DEPOT-PED 3-month (11.25 mg and 30 mg): 1 injection/12 weeks
   G. Eligard 7.5 mg: 1 injection/4 weeks
   H. Eligard 22.5 mg: 1 injection/12 weeks
   I. Eligard 30 mg: 1 injection/16 weeks
   J. Eligard 45 mg: 1 injection/24 weeks
   K. leuprolide acetate solution for injection: 2 vials/28 days

Therapeutic Class Overview
Leuprolide

Therapeutic Class

- **Overview/Summary:** Leuprolide (Eligard®, Lupron Depot®, Lupron Depot-PED®) is a synthetic analog of luteinizing hormone-releasing hormone (LHRH), otherwise known as a gonadotropin-releasing hormone (GnRH), which is Food and Drug Administration-approved for the management of endometriosis, palliative treatment of advanced prostate cancer, preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata in combination with iron therapy, and treatment of central precocious puberty. The agent is available as an aqueous solution for daily subcutaneous administration; a suspension for subcutaneous administration every one, three, four, or six months; or a depot formulation for intramuscular administration every one, three, four, or six months.[1-6] Similar to other agents in the class, upon initial administration of leuprolide, there is an increase in luteinizing hormone (LH) and follicle stimulating hormone (FSH) which leads to transient increases in estrogen regulation of the pituitary gland which results in a sustained decrease in LH and FSH secretion, and a marked reduction of ovarian and testicular steroidogenesis. Consequently, tissues and functions that depend on gonadal steroids for their maintenance become quiescent.[1-7] Currently, the daily subcutaneous injection of leuprolide is available generically. Pain is the most common symptom associated with endometriosis, particularly pelvic pain and/or dysmenorrhea. The precise pathogenesis of endometriosis has not been clearly defined.[8] Optimal management of endometriosis is unclear. There is no high quality evidence to support the superiority of one medical treatment over another; therefore, treatment decisions require individualization. Decisions may be based on the severity of symptoms, the extent and location of the disease, whether there is a desire for pregnancy, patient age, adverse events, surgical complication rates, and cost.[9,10] According to the American Society for Reproductive Medicine, oral contraceptives, progestogens, danazol, GnRH agonists, and anti-progestogens have all been utilized as medical treatments for endometriosis.[10] According to the National Comprehensive Cancer Network (NCCN), androgen deprivation therapy is commonly used in the treatment of prostate cancer, and is accomplished through surgical or medical castration (using an LHRH agonist or antagonist with or without an anti-androgen), which are equally effective. Androgen deprivation therapy is primarily administered as primary systemic therapy in advanced disease, but also plays an important role, when administered in combination with radiation therapy, for the management of localized or locally advanced prostate cancer. The NCCN does not distinguish among available GnRH agonists.[11] Uterine leiomyomas, otherwise known as uterine fibroids, are the most common solid pelvic tumors in women. . Currently, hysterectomy is the only definitive treatment option, and eliminates the possibility of recurrence; however, women who desire future childbearing or to retain their uteri require alternative management strategies. Alternatives include contraceptive steroids (estrogen and progestin combinations, progestins), nonsteroidal anti-inflammatory drugs (NSAIDs), GnRH agonists, aromatase inhibitors, progesterone modulators, and alternative surgical procedures such as myomectomy and uterine artery embolization. Use of GnRH agonists leads to amenorrhea in most women and provides a 35 to 65% reduction in leiomyoma volume within three months of treatment. Disadvantages associated with GnRH agonists include gradual recurrent growth of leiomyomas after cessation of treatment, and a limited duration of treatment (six months) due to significant symptoms of pseudomenopause and an adverse impact on bone mineral associated with these agents.[12] Precocious puberty is defined as the onset of secondary sexual development before the age of eight in girls and nine in boys. GnRH analogs are used as primary treatment of gonadotropin-dependent precocious puberty, with the primary goal to allow the child to grow to a normal adult height. The decision to prescribe a GnRH agonist depends on the child's age, the rate of pubertal progression, height velocity, and the estimated adult height as determined from the rate of bone age advancement.[13]

Table 1. Current Medications Available in Therapeutic Class[1-7]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Leuprolide* (Eligard®, Lupron Depot®, Lupron Depot-PED®)	Management of endometriosis, including pain relief and reduction from endometriotic lesions (Lupron Depot® 3.75 and 11.25 mg). Palliative treatment of advanced prostate cancer (Eligard®; leuprolide; Lupron Depot® 7.5, 22.5, 30, and 45 mg). Preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata in combination with iron therapy (Lupron Depot® 3.75 and 11.25 mg). Treatment of children with central precocious puberty (Lupron Depot-PED®).	Injection: 1 mg/0.2 mL Intramuscular injection (Lupron Depot®): 3.75 mg 7.5 mg 11.25 mg 22.5 mg 30 mg 45 mg Intramuscular injection pediatric (Lupron Depot-PED®): 7.5 mg 11.25 mg 15 mg 30 mg Subcutaneous injection (Eligard®): 7.5 mg 22.5 mg 30 mg 45 mg	✔

Evidence-based Medicine

- Clinical trials have demonstrated safety and efficacy in the formulations' respective Food and Drug Administration-approved indications.[14-34]
- For the management of endometriosis, clinical trial data consistently demonstrate the effectiveness of leuprolide in improving pain-related symptoms.[14-21]
- In a head-to-head trial comparing once monthly to every three month dosing of leuprolide, both treatment regimens demonstrated efficacy. Specifically, both regimens achieved ovarian suppression, lesion regression, and provided relief from pain. Better patient acceptability was recorded with every three month injections of leuprolide.[14]
- A meta-analysis comparing luteinizing-hormone releasing hormone (LHRH) agonists to orchiectomy and anti-androgens reported that survival after therapy with LHRH agonists in men with advanced prostate cancer was equivalent to that after orchiectomy; however, survival rates may be lower if an anti-androgen was used as monotherapy.[24]
- Many trials have compared combined androgen blockade (castration plus an anti-androgen) to conventional medical or surgical castration. The use of combined androgen blockade in advanced prostate cancer is controversial since meta-analyses showed a small survival benefit with the addition of an anti-androgen to medical or surgical castration.[26,27]
- Limited clinical trial data was identified evaluating leuprolide for the treatment of central precocious puberty; however, available data demonstrate that treatment with leuprolide results in effective

suppression of puberty. Furthermore, a variety of treatment strategies have been evaluated, and evidence suggests that multi-monthly injections (e.g., every three months) are effective, but higher doses may be required.[29-31]

- Results from a placebo-controlled trial of anemic women with uterine leiomyomas scheduled to undergo surgical management, demonstrate that three months of preoperative treatment with leuprolide 3.75 or 7.5 mg once monthly, in combination with iron therapy, was superior in treating anemia, in reducing uterine and myoma volume, and in alleviating bleeding and other leiomyomata - related symptoms.[33]

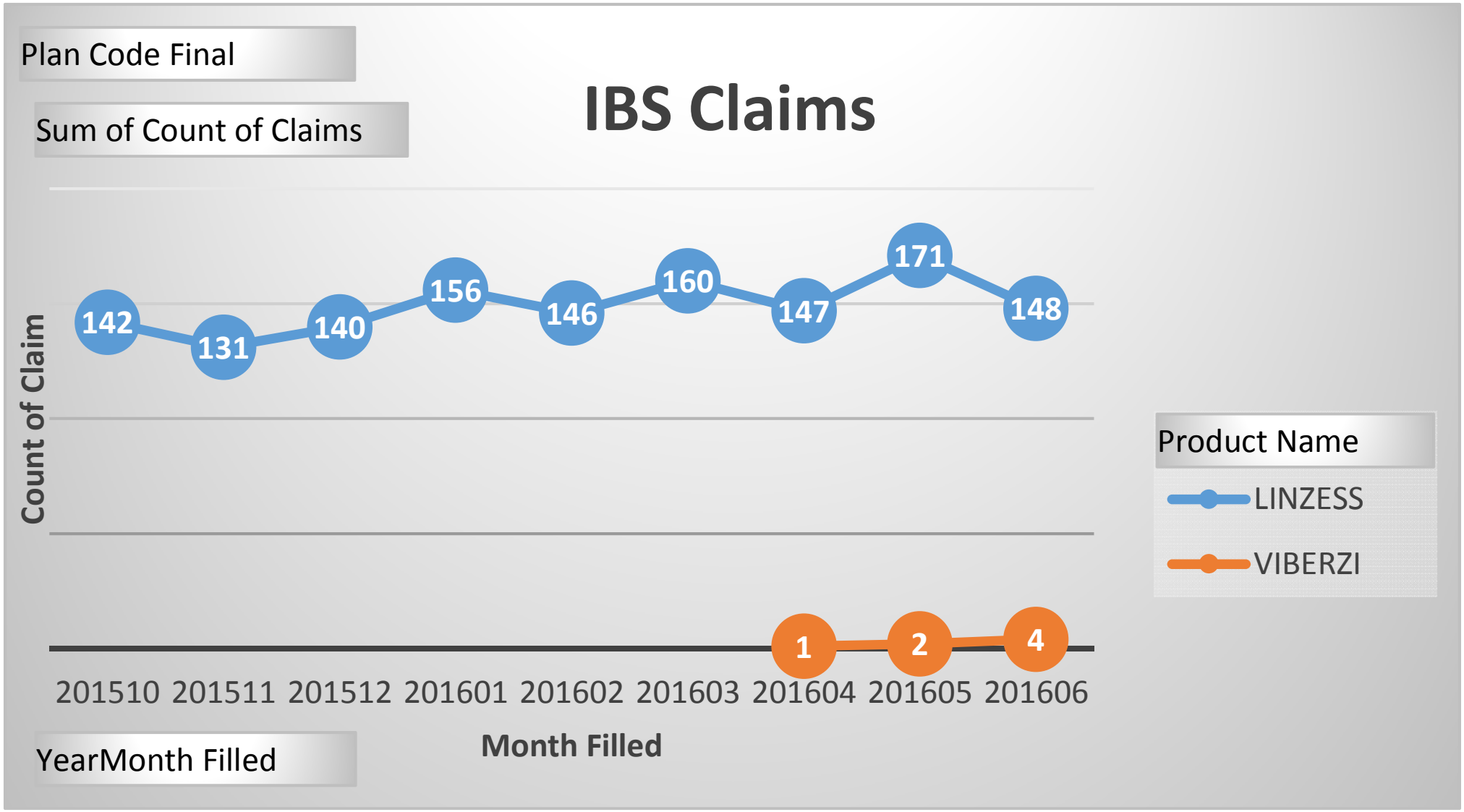
Key Points within the Medication Class

- According to Current Clinical Guidelines:[10-12,35]
    - According to the American Society for Reproductive Medicine, oral contraceptives, progestogens, danazol, GnRH agonists, and anti-progestogens have all been utilized as medical treatments for endometriosis. There is no high quality evidence to support the superiority of one medical treatment over another; therefore, treatment decisions require individualization.
    - After an appropriate pretreatment evaluation (to exclude other causes of chronic pelvic pain) and failure of initial treatment with oral contraceptives and nonsteroidal antiinflammatory drugs (NSAIDS), empiric therapy with a three-month course of a GnRH agonist is appropriate for the treatment of endometriosis. When relief of pain from treatment with a GnRH agonist supports continued therapy, the addition of add-back therapy reduces or eliminates GnRH agonist-induced bone mineral loss and provides symptomatic relief without reducing the efficacy of pain relief.
    - According to the NCCN, LHRH agonists and antagonists are commonly utilized as primary androgen deprivation therapy in patients with advanced prostate cancer. The NCCN does not distinguish among available LHRH agonists.
    - Potential alternatives to hysterectomy in the treatment of uterine leiomyomas include contraceptive steroids (estrogen and progestin combinations, progestins), nonsteroidal anti-inflammatory drugs, GnRH agonists, aromatase inhibitors, progesterone modulators, and alternative surgical procedures such as myomectomy and uterine artery embolization. With regards to GnRH agonists, treatment leads to amenorrhea in most women and provides a 35 to 65% reduction in leiomyoma volume within three months of treatment. Disadvantages associated with GnRH agonists include gradual recurrent growth of leiomyomas after cessation of treatment, and a limited duration of treatment (six months) due to significant symptoms of pseudomenopause and an adverse impact on bone mineral associated with these agents.
- Other Key Facts:
    - The daily subcutaneous injection is available generically.

References

1. Eligard® [package insert]. Fort Collins (CO): Tolmar Pharmaceuticals; 2016 Feb.
2. Leuprolide [package insert]. Princeton (NJ): Sandoz Inc.; 2011 Jan.
3. Lupron Depot® 3.75 mg [package insert]. North Chicago (IL): AbbVie, Inc.; 2013 Oct.
4. Lupron Depot® 11.25 mg [package insert]. North Chicago (IL): AbbVie, Inc.; 2013 Oct.
5. Lupron Depot® 7.5, 22.5, 30, and 45 mg [package insert]. North Chicago (IL): AbbVie, Inc.; 2016 Jun.
6. Lupron Depot-PED® [package insert]. North Chicago (IL): Abbott Laboratories; 2013 Mar.
7. Micromedex® Healthcare Series [database on the Internet]. Greenwood Village (CO): Thomson Reuters (Healthcare) Inc.; Updated periodically [cited 2016 Jun]. Available from: http://www.thomsonhc.com/.
8. Schenken RS. Pathogenesis, clinical features, and diagnosis of endometriosis. UTD. In: Basow DS (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2016 [cited 2016 Jun]. Available from: http://www.utdol.com/utd/index.do.
9. Schenken RS. Endometriosis: Treatment of pelvic pain. In: Basow DS (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2016 [cited 2016 Jun]. Available from: http://www.utdol.com/utd/index.do.
10. Practice Committee of the American Society for Reproductive Medicine. Treatment of pelvic pain associated with endometriosis: a committee opinion. Fertil Steril. 2014 Apr;101(4):927-35.
11. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: prostate cancer [guideline on the internet]. Fort Washington (PA): NCCN; Version.3.2016 [cited June 2016]. Available from: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.

12. No authors listed. ACOG practice bulletin. Alternatives to hysterectomy in the management of leiomyomas. Obstet Gynecol. 2008 Aug;112(2 Pt 1):387-400.
13. Harrington J and Palmert MR. Treatment of precocious puberty. In: Basow DS (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2016 [cited 2016 Jun]. Available from: http://www.utdol.com/utd/index.do.
14. Crosignani PG, De Cecco L, Gastaldi A, Venturini PL, Oldani S, Vegetti W, et al. Leuprolide in a three-monthly vs a monthly depot formulation for the treatment of symptomatic endometriosis: a pilot study. Human Reproduction. 1996;11(12):2732-5.
15. Ling FW; Pelvic Pain Study Group. Randomized controlled trial of depot leuprolide in patients with chronic pelvic pain and clinically suspected endometriosis. Obstet Gynecol. 1999;93:51-8.
16. Busacca M, Somigliana E, Bianchi S, De Marinis S, Calia C, Candiani M, et al. Post-operative GnRH analogue treatment after conservative surgery for symptomatic endometriosis stage III-IV: a randomized controlled trial. Human Reproduction. 2001;16(11):2399-402.
17. Wright S, Valdes CT, Dunn RC, Fraklin RR. Short-term Lupron or danazol therapy for pelvic endometriosis (abstract). Fertil Steril. 1995 Mar;63(3):504-7.
18. Strowitzki T, Marr J, Gerlinger C, Faustmann T, Seitz C. Dienogest is as effective as leuprolide acetate in treating the painful symptoms of endometriosis: a 24-week, randomized, multicentre, open-label trial. Human Reproduction. 2010;25(3):633-41.
19. Crosignani PG, Luciano A, Ray A, Berggvist A. Subcutaneous depot medroxyprogesterone acetate vs leuprolide acetate in the treatment of endometriosis-associated pain. Hum Reprod. 2006 Jan;21(1):248-56.
20. Schlaff WD, Carson SA, Luciano A, Ross D, Berggvist A. Subcutaneous injection of depot medroxyprogesterone acetate compared to leuprolide acetate in the treatment of endometriosis-associated pain. Fertil Steril. 2006 Feb;85(5):314-25.
21. Brown J, Pan A, Hart RJ. Gonadotropin-releasing hormone analogues for pain associated with endometriosis. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD008475. DOI: 10.1002/14651858.CD008475.pub2.
22. Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola RS, et al. Survival following primary androgen deprivation therapy among men with localized prostate cancer. JAMA. 2008 Jul 9;300(2):173-81.
23. No authors listed. Leuprolide vs diethylstilbestrol for metastatic prostate cancer (abstract). Leuprolide Study Group. N Engl J Med. 1984 Nov 15;311:1281-6.
24. Seidenfeld J, Samson DJ, Hasselblad V, Aronson N, Albersten PC, Bennett CL, et al. Single-therapy androgen suppression in men with advanced prostate cancer: a systematic review and meta-analysis. Ann Intern Med. 2000;132:566-77.
25. Kunath F, Grobe HR, Rücker G, Motschall E, Antes G, Dahm P, et al. Non-steroidal antiandrogen monotherapy compared with luteinising hormone-releasing hormone agonists or surgical castration monotherapy for advanced prostate cancer. Cochrane Database Syst Rev. 2014 Jun 30;(6):CD009266.
26. No authors listed. Maximum androgen blockade in advanced prostate cancer: an overview of the randomized trials. Prostate Cancer Trialists' Collaborative Group. Lancet. 2000 Apr 29;355:1491-8.
27. Schmitt B, Wilt TJ, Schellhammer PF, DeMasi V, Sartor O, Crawford ED, et al. Combined androgen blockade with nonsteroidal antiandrogens for advanced prostate cancer: a systematic review. Urology. 2001 Apr;57(4):727-32.
28. Crawford ED, Moul JW, Sartor O, Shore ND. Extended release, 6-month formulations of leuprolide acetate for the treatment of advanced prostate cancer: achieving testosterone levels below 20 ng/dl. Expert Opin Drug Metab Toxicol. 2015;11(9):1465-74.
29. Fuld K, Chi C, Neely EK. A randomized trial of one- and three-month depot leuprolide doses in the treatment of central precocious puberty. J Pediatr. 2011;159:982-7.
30. Mericq V, Lammoglia JJ, Unanue N, Villaroel C, Hernandez MI, Avila A, et al. Comparison of three doses of leuprolide acetate in the treatment of central precocious puberty: preliminary results. Clin Endocrin. 2009;71:686-90.
31. Lee PA, Klein K, Mauras N, Lev-Vaisler T, Bacher P. 36-month treatment experience of two doses of leuprolide acetate 3-month depot for children with central precocious puberty. J Clin Endocrinol Metab. 2014 Sep;99(9):3153-9.
32. Jasonni VM, D'Anna R, Mancuso A, Caruso C, Corrado F, Leonardi I. Randomized double-blind study evaluating the efficacy on uterine fibrosis shrinkage and on intra-operative blood loss of different length of leuprolide acetate depot treatment before myomectomy. Acta Obstet Gynecol Scand. 2001;80:956-8.
33. Stovall TG, Muneyyirci-Delale O, Summitt RL, Scialli AR; The Leuprolide Acetate Study Group. GnRH agonist and iron vs placebo and iron in the anemic patient before surgery for leiomyomas: a randomized controlled trial. Obstet Gynecol. 1995;86:65-71.
34. Lethaby A, Vollenhoven B, Sowter MC. Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids. Cochrane Database of Systematic Reviews 2001, Issue 2. Art. No.: CD000547. DOI:10.1002/14651858.CD000547.
35. No authors listed. ACOG practice bulletin. Medical management of endometriosis. Number 114, July 2010 (replaces Practice Bulletin Number 11, December 1999). Clinical management guidelines for obstetrician-gynecologists. ACOG Committee on Practice Bulletins-Gynecology. Obstet Gynec. 2010;116(1).


Plan Code Final
Sum of Count of Claims
IBS Claims
Count of Claim
142
131
140
156
146
160
147
171
148
1
2
4
201510 201511 201512 201601 201602 201603 201604 201605 201606
Month Filled
YearMonth Filled
Product Name
LINZESS
VIBERZI

DIVISION OF HEALTH CARE FINANCING AND POLICY
NEVADA MEDICAID
DRUG USE REVIEW (DUR) BOARD
PROPOSED PRIOR AUTHORIZATION CRITERIA

Therapeutic Class: Irritable-Bowel Syndrome Agents
Last Reviewed by the DUR Board: N/A

1. **Coverage and limitations:**

   Approval of medications used for the treatment of Irritable-Bowel Syndrome will be given if the following criteria are met. Clinical criteria for these agents in other diagnoses may apply.

   A. The recipient is 18 years of age or older
   AND
   B. The requested agent is being used for an appropriate indication
   AND
   C. Requests for a diagnosis of Irritable-bowel syndrome with constipation (IBS-C) must meet all of the following criteria:
      1) There is documentation in the recipient's medical record indicating an inadequate response, adverse reaction, or contraindication to 1 agent from three of the four traditional laxative therapy classes:
         a. Bulk forming laxatives
         b. Osmotic laxatives
         c. Saline laxatives
         d. Stimulant laxatives
      2) Request for lubiprostone in IBS-C: Recipient must be female
      3) The requested dose is appropriate based on indication and age
         a. Linaclotide: 145 µg daily
         b. Lubiprostone: 290 µg daily

   OR

   D. Requests for a diagnosis of Irritable-bowel syndrome with constipation (IBS-D) must meet all of the following criteria:
      1) Prescriber is a gastroenterologist or there is documentation in the recipient's medical record that a consultation was done by a gastroenterologist
      2) The requested dose is appropriate based on indication and age
         a. Alosetron: 0.5 mg twice daily or 1 mg twice daily
         b. Eluxadoline: 75 mg twice daily or 100 mg twice daily
         c. Rifaximin: 550 mg three times a day for 14 days
      3) One of the following:
         a. Inadequate response or adverse reaction to THREE of the following:
            I) Loperamide
            II) diphenoxylate/atropine
            III) Bile acid sequestrant (e.g., cholestyramine, colestipol, colesevelam)
            IV) TCAs
            V) SSRIs

            OR

         b. If inadequate response or adverse reaction to less than THREE agents above (I to VII), contraindication to ALL agents not tried.

2. **Prior Authorization Guidelines:**
   A. Prior authorization will be given for an appropriate length of therapy based on the requested agent and diagnosis not to exceed one year.

3. **Quantity Limitations**:
   A. Linaclotide (Linzess®): 1 capsule/day
   B. Lubiprostone (Amitiza®): 2 capsules/day
   C. Alosetron (Lotronex®): 2 tablets/day
   D. Eluxadoline (Viberzi®): 2 tablets/day
   E. Rifaximin (Xifaxan®) 550 mg: 3 tablets/day (42 tablets/Rx)
   F. Rifaximin (Xifaxan®) 200 mg: 3 tablets/day (9 tablets/Rx)

Therapeutic Class Overview
Irritable Bowel Syndrome Agents

Therapeutic Class Overview/Summary:
This review will focus on agents used for the treatment of Irritable Bowel Syndrome (IBS).[1-5] IBS is a gastrointestinal syndrome characterized primarily by non-specific chronic abdominal pain, usually described as a cramp-like sensation, and abnormal bowel habits, either constipation or diarrhea, in which there is no organic cause. Other common gastrointestinal symptoms may include gastroesophageal reflux, dysphagia, early satiety, intermittent dyspepsia and nausea. Patients may also experience a wide range of non-gastrointestinal symptoms. Some notable examples include sexual dysfunction, dysmenorrhea, dyspareunia, increased urinary frequency/urgency and fibromyalgia-like symptoms.[6] IBS is defined by one of four subtypes. IBS with constipation (IBS-C) is the presence of hard or lumpy stools with ≥25% of bowel movements and loose or watery stools with <25% of bowel movements. When IBS is associated with diarrhea (IBS-D) loose or watery stools are present with ≥25% of bowel movements and hard or lumpy stools are present with <25% of bowel movements. Mixed IBS (IBS-M) is defined as the presence of hard or lumpy stools with ≥25% and loose or water stools with ≥25% of bowel movements. Final subtype, or unsubtyped, is all other cases of IBS that do not fall into the other classes. Pharmacological therapy for IBS depends on subtype.[7]

While several over-the-counter or off-label prescription agents are used for the treatment of IBS, there are currently only two agents approved by the Food and Drug Administration (FDA) for the treatment of IBS-C and three agents approved by the FDA for IBS-D. Of note, each agent has a unique mechanism of action.[1-5] Agents used for the treatment of IBS-C include linaclotide (Linzess®) and lubiprostone (Amitiza®). Linaclotide is a guanylate cyclase-C (GC-C) agonist. It achieves improved gastrointestinal (GI) transit and reduced intestinal pain via activation of GC-C locally, on the luminal surface of the intestinal epithelium. Activation of GC-C stimulates the secretion of chloride and bicarbonate into the intestinal lumen while also decreasing the activity of pain-sensing nerves.[1] Lubiprostone is a locally acting chloride channel activator acting specifically at chloride channel-2 (CIC-2) receptors in the intestine. By increasing intestinal fluid secretion, lubiprostone increases motility in the intestine.[2] Agents used for the treatment of IBS-D include alosetron (Lotronex®), eluxadoline (Viberzi®) and rifaximin (Xifaxan®). Alosetron is a potent and selective serotonin-3 (5-HT_3) receptor antagonist. 5-HT3 receptors are ligand-gated cation channels that are extensively distributed on enteric neurons in the human gastrointestinal tract, as well as other peripheral and central locations. Activation of these channels and the resulting neuronal depolarization affect the regulation of visceral pain, colonic transit, and gastrointestinal secretions.[3] Eluxadoline (Viberzi®) is a μ-opioid receptor agonist/δ-opioid receptor antagonist/κ-receptor agonist. It is a locally active visceral analgesic, with low systemic absorption and bioavailability. The μ-opioid agonist activity works by inhibiting gastrointestinal (GI) motility and secretion and the δ-opioid receptor antagonism works by mitigating against the constipating effects of unopposed peripherally acting μ-opioid receptor agonist.[4] Rifaximin (Xifaxan®) is a semi-synthetic, non-systemic, broad-spectrum antibiotic and is a structural analog of rifampin. The proposed mechanism of action involves inhibition of bacterial RNA synthesis by binding to the beta-subunit of bacterial DNA-dependent RNA polymerase.[5]

Table 1a. IBS-C Current Medications Available[1-2]

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Linaclotide (Linzess®)	Chronic idiopathic constipation in adults, irritable bowel syndrome with constipation in adults	Capsule: 145 μg 290 μg	-
Lubiprostone (Amitiza®)	Chronic idiopathic constipation in adults, irritable bowel syndrome with constipation in adult women, opioid-induced constipation in adults with chronic non-cancer pain	Capsule: 8 μg 24 μg	-

Table 1b. IBS-D Current Medications Available[3-5]

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Alosetron (Lotronex®*)	Irritable bowel syndrome with diarrhea in adult women	Tablet: 0.5 mg 1 mg	-
Eluxadoline (Viberzi®)	Irritable bowel syndrome with diarrhea in adults	Tablet: 75 mg 100 mg	-
Rifaximin (Xifaxan®)	Irritable bowel syndrome with diarrhea in adults, reduce the risk of recurrent overt hepatic encephalopathy in adults, travelers' diarrhea in adults and children 12 years of age or older	Tablet: 200 mg 550 mg	-

*Generic available in at least one dosage form or strength.

Evidence-based Medicine

- Clinical trials have been shown to be safe and effective for the treatment of IBS-C or IBS-D.[1-5,8-16]
  - The FDA approval of linaclotide was based on four phase III, double-blind, placebo-controlled trials ranging from 12 to 26 weeks.[1] In the first trial (N=804) and the second trial (N=800), patients with IBS-C aged 18 and over were randomized to either linaclotide 290 µg or placebo. Treatment with linaclotide was associated with statistically significant changes in the proportion of patients who experienced ≥30% improvement in the daily worst abdominal pain score and increase of ≥1 in complete spontaneous bowel movement (CSBM) for at least 6 out of 12 weeks when compared to placebo. In addition, a greater proportion of patients treated with linaclotide were considered responders at 12 weeks in both trials.[1,8,9]
  - Safety and efficacy of lubiprostone in adult women with IBS-C was established in two similar double-blind, placebo-controlled studies of similar design. A mostly female study population (91.6%) of patients with IBS-C was randomized to receive lubiprostone 8 µg twice daily or matching placebo twice daily for 12 weeks. In a combined analysis, the percentage of patients in Study 1 qualifying as an "overall responder" was 18.2% in the group receiving lubiprostone 8 µg twice daily compared to 9.8% of patients receiving placebo twice daily (P=0.009). In Study 2, 17.7% of patients in the lubiprostone 8 µg group were "overall responders" versus 10.4% of patients in the placebo group (P=0.031).[10]
  - Several meta-analyses and systematic reviews evaluating alosetron and/or the 5-HT_3 antagonists as a class have been performed.[11-13]
    - An analysis by Andresen et al demonstrated that as a class, the 5-HT_3 antagonists significantly improve symptoms of non-constipating or diarrhea-predominant IBS in both men and women compared to placebo. These agents were also associated with a greater increase in the risk of becoming constipated compared to placebo.[11]
    - Cremonini et al demonstrated that alosetron treatment positively impacts global symptoms, and pain and discomfort in non-constipating IBS female patients. This analysis also showed an increased chance in developing constipation with alosetron compared to placebo.[12]
    - Ford et al evaluated all of the 5-HT_3 antagonists for the treatment of IBS. Results demonstrated that alosetron, along with others, are effective IBS treatments compared to placebo. Evaluation of 11 trials of patients receiving alosetron or cilansetron demonstrated that 49% of the active treatment group experienced persistent IBS symptoms after treatment cessation compared to 64% of the placebo group (P value not reported).[13]
  - The safety and efficacy of eluxadoline in the treatment of IBS-D was established in two identical randomized, multi-center, double-blind, placebo-controlled phase III clinical trials in

adults with IBS-D (IBS-3001 and IBS-3002). Both trials were 26 weeks long. Individuals were randomized to receive twice daily placebo, eluxadoline 75 mg or eluxadoline 100 mg.[14,15]
    - For the IBS-3001 trial, the proportion of composite responders for the 75 mg and 100 mg treatment groups had a statistically greater response than placebo for weeks 1 to 12 (P<0.025) and weeks 1 to 26 for the 100 mg treatment group (P<0.001).
    - In the IBS-3002 trial, the proportion of composite responders for the eluxadoline 75 mg and 100 mg groups had a statistically greater response than placebo for weeks 1 to 12 (P<0.001) and weeks 1 to 26 (P=0.001). The onset for response was noted to be within the first week of dosing in both trials.[14,15]
  - The safety and efficacy of rifaximin for the treatment of IBS-D was evaluated in three randomized, double-blind, placebo-controlled trials.
    - Two studies, TARGET 1 and TARGET 2, evaluated rifaximin 550 mg three times a day for 14 days in adult patients. There were significantly more patients in the rifaximin group than in the placebo group that had adequate relief of global IBS symptoms for at least two of the first four weeks after treatment in both TARGET 1 (40.8% vs 31.2%; P=0.01) and TARGET 2 (40.6% vs 32.2%; P=0.03) as well as combined (40.7% vs 31.7%; P<0.001).[5,16]
    - Another study, TARGET 3, evaluated retreatment with rifaximin 550 mg three times daily for 14 days who had previously responded to rifaximin, but who had experienced a recurrence of IBS-related symptoms (abdominal pain or mushy/watery stool). After the initial rifaximin treatment course, patients who were considered responders (N=1,257, 49%) were followed for 20 treatment free weeks. Overall, a numerically larger number of receiving rifaximin were month responders for both abdominal pain and stool consistency when compared to placebo (125 [38%] vs 97 [31%], respectively; no P value reported). The response rate difference was 7% (95% confidence interval, 1.2% to 11.6%, no P value reported).[5]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - Current clinical guidelines recommend the use of linaclotide, lubiprostone or other laxatives for the treatment of IBS-C.[18-20]
  - Due to limited therapeutic options and efficacy data for the treatment of IBS-D, clinical guidelines have consistently provided only moderate or weak recommendations for the use of all agents, new and old.All current clinical guidelines suggest rifaximin, alosetron, TCAs, SSRIs, and antispasmodics as effective, but their place in therapy is not well defined and varies by guideline. Loperamide was granted a conditional recommendation by the American Gastrointestinal Association (AGA) due to its usefulness as a potential adjunctive therapy for the management of diarrhea, however the American College of Gastroenterology (ACG) and World Gastroenterology Organization Global Guidelines do not recommend its use due to no relief of the global symptoms of IBS-D. Only the World Gastroenterology Organization mentions the use of eluxadoline, but acknowledges that although it has been approved for use in the United States, its position in the management of IBS is difficult to define at this time.[18-20]

- Other Key Facts:
  - There is a lack of head-to head data with these agents.
  - Linaclotide is administered twice daily and lubiprostone is administered once daily.[1-2]
  - Rifaximin is administered three times a day for 14 days. Other agents are administered twice daily.[3-5]
  - Linaclotide is contraindicated in pediatric patients <6 years of age.[1]
  - Alosetron and eluxadoline are contraindicated in patients with severe hepatic dysfunction (Child-Pugh class C).[3,4]

References

1. Linzess® [package insert]. Cambridge (MA): Ironwood Pharmaceuticals, Inc.; 2016 Apr.
2. Amitiza® [package insert]. Deerfield (IL): Takeda Pharmaceuticals America, Inc.; 2013 Apr.
3. Lotronex® [package insert]. San Diego (CA): Prometheus Laboratories, Inc.; 2016 Jan.
4. Viberzi® [package insert]. Parsippany (NJ): Actavis Pharma, Inc.; 2016 Jan.
5. Xifaxan® [package insert]. Bridgewater (NJ): Salix Pharmaceuticals; 2015 Nov.
6. Wald A. Clinical manifestations and diagnosis of irritable bowel syndrome in adults. In: Post T, ed. UpToDate. Waltham, MA: UpToDate; 2016. Available from: http://www.uptodate.com/ [cited 3 June 2016].
7. Wald A. Treatment of irritable bowel syndrome in adults. In: Post T, ed. UpToDate. Waltham, MA: UpToDate; 2016. Available from: http://www.uptodate.com/ [cited 3 June 2016].
8. Chey WD, Lembo AJ, Lavins BJ, Shiff SJ, Kurtz CB, Currie MG, et al. Linaclotide for irritable bowel syndrome with constipation: A 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. Am J Gastroenterol 2012; 107:1702-12.
9. Rao S, Lembo AJ, Shiff SJ, Lavins BJ, Currie MG, Jia XD, et al. A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. Am J Gastroenterol 2012; 107:1714-24.
10. Drossman DA, Chey WD, Johanson JF, Fass R, Scott C, Panas R, et al. Clinical trial: lubiprostone in patients with constipation-associated irritable bowel syndrome--results of two randomized, placebo-controlled studies. Aliment Pharmacol Ther. 2009 Feb 1;29(3):329-41. doi: 10.1111/j.1365-2036.2008.03881.x. Epub 2008 Nov 4.
11. Andresen V, Montori VM, Keller J, West C, Layer P, Camilleri M. Effects of 5-Hydroxytryptamine (Serotonin) Type 3 Antagonists on Symptoms Relief and Constipation in Nonconstipated Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Clinical Gastroenterology and Hepatology. 2008;6:545-55.
12. Cremonini F, Delgado-Aros S, Camilleri M. Efficacy of alosetron in irritable bowel syndrome: a meta-analysis of randomized controlled trials. Neurogastroenterol Motil. 2003;15:79-86.
13. Ford AC, Brandt LJ, Young C, Chey WD, Foxx-Orenstein AE, Moayyedi P. Efficacy of 5-HT3 Antagonists and 5-HT4 Agonists in Irritable Bowel Syndrome: Systematic Review and Meta-Analysis. Am J Gastroenterol. 2009;104:1831-43.
14. Viberzi® (eluxadoline) product dossier V3.1. 2015 Nov. 18. Actavis. Data on file.
15. Lembo AJ, Lacy BE, Zuckerman MJ, Schey R, Dove LS, Andrae DA, et al. Eluxadoline for irritable bowel syndrome with diarrhea. N Eng J Med. 2016 Jan 21; 374(3):242-253.
16. Pimentel M, Lembo A, Chey WD, Zakko S, Ringel Y, Yu J, et al. Rifaximin therapy for patients with irritable bowel syndrome without constipation. N Engl J Med. 2011 Jan 6;364(1):22-32. doi: 10.1056/NEJMoa1004409.
17. Weinberg DS, Smalley W, Heidelbaugh JJ, Sultan S. American Gastroenterological Association Institute: Guideline on the Pharmacological Management of Irritable Bowel Syndrome. Gastroenterol. 2014;147:1146-48.
18. Ford AC, Moayyedi P, Lacy BE, Lembo AJ, Saito YA, Schiller LR, et al. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. Am J Gastroenterol. 2014;109 (1):S2 – S26.
19. Quigley EM, Fried M, Gwee KA, Khalif I, Hungin P, Lindberg G, et al. World Gastroenterology Organisation Global Guidelines: Irritable Bowel Syndrome: a Global Perspective. Milwaukee (WI); 2015 Sep. Available from: http://www.worldgastroenterology.org/guidelines/global-guidelines/irritable-bowel-syndrome-ibs/irritable-bowel-syndrome-ibs-english.

Z. Cymbalta® (duloxetine)

Therapeutic Class: Sertonin-Norepinephrine Reuptake Inhibitor (SNRI)
Last Reviewed by the DUR Board: July 25, 2013

Cymbalta® is subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the Social Security Act and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

Approval will be given if the following criteria are met and documented. Recipients must meet at least one diagnosis listed below:

a. Diabetic Peripheral Neuropathy (DPN):

1. If an ICD code for Diabetes with Neurological Manifestations is documented on the prescription and transmitted on the claim; or

2. Completion of a prior authorization documenting a diagnosis of Diabetes with Neurological Manifestations.

b. Fibromyalgia:

1. If an ICD code for Fibromyalgia, Myalgia and Myositis unspecified is documented on the prescription and transmitted on the claim; or

2. Completion of a prior authorization documenting a diagnosis of Fibromyalgia and/or Myalgia and Myositis, unspecified.

c. Chronic Musculoskeletal Pain:

The recipient must meet one of the following:

1. The recipient has experienced an inadequate response or adverse event to at least two oral or topical non-steroidal anti-inflammatory drug (NSAIDS); or

2. The recipient has an allergy or contraindication to two NSAIDS.

d. Generalized Anxiety Disorder:

The recipient must meet the following:

1. The recipient has experienced an inadequate response or adverse event to at least two antidepressants from any of the following classes: selective

serotonin reuptake inhibitors, tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors or buspirone.

e. Major Depressive Disorder:

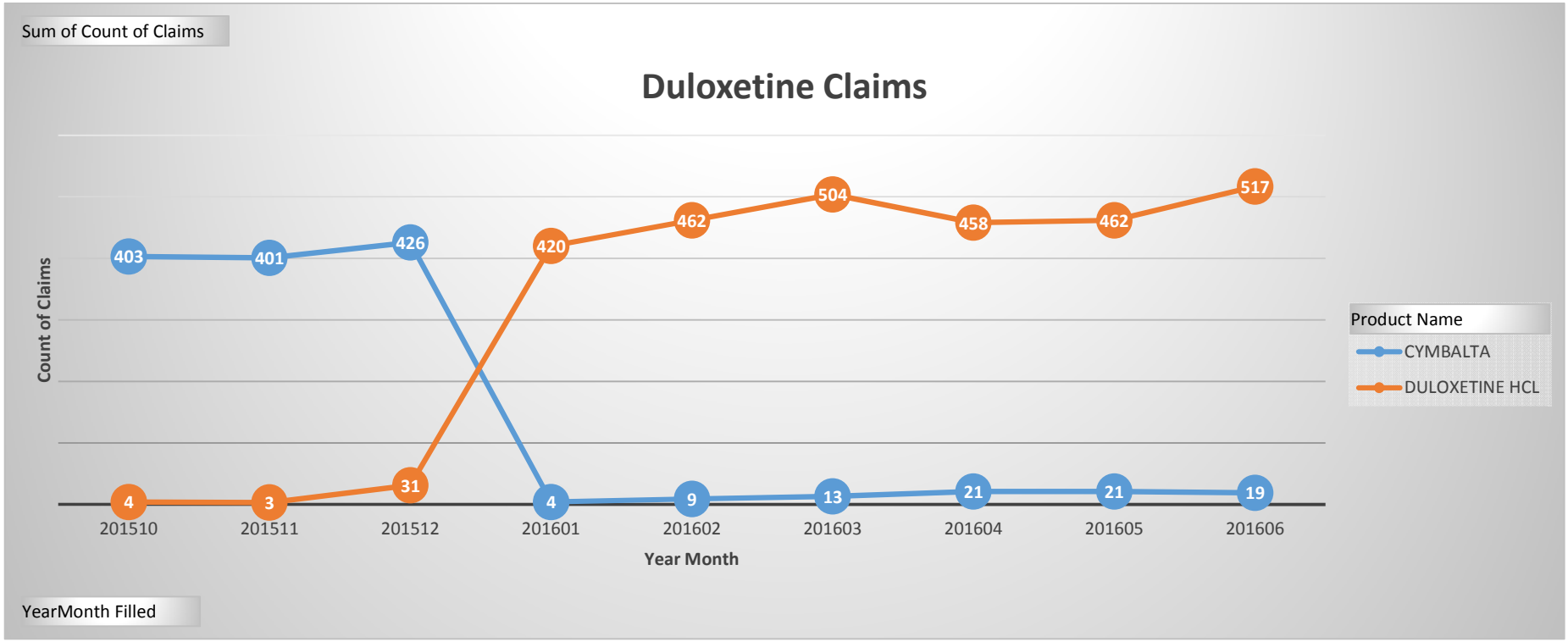
The recipient must meet the following:

1. The recipient has experienced an inadequate response, and/or adverse event and/or an allergy and/or contraindication to at least two antidepressants.

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


Sum of Count of Claims
Duloxetine Claims
Count of Claims
403
401
426
4
4
9
13
21
21
19
4
3
31
420
462
504
458
462
517
201510
201511
201512
201601
201602
201603
201604
201605
201606
Year Month
Product Name
CYMBALTA
DULOXETINE HCL
YearMonth Filled

Therapeutic Class Overview
Serotonin and Norepinephrine Reuptake Inhibitors

Overview/Summary:
The serotonin and norepinephrine reuptake inhibitors (SNRIs) are Food and Drug Administration (FDA)-approved to treat a variety of mental and nonpsychiatric disorders. FDA-approved indications vary by drug but may include anxiety disorders, depressive disorders, eating disorders (bulimia nervosa) and premenstrual dysphoric disorder. Some of the SNRIs are also approved to treat nonpsychiatric conditions such as chronic musculoskeletal pain, diabetic peripheral neuropathy, fibromyalgia, insomnia, moderate to severe vasomotor symptoms associated with menopause, nocturnal enuresis and tobacco abuse.[1-10] The American Hospital Formulary Service (AHFS) classifies the SNRIs as antidepressants. Altogether, the AHFS lists six different antidepressant subclasses with the other antidepressant classes being monoamine oxidase inhibitors (MAOIs), selective serotonin-reuptake inhibitors (SSRIs), serotonin modulators, tricyclic antidepressants (TCAs) and miscellaneous agents.[2]

The SNRIs include desvenlafaxine, desvenlafaxine succinate, duloxetine, levomilnacipran, milnacipran and venlafaxine. The exact mechanisms by which these agents exert their therapeutic effect is not fully understood. SNRIs block the presynaptic reuptake of two neurotransmitters, serotonin and norepinephrine, at their respective transporters in the central nervous system. By preventing the reuptake of serotonin and norepinephrine in the presynaptic cleft, there is an increased sustained level of these neurotransmitters to act on their specific receptors.[3-11]

The SNRIs have been shown to be efficacious when compared to placebo for their FDA indications and results of other clinical trials have generally not demonstrated one antidepressant to be significantly more effective than another. Specifically, venlafaxine and duloxetine have also been shown to be comparable to other antidepressants and to each other. Currently head to head trials in the class is limited.[12-109]

Table 1. Current Medications Available in the Therapeutic Class[1-2,5-13]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Desvenlafaxine (Khedezla®)	Treatment of major depressive disorder	Extended-release tablet: 50 mg 100 mg	-
Desvenlafaxine succinate (Pristiq®)	Treatment of major depressive disorder	Extended-release tablet: 25 mg 50 mg 100 mg	-
Duloxetine (Cymbalta®*, Irenka®*)	Management of chronic musculoskeletal pain, fibromyalgia, neuropathic pain associated with diabetic peripheral neuropathy, and for the treatment of generalized anxiety disorder, major depressive disorder, panic disorder with or without agoraphobia, and social anxiety disorder	Delayed-release capsule: 20 mg (Cymbalta®) 30 mg (Cymbalta®) 40 mg (Irenka®) 60 mg (Cymbalta®)	✔
Levomilnacipran (Fetzima®)	Treatment of major depressive disorder	Extended-release capsules: 20 mg 40 mg 80 mg 120 mg	-

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Milnacipran (Savella®)	Management of fibromyalgia	Tablet: 12.5 mg 25 mg 50 mg 100 mg	-
Venlafaxine* (Effexor XR ®*)	Treatment of generalized anxiety disorder, major depressive disorder, panic disorder with or without agoraphobia, and social anxiety disorder	Extended-release capsule (Effexor XR®): 37.5 mg 75 mg 150 mg Extended-release tablet: 37.5 mg 75 mg 150 mg 225 mg Tablet: 25 mg 37.5 mg 50 mg 75 mg 100 mg	✔

*Generic available in at least one dosage form or strength.

Evidence-based Medicine

- The results of clinical trials have generally not demonstrated one antidepressant to be significantly more effective than another. The majority of clinical studies support the conclusion that antidepressants are of equivalent efficacy when administered in comparable doses. The choice of an antidepressant is influenced by the patient's diagnosis, current medical history, past history of response, the potential for drug-drug interactions and the adverse events profile. Treatment failure to one antidepressant class or to any specific antidepressant within a class does not predict treatment failure to another antidepressant agent, either within or outside of the same drug class. The SNRIs have been shown to be efficacious when compared to placebo for their FDA indications. Venlafaxine and duloxetine have also been shown to be comparable to other antidepressants and to each other. Currently head to head trials in the class is limited.[12-109]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - National and international treatment guidelines for the treatment of depression state:[110-113]
    - Selecting an agent should be driven by anticipated side effects, tolerability, patient preference, and quantity and quality of available clinical data, and that the effectiveness of antidepressants is usually comparable within and between medication classes.
    - Medications that can be considered first-line therapy for most patients include SSRIs, SNRIs, mirtazapine, or bupropion, while MAOIs)should be reserved for patients who are unresponsive to other available medications. These guidelines do not recommend one SSRI, SNRI or MAOI over another.
  - Antidepressants are recommended as first-line treatment for GAD, with the following agents considered treatment options: SSRIs, SNRIs, and nonsedating TCAs.[114-116]

  - For the treatment of neuropathic pain, the SNRIs are recommended as initial therapy along with TCAs and anticonvulsants.[122-126]
- Other Key Facts:
  - All of the SNRI products have a Black Box Warning regarding the potential for antidepressants to increase suicidal thoughts in children and young adults.[3-11]
  - Duloxetine is the only agent FDA-approved for use in children, specifically for the diagnosis of general anxiety disorder.[5,6]
  - Generally, SNRIs are administered once-daily, however milnacipran and immediate release venlafaxine are administer twice a day.[3-11]
  - Generic products are available for duloxetine and both immediate- and extended-release formulations of venlafaxine.

References

1. Micromedex® Healthcare Series [database on the Internet]. Greenwood Village (CO): Thomson Micromedex; 2014 [cited 2014 Jan 25]. Available from: http://www.thomsonhc.com.
2. Selective Serotonin- and Norepinephrine-Reuptake Inhibitors 28:16.04.16. In: McEvoy GK, editor; American Hospital Formulary Service. AHFS Drug Information – 58th Ed. 2016 [monograph on the Internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2016 [cited 2016 Jun 6]. Available from: http://online.statref.com.
3. Pristiq® [prescribing information]. Indianapolis (IN): Lilly USA, LLC; 2015 Mar.
4. Khedezla® [prescribing information]. Wilmington (NC): Osmotica Pharmaceutical Corp; 2014 June.
5. Cymbalta® [prescribing information]. Indianapolis (IN): Lilly USA, LLC; 2015 Jun.
6. Irenka® [prescribing information]. Baltimore (MD): Lupin Pharma; 2015 May.
7. Fetzima® [package insert]. St. Louis, MO: Forest Laboratories, Inc.; 2014 July.
8. Savella® [package insert]. New York (NY): Forest Pharmaceuticals, Inc.; 2015 Jan.
9. Effexor XR® [prescribing information]. Philadelphia (PA): Wyeth Pharmaceuticals, Inc.; 2015 Aug.
10. Venlafaxine tablet [prescribing information]. Tampa (FL): TruPharma, LLC; 2016 Mar.
11. Venlafaxine extended release tablet [prescribing information]. Smyrna (GA): Upstate Pharma, LLC; 2015 Jun.
12. Ferguson J, Tourian KA, Manley AL, Padmanadhan SK, Nichols A. An evaluation of the efficacy, safety, and tolerability of desvenlafaxine in the long-term treatment of elderly outpatients with major depressive disorder. Prim Psychiatry. 2010;17(1):66-73.
13. Soares CN, Thase ME, Clayton A, Guico-Pabia CJ, Focht K, Jiang Q, et al. Open-label treatment with desvenlafaxine in postmenopausal women with major depressive disorder not responding to acute treatment with desvenlafaxine or escitalopram. CNS Drugs. 2011;25(3):227-38.
14. Dunlop BW, Reddy S, Yang L, Lubaczewski S, Focht K, Guico-Pabia CJ. Symptomatic and functional improvement in employed depressed patients. A double-blind clinical trial desvenlafaxine vs placebo. J Clin Psychopharmacol. 2011;31:569-76.
15. Liebowitz MR, Yeung PP, Entsuah R. A randomized, double-blind, placebo-controlled trial of desvenlafaxine succinate in adult outpatients with major depressive disorder. J Clin Psychiatry. 2007;68:1663-72.
16. Boyer P, Montgomery S, Lepola U, Germain JM, Brisard C, Ganguly R, et al. Efficacy, safety, and tolerability of fixed-dose desvenlafaxine 50 and 100 mg/day for major depressive disorder in a placebo-controlled trial. Int Clin Psychopharmacol. 2008;23:243-53.
17. Liebowitz MR, Manley AL, Padmanabhan SK, Ganguly R, Tummala R, Tourian KA. Efficacy, safety and tolerability of desvenlafaxine 50 and 100 mg/day in outpatients with major depressive disorder (abstract). Curr Med Res Opin. 2008 Jul;24(7):1877-90.
18. Kornstein SG, Jiang Q, Reddy S, Musgnung JJ, Guico-Pabia CJ. Short-term efficacy and safety of desvenlafaxine in a randomized, placebo-controlled study of perimenopausal and postmenopausal women with major depressive disorder. J Clin Psychiatry. 2010;71(8):1088-96.
19. Feiger AD, Tourian KA, Rosas GR, Padmanabhan SK. A placebo-controlled study evaluating the efficacy and safety of flexible-dose desvenlafaxine treatment in outpatients with major depressive disorder. CNS Spectr. 2009;14(1):41-50.
20. Septien-Velez L, Pitrosky B, Padmanabhan SK, Germain JM, Tourian KA. A randomized, double-blind, placebo-controlled trial of desvenlafaxine succinate in the treatment of major depressive disorder. Int Clin Psychopharmacology. 2007;22:338-47.
21. Rickels K, Montgomery SA, Tourian KA, Guelfi JD, Pitrosky B, Padmanabhan SK, et al. Desvenlafaxine for the prevention of relapse in major depressive disorder. Results of a randomized trial. J Clin Psychopharmacol. 2010;30:18-24.
22. Demartinis NA, Yeung PP, Entsuah R, Manley AL. A double-blind, placebo-controlled study of the efficacy and safety of desvenlafaxine succinate in the treatment of major depressive disorder. J Clin Psychiatry. 2007;69:677-88.
23. Clayton AH, Kornstein SG, Rosas G, Guico-Pabia C, Tourian KA. An integrated analysis of the safety and tolerability of desvenlafaxine compared to placebo in the treatment of major depressive disorder (abstract). CNS Spectr. 2009 Apr;14(4):183-95.
24. Thase ME, Kornstein SG, Germain JM, Jiang Q, Guico-Pabia C, Ninan PT. An integrated analysis of the efficacy of desvenlafaxine compared to placebo in patients with major depressive disorder. CNS Spectr. 2009;14:144-54.
25. Tourian K, Wang Y, Ii Y. A 10-month, open-label evaluation of desvenlafaxine in Japanese outpatients with major depressive disorder. International Clinical Psychopharmacology. 2013 Jul;28(4):206-13.
26. Rosenthal JZ, Boyer P, Vialet C, Hwang E, Tourian KA. Efficacy and safety of desvenlafaxine 50 mg/d for prevention of relapse in major depressive disorder: a randomized controlled trial. Journal of Clinical Psychiatry. 2013 Feb;74(2):158-66.

27. Clayton AH, Reddy S, Focht K, Musgnung J, Fayyad R. An evaluation of sexual functioning in employed outpatients with major depressive disorder treated with desvenlafaxine 50 mg or placebo. Journal of Sexual Medicine. 2013 Mar;10(3):768-76.
28. Gaynor PJ, Gopal M, Zheng W, Martinez JM, Robinson MJ, Hann D, et al. Duloxetine vs placebo in the treatment of major depressive disorder and associated painful physical symptoms: a replication study. Curr Med Res Opin. 2011;27:1859-67.
29. Gaynor PJ, Gopal M, Zheng W, Martinez JM, Robinson MJ, Marangell LB. A randomized placebo-controlled trial of duloxetine in patients with major depressive disorder and associated painful physical symptoms. Curr Med Res Opin. 2011;27:1849-58.
30. Acharya N, Rosen AS, Polzer JP, D'Souza DN, Perahia DG, Cavazzoni PA, Baldessarini RJ. Duloxetine: meta-analyses of suicidal behaviors and ideation in clinical trials for major depressive disorder J Clin Psychopharmacol. 2006;26(6):587-94.
31. Mancini M, Sheehan DV, Demyttenaere K, Amore M, Deberdt W, Quail D, Sagman D. Evaluation of the effect of duloxetine treatment on functioning as measured by the Sheehan disability scale: pooled analysis of data from six randomized, double-blind, placebo-controlled clinical studies. International Clinical Psychopharmacology. 2012 Nov;27(6):298-309.
32. Asnis GM, Bose A, Gommoll CP, Chen C, Greenberg WM. Efficacy and safety of levomilnacipran sustained release 40, 80, or 120 mg in major depressive disorder: A phase 3, randomized, double-blind, placebo-controlled study. Journal of Clinical Psychiatry. 2013 Mar;74(3):242-8.
33. Bakish D, Bose A, Gommoll C, Chen C, Nunez R, Greenberg WM, Liebowitz M, Khan A. Levomilnacipran ER 40 and 80 mg in patients with major depressive disorder: a phase III, randomized, double-blind, fixed-dose, placebo-controlled study. Journal of Psychiatry & Neuroscience. 2013 Oct 22 [Epub ahead of print]; 38(6):1-10. PMID: 24144196.
34. Sambunaris A, Bose A, Gommoll CP, Chen C, Greenberg WM, Sheehan DV. A phase III, double-blind, placebo-controlled, flexible-dose study of levomilnacipran extended-release in patients with major depressive disorder. Journal of Clinical Psychopharmacology. 2013 Nov 27 [Epub ahead of print]; 34(1):1-10. PMID: 24172209
35. Montgomery, Stuart A, Mansuy, Lucilla, Ruth, Adam, Bose, Anjana, Li, Hua, Li, Dayong. Efficacy and safety of levomilnacipran sustained release in moderate to severe major depressive disorder: a randomized, double-blind, placebo-controlled, proof-of-concept study. Journal of Clinical Psychiatry. 2013 Apr;74(4):363-9.
36. Vis PM, van Baardewijk M, Einarson TR. Duloxetine and venlafaxine-XR in the treatment of major depressive disorder: a meta-analysis of randomized clinical trials. Ann Pharmacother. 2005;39(11):1798-807.
37. Perahia DG, Pritchett YL, Kajdasz DK, Bauer M, Jain R, Russell JM, et al. A randomized, double-blind comparison of duloxetine and venlafaxine in the treatment of patients with major depressive disorder. J Psychiatr Res. 2008;42:22-34.
38. Van Baardewijk M, Vis PMJ, Einarson TR. Cost effectiveness of duloxetine compared to venlafaxine-XR in the treatment of major depressive disorder. Curr Med Res Opin. 2005;21(8):1271-9.
39. Soares CN, Thase ME, Clayton A, et al. Desvenlafaxine and escitalopram for the treatment of postmenopausal women with major depressive disorder. Menopause 2010;17:700-11.
40. Nierenberg AA, Greist JH, Mallinckrodt CH, Prakash A, Sambunaris A, Tollefson GD, Wohlreich MM. Duloxetine vs escitalopram and placebo in the treatment of patients with major depressive disorder: onset of antidepressant action, a non-inferiority study. Curr Med Res Opin. 2007 Feb;23(2):401-16.
41. Pigott TA, Prakash A, Arnold LM, et al. Duloxetine vs escitalopram and placebo: an 8-month, double-blind trial in patients with major depressive disorder. Curr Med Res Opin 2007;23:1303-18.
42. Wade A, Gembert K, Florea I, et al. A comparative study of the efficacy of acute and continuation treatment with escitalopram vs duloxetine in patients with major depressive disorder. Curr Med Res Opin 2007;23:1605-14.
43. Khan A, Bose A, Alexopoulos GS, Gommoll C, Li D, Gandhi C. Double-blind comparison of escitalopram and duloxetine in the acute treatment of major depressive disorder. Clin Drug Investig. 2007;27(7):481-92.
44. Goldstein DJ, Mallinckrodt C, Lu Y, Demitrack MA. Duloxetine in the treatment of major depressive disorder: a double-blind clinical trial (abstract). J Clin Psychiatry. 2002 Mar;63(3):225-31.
45. Detke MJ, Wiltse CG, Mallinckrodt CH, McNamara RK, Demitrack MA, Bitter I. Duloxetine in the acute and long-term treatment of major depressive disorder: a placebo- and paroxetine-controlled trial. Eur Neuropsychopharmacol. 2004;14:457-70.
46. Goldstein DJ, Lu Y, Detke MJ, Wiltse C, Mallinckrodt C, Demitrack MA. Duloxetine in the treatment of depression a double-blind placebo-controlled comparison with paroxetine. J Clin Psychopharmacol. 2004;24:389-99.
47. Perahia DG, Wang F, Mallinckrodt CH, Walker DJ, Detke MJ. Duloxetine in the treatment of major depressive disorder: a placebo- and paroxetine-controlled trial. Eur Psychiatry. 2006;21(6):367-78.
48. Rosso G, Rigardetto S, Bogetto F, Maina G. A randomized, single-blind, comparison of duloxetine with bupropion in the treatment of SSRI-resistant major depression. J Affect Disord. 2012;136:172-6.
49. Katona C, Hansen T, Olsen CK. A randomized, double-blind, placebo-controlled, duloxetine-referenced, fixed-dose study comparing the efficacy and safety of Lu AA21004 in elderly patients with major depressive disorder. 2012 July 1;27(4):215-23.
50. Mahableshwarkar AR, Jacobsen PL, Chen Y. A randomized, double-blind trial of 2.5 mg and 5 mg vortioxetine (Lu AA21004) vs placebo for 8 weeks in adults with major depressive disorder. Current Medical Research & Opinion. 2013 March 29(3):217-26.
51. Lenox-Smith AJ, Jiang Q. Venlafaxine extended release vs citalopram in patients with depression unresponsive to a selective serotonin reuptake inhibitor. Int Clin Psychopharmacol. 2008;23:113-9.
52. Montgomery SA, Huusom AK, Bothmer J. A randomised study comparing escitalopram with venlafaxine XR in primary care patients with major depressive disorder. Neuropsychobiology. 2004;50(1):57-64.
53. Bielski RJ, Ventura D, Chang C. A double-blind comparison of escitalopram and venlafaxine extended-release in the treatment of major depressive disorder. J Clin Psychiatry. 2004;65:1190-6.
54. Nemeroff CB, Michael E. A double-blind, placebo-controlled comparison of venlafaxine and fluoxetine treatment in depressed outpatients. J Psychiatr Res. 2007;41:351-9.
55. Rudolph RL, Feiger AD. A double-blind, randomized, placebo-controlled trial of once-daily venlafaxine extended release (XR) and fluoxetine for the treatment of depression. J Affective Disorders. 1999:56:171-81.
56. Mazeh D, Shahal B, Aviv A, et al. A randomized, single-blind, comparison of venlafaxine with paroxetine in elderly patients suffering from resistant depression. Int Clin Psychopharmacol. 2007;22:371-5.

57. Richard IH, McDermott MP, Kurlan R, Lyness JM, Como PG, Pearson N, et al. A randomized, double-blind, placebo-controlled trial of antidepressants in Parkinson disease. Neurology. 2012;78:1229-36.
58. Hewett K, Chrzanowski W, Schmitz M, Savela A, Milanova V, Gee M, et al. Eight-week, placebo-controlled, double-blind comparison of the antidepressant efficacy and tolerability of bupropion XR and venlafaxine XR. J Psychopharmacol. 2009;23:531-8.
59. Benkert O, Grunder G, Wetzel H, et al: A randomized, double-blind comparison of a rapidly escalating dose of venlafaxine and imipramine in inpatients with major depression and melancholia. J Psychiatr Res. 1996:30(6):441-51.
60. Guelfi D, Ansseau M, Timmerman L, et al. Mirtazapine vs venlafaxine in hospitalized severely depressed patients with melancholic features. J Clin Psychopharmacol. 2001;21:425-31.
61. Kok RM, Nolen WA, Heeren TJ. Venlafaxine vs nortriptyline in the treatment of elderly depressed inpatients: a randomised, double-blind, controlled trial. Int J Geriatr Psychiatry. 2007;22:1247-54.
62. Rush AJ, Trivedi MH, Stewart JW, Nierenberg AA, Fava M, Kurian BT, et al. Combining medications to enhance depression outcomes (CO-MED): acute and long-term outcomes of a single-blind randomized study. Am J Psychiatry. 2011;168:689-701.
63. Morris DW, Budhwar N, Husain M, Wisniewski SR, Kurian BT, Luther JF, et al. Depression treatment in patients with general medical conditions: results from the CO-MED trial. Ann Fam Med. 2012;10:23-33.
64. Kerber KB, Wisniewksi SR, Luther JF, Leuchter AF, D'Empaire I, Trivedi MH, et al. Effects of heart disease on depression treatment: results from the COMED study. General Hospital Psychiatry. 2012;34:24-34.
65. Martinez JM, Katon W, Greist JH, et al. A pragmatic 12-week, randomized trial of duloxetine vs generic selective serotonin-reuptake inhibitors in the treatment of adult outpatients in a moderate-to-severe depressive episode. Int Clin Psychopharmacol. 2012;27:17-26.
66. Cipriani A, Brambilla P, Furukawa T, Geddes J, Gregis M, Hotopf M, et al. Fluoxetine vs other types of pharmacotherapy for depression. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD004185.
67. de Silva VA, Hanwella R. Efficacy and tolerability of venlafaxine vs specific serotonin reuptake inhibitors in treatment of major depressive disorder: a meta-analysis of published studies. International Clinical Psychopharmacology. 2012 Ja;27(1):8-16.
68. Walsh BT, Seidman SN, Sysko R, et al. Placebo response in studies of major depression: variable, substantial, and growing. JAMA. 2002;287:1840-7.
69. Geddes JR, Carney SM, Davies C, et al. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. Lancet. 2003;361:653-61.
70. Cipriani A, Furukawa TA, Salanti G, Geddes JR, Higgins JP, Churchill R, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. Lancet. 2009;373:746-58.
71. Mease PJ, Russell IJ, Kajdasz DK, Wiltse CG, Detke MJ, Wohlreich MM, et al. Long-term safety, tolerability, and efficacy of duloxetine in the treatment of fibromyalgia. Semin Arthritis Rheum. 2010;39:454-64.
72. Russell IJ, Mease PJ, Smith TR, Kajdasz DK, Wohlreich MM, Detke MJ, et al. Efficacy and safety of duloxetine for treatment of fibromyalgia in patients with or without major depressive disorder: Results from a six-month, randomized, double-blind, placebo-controlled, fixed-dose trial. Pain. 2008;136:432-44.
73. Arnold LM, Hudson JI, Wang F, Wohlreich MM, Prakash A, Kajdasz DK, et al. Comparisons of the efficacy and safety of duloxetine for the treatment of fibromyalgia in patients with vs without major depressive disorder. Clin J Pain. 2009;25:461-8.
74. Arnold LM, Zhang S, Pangallo BA. Efficacy and safety of duloxetine 30 mg/day in patients with fibromyalgia: a randomized, double-blind, placebo-controlled study. Clinical Journal of Pain. 2012 Nov-Dec;28(9):775-81.
75. Hauser W, Urrutia G, Tort S, Uceyler N, Walitt B. Serotonin and noradrenaline reuptake inhibitors (SNRIs) for fibromyalgia syndrome. Cochrane Database Syst Rev. 2013 Jan 31;1:CD010292.
76. Clauw DJ, Mease P, Palmer RH, Gendreau RM, Wang Y. Milnacipran for the treatment of fibromyalgia in adults: a 15-week, multicenter, randomized, double-blind, placebo-controlled, multiple-dose clinical trial. Clinical Therapeutics. 2008;30(11):1988-2004.
77. Mease PJ, Clauw DJ, Gendreau RM, Rao SG, Kranzler J, Chen W, et al. The efficacy and safety of milnacipran for treatment of fibromyalgia: a randomized, double-blind, placebo-controlled trial. J Rheumatol. 2009; 36:398-409.
78. Vitton O, Gendreau M, Gendreau J, Kranzler J, Rao SG. A double-blind placebo-controlled trial of milnacipran in the treatment of fibromyalgia. Hum Psychopharmacol Clin Exp. 2004;19:S27-S35.
79. Hauser W, Petzke F, Sommer C. Comparative efficacy and harms of duloxetine, milnacipran, and pregbabalin in fibromyalgia syndrome (abstract). J Pain. 2010 Jun;11(6):505-21.
80. Rynn M, Russell J, Erickson J, Detke MJ, Ball S, Dinkel J, et al. Efficacy and safety of duloxetine in the treatment of generalized anxiety disorder: a flexible-dose, progressive-titration, placebo-controlled trial. Depression and Anxiety. 2008;25:182-9.
81. Koponen H, Allgulander G, Erickson J, Dunayevich E, Pritchett Y, Detke MJ, et al. Efficacy of duloxetine for the treatment of generalized anxiety disorder: implications for primary care physicians. Prim Care Companion J Clin Psychiatry. 2007;9:100-7.
82. Davidson JRT, Wittchen HU, Llorca PM, Erickson J, Detke M, Ball SG, et al. Duloxetine treatment for relapse prevention in adults with generalized anxiety disorder: a double-blind placebo-controlled trial. Eur Neuropschopharmacol. 2008;18:673-81.
83. Hartford J, Kornstein S, Liebowitz M, Pigott T, Russell J, Detke M, et al. Duloxetine as an SNRI treatment for generalized anxiety disorder: results from a placebo and active-controlled trial. Int Clin Psychopharmacol. 2007;22:167-74.
84. Nicolini H, Bakish D, Duenas H, Spann M, Erickson J, Hallberg C, et al. Improvement of psychic and somatic symptoms in adult patients with generalized anxiety disorder: examination from a duloxetine, venlafaxine extended-release and placebo-controlled trial. Psychol Med. 2009;39:267-76.
85. Bose A, Korotzer A, Gommoll C, et al. Randomized placebo-controlled trial of escitalopram and venlafaxine XR in the treatment of generalized anxiety disorder. Depress Anxiety 2008;25:854-61.
86. Schmitt R, Gazalle FK, Lima MS, Cunha A, Souza J, Kapczinski F. The efficacy of antidepressants for generalized anxiety disorder: a systematic review and meta-analysis. Rev Bras Psiquiatr. 2005 Mar;27(1):18-24.
87. Wernicke J, Lledo A, Raskin J, Kajdasz DK, Wang F. An evaluation of the cardiovascular safety profile of duloxetine. Drug Safety. 2007;30(5):437-55.

88. Skljarevski V, Zhang S, Chappell AS, Walker DJ, Murray I, Backonja M. Maintenance of effect of duloxetine in patients with chronic low back pain: a 41-week uncontrolled, dose-blinded study. Pain Med. 2010;11:648-57.
89. Skljarevski V, Desaiah D, Liu-Seifert H, Zhang Q, Chappell AS, Detke MJ, et al. Efficacy and safety of duloxetine in patients with chronic low back pain. Spine. 2010;35:E578-85.
90. Chappell AS, Ossanna MJ, Liu-Seifert H, Iyengar S, Skljarevski V, Li LC, et al. Duloxetine, a centrally acting analgesic, in the treatment of patients with osteoarthritis knee pain: a 13-week, randomized, placebo-controlled trial. Pain. 2009;146:253-60.
91. Chappell AS, Desaiah D, Liu-Seifert H, Zhang S, Skljarevski V, Belenkov Y, et al. A double-blind, randomized, placebo-controlled study of the efficacy and safety of duloxetine for the treatment of chronic pain due to osteoarthritis of the knee. Pain Pract. 2010;11:33-41.
92. Skljarevski V, Zhang S, Desaiah D, Alaka KJ, Palaciaos S, Miazgowski T, et al. Duloxetine vs placebo in patients with chronic low back pain: a 12-week, fixed-dose, randomized, double-blind trial. J Pain. 2010;11:1282-90.
93. Skljarevski V, Ossanna M, Liu-Seifert H, Zhang Q, Chappell A, Iyengar S, et al. A double-blind, randomized trial of duloxetine vs placebo in the management of chronic low back pain. Eur J Neurol. 2009;16:1041-8.
94. Frakes EP, Risser RC, Ball TD, Hochberg MC, Wohlreich MM. Duloxetine added to oral nonsteroidal anti-inflammatory drugs for treatment of knee pain due to osteoarthritis: results of a randomized, double-blind, placebo-controlled trial. Curr Med Res Opin. 2011;27:2361-72.
95. Mazza M, Mazza O, Pazzaglia C, et al. Escitalopram 20 mg vs duloxetine 60 mg for the treatment of chronic low back pain. Expert Opin Pharmacother. 2010;11:1049-52.
96. Yan G, Guang N, Wei-ping J, Zhi-guang Z, Zhang-rong X, Zhi-min L, et al. Duloxetine vs placebo in the treatment of patients with diabetic neuropathic pain in China. Chin Med J. 2010;123(22):3184-92.
97. Armstrong DG, Chappell AS, Le TK, Kajdasz DK, Backonja M, D'Souza DN, et al. Duloxetine for the management of diabetic peripheral neuropathic pain: evaluation of functional outcomes. Pain Med. 2007 Jul-Aug;8(5):410-8.
98. Kajdasz DK, Iyengar S, Desaiah D, Backonja MM, Farrar JT, Fishbain DA, et al. Duloxetine for the management of diabetic peripheral neuropathic pain: evidence-based findings from post hoc analysis of three multicenter, randomized, double-blind, placebo-controlled, parallel-group studies. Clin Ther. 2007;29:2536-46.
99. Wernicke J, Lledo A, Raskin J, Kajdasz DK, Wang F. An evaluation of the cardiovascular safety profile of duloxetine. Drug Safety. 2007;30(5):437-55.
100. Lunn MPT, Hughes RAC, Wiffen PJ. Duloxetine for treating painful neuropathy or chronic pain. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.CD007115.
101. Kaur H, Hota D, Bhansali A, et al. A comparative evaluation of amitriptyline and duloxetine in painful diabetic neuropathy: a randomized, double-blind, cross-over clinical trial. Diabetes Care. 2011;34:818-22.
102. Wernicke JF, Wang F, Pritchett YL, Smith TR, Raskin J, D'Souza DN, et al. An open-label 52-week clinical extension comparing duloxetine with routine care in patients with diabetic peripheral neuropathic pain. Pain Medicine. 2007;8(6):503-13.
103. Raskin J, Smith TR, Wong K, Pritchett YL, D'Souza DN, Iyengar S, et al. Duloxetine vs routine care in the long-term management of diabetic peripheral neuropathic pain. J Palliative Med. 2006;9(1):29-40.
104. Boyle J, Eriksson ME, Gribble L, Gouni R, Johnsen S, Coppini DV, et al. Randomized, placebo-controlled comparison of amitriptyline, duloxetine, and pregabalin in patients with chronic diabetic peripheral neuropathic pain: impact on pain, polysomnographic sleep, daytime functioning, and quality of life. Diabetes Care. 2012 Dec;35(12):2451-8.
105. Tanenberg RJ, Irving GA, Risser RC, Ahl J, Robinson MJ, Skljarevski V, et al. Duloxetine, pregabalin, and duloxetine plus gabapentin for diabetic peripheral neuropathic pain management in patients with inadequate pain response to gabapentin: an open-label, randomized, noninferiority comparison. Mayo Clin Proc. 2011;86(7):615-24.
106. Quilici S, Chancellor J, Lothgren M, Simon D, Said G, Le TK, et al. Meta-analysis of duloxetine vs pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain. BMC Neurology. 2009;9:6-19.
107. Ney JP, Devine EB, Watanabe JH, Sullivan SD. Comparative efficacy of oral pharmaceuticals for the treatment of chronic peripheral neuropathic pain: meta-analysis and indirect treatment comparisons. Pain Med. 2013 May;14(5):706-19.
108. Denys D, van der Wee N, van Megen HJ, Westenberg HG. A double blind comparison of venlafaxine and paroxetine in obsessive-compulsive disorder. J Clin Psychopharmacol. 2003;23:568-75.
109. Pollack M, Mangano R, Entsuah R, et al. A randomized controlled trial of venlafaxine ER and paroxetine in the treatment of outpatients with panic disorder. Psychopharmacology (Berl). 2007;194:233-42
110. American Psychiatric Association (APA). Practice Guideline for the Treatment of Patients With Major Depressive Disorder, Third Edition [guideline on the internet]. Arlington, Virginia: American Psychiatric Association; 2010 [cited 2014 Jan 25]. Available from: http://psychiatryonline.org/content.aspx?bookid=28&sectionid=1667485.
111. National Institute for Health and Care Excellence (NICE). Depression in adults: The treatment and management of depression in adults [guideline on the internet]. London, England, UK: National Institute for Health and Care Excellence; 2009 [cited 2014 Jan 25]. Available from: http://publications.nice.org.uk/depression-in-adults-cg90.
112. Qaseem A, Snow V, Denberg T, Forciea MA, Owens DK, Clinical Efficacy Assessment Subcommittee of American College of Physicians. Using second-generation antidepressants to treat depressive disorders: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2008;18;149:725-33.
113. Birmaher B, Brent D, AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with depressive disorders. American Academy of Child and Adolescent Psychiatry (AACAP). J Am Acad Child Adolesc Psychiatry. 2007;46:1503-26.
114. National Institute for Clinical Excellence. Generalized anxiety disorder and panic disorder (with or without agoraphobia) in adults. National Institute for Clinical Excellence; 2011 Jan [cited 2014 Jan]. Available at: http://www.nice.org.uk/nicemedia/live/13314/52599/52599.pdf.
115. Stein M, Goin M, Pollack M, Roy-Byrne P, Sareen J, Simon NM, et al. Practice guideline for the treatment of patients with panic disorder, second edition. American Psychiatric Association; 2009 [cited 2014 Jan]. Available at: http://psychiatryonline.org/data/Books/prac/PanicDisorder_2e_PracticeGuideline.pdf.

116. Connolly S, Bernstein G; Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with anxiety disorders. American Academy of Child and Adolescent Psychiatry. J Am Acad Child Adolesc Psychiatry. 2007;46(2):267-83.
117. Chou R, Qaseem A, Snow V, Casey D, Cross JT Jr, Shekelle P, 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 Intern Med. 2007;147:478-91.
118. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, Towheed T, Welch V, Wells G, Tugwell P; 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.
119. American Academy of Orthopedic Surgeons: Clinical practice guideline on the treatment of osteoarthritis of the knee (non-arthroplasty). Rosemont (IL): 2013 [Guideline on the internet] [cited 2014 Jant] Available from: http://www.aaos.org/research/guidelines/OAKguideline.pdf.
120. Carville SF, Arendt-Nielsen S, Bliddal H, Blotman F, Branco JC, Buskila D, et al. EULAR evidence-based recommendations for the management of fibromyalgia syndrome. Ann Rheum Dis. 2008;67:536-41.
121. Buckhardt C, Goldenberg D, Crofford L, et al. Guideline for the management of fibromyalgia syndrome pain in adults and children. American Pain Society (APS); 2005 [cited 2014 Jant]. Available at: http://www.ampainsoc.org/pub/fibromyalgia.htmI.
122. Attal N, Cruccu G, Baron R, Haanpaa M, Hansson P, Jensen TS, et al. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. Eur J Neurol. 2010 Sep;17(9):1113-e88.
123. Bril V, England J, Franklin GM, Backonja M, Cohen J, Del Toro D, 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.
124. Handelsman Y, Mechanick JI, Blonde L, Grunberger G, Bloomgarden ZT, Bray GA, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for developing a diabetes mellitus comprehensive care plan. Endocr Pract. 2011 Mar-Apr;17 Suppl 2:1-53.
125. Boulton AJ, Vinkik AL, Arezzo JC, Bril V, Feldman EL, Freeman R, et al. Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care. 2005;28(4):956-62.
126. Dubinsky RM, Kabbani H, El-Chami, Boutwell C, Ali H; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: treatment of postherpetic neuralgia: an evidence-based report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2004;63:959.

P. Xolair® (Omalizumab)

Therapeutic Class: Respiratory Monoclonal Antibody Agents
Last Reviewed by the DUR Board: April 23, 2015

Xolair® (Omalizumab) is subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the Social Security Act and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

Approval will be given if the following criteria are met and documented: Recipients must meet at least one condition (a. or b.) listed below:

a. The recipient must have a diagnosis of moderate to severe persistent asthma; and

The recipient must meet all of the following criteria:

1. The recipient must be age 12 years or older; and

2. The recipient must have tried and failed, or have a contraindication to inhaled oral corticosteroids; and

3. The recipient must have tried and failed, or have a contraindication to an oral second generation antihistamine; and

4. The recipient must have tried and failed, or have a contraindication to a leukotriene receptor antagonist; and

5. The prescriber must be either a pulmonologist or allergist/immunologist; and

6. The recipient must have a history of a positive skin test or Radioallergosorbent (RAST) test to a perennial aeroallergen; and

7. The recipient must have had a pretreatment serum total Immunoglobulin E (IgE) level; and

8. The recipient's current weight must be recorded; and

9. The requested dose is appropriate for the recipient’s pre-treatment serum IgE and body weight.

b. The recipient has a diagnosis of chronic idiopathic urticaria (CIL), and

The recipient must meet all of the following criteria:

1. The recipient is age 12 years or older; and

2. The recipient must have tried and failed, or have a contraindication to two oral second generation antihistamines; and

3. The recipient must have tried and failed, or have a contraindication to an oral second generation antihistamine in combination with a leukotriene receptor antagonist; and

4. The prescriber must be either an allergist/immunologist, dermatologist or a rheumatologist.

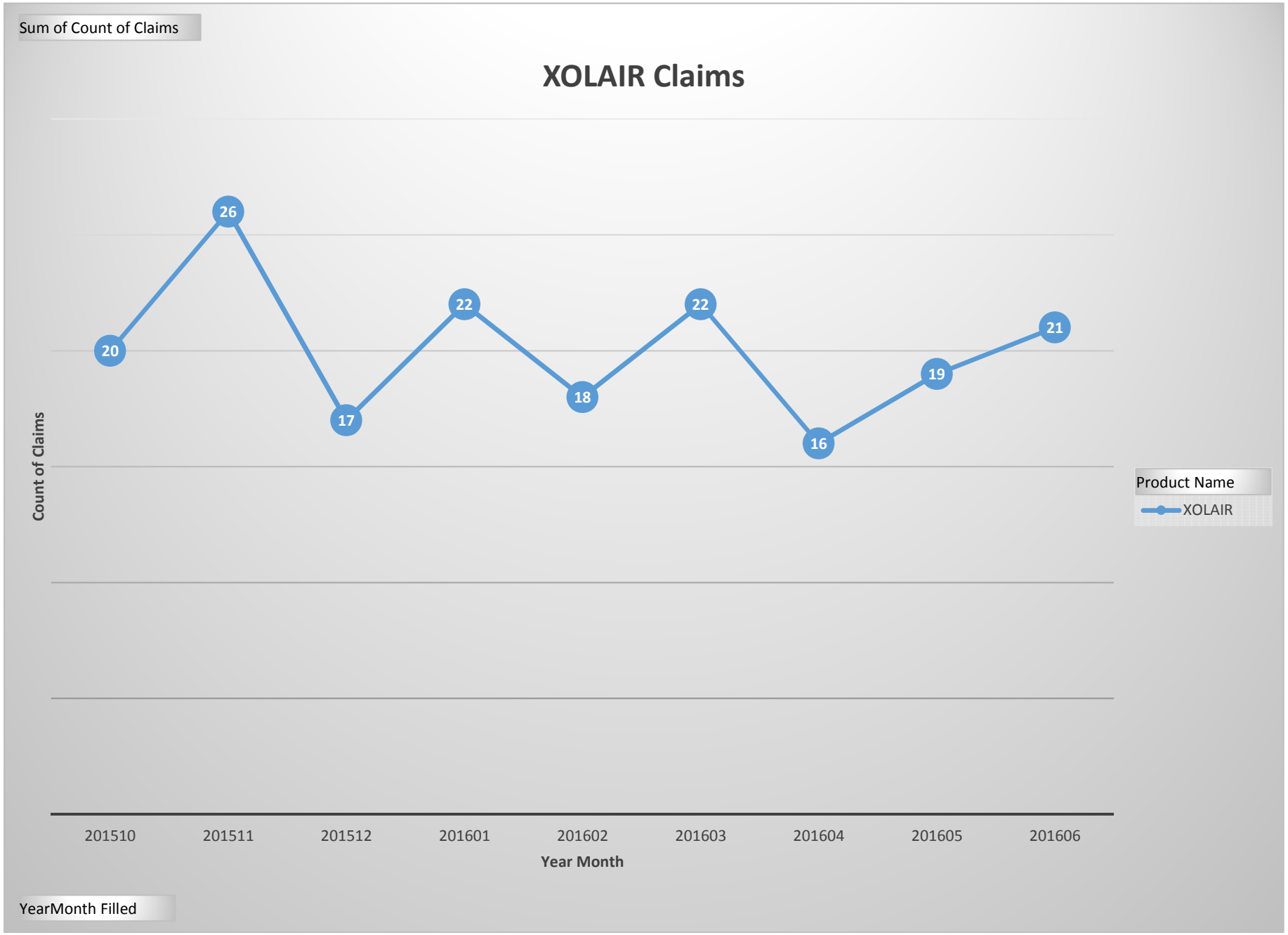
2. Prior Authorization Guidelines

a. Prior Authorization approval will be for 12 months.

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

Table 1: Dosing for Xolair® (omalizumab)*

Pre-treatment Serum IgE (IU/mL)	Body Weight (kg)			
	30-60	**>60-70**	**>70-90**	**>90-150**
≥30-100	150 mg	150 mg	150 mg	300 mg
>100-200	300 mg	300 mg	300 mg	225 mg
>200-300	300 mg	225 mg	225 mg	300 mg
>300-400	225 mg	225 mg	300 mg	
>400-500	300 mg	300 mg	375 mg	
>500-600	300 mg	375 mg		
>600-700	375 mg	**DO NOT DOSE**		
Every 2 Weeks Dosing				
Every 4 Weeks Dosing				


Sum of Count of Claims
XOLAIR Claims
Count of Claims
26
20
17
22
18
22
16
19
21
201510
201511
201512
201601
201602
201603
201604
201605
201606
Year Month
Product Name
XOLAIR
YearMonth Filled

DIVISION OF HEALTH CARE FINANCING AND POLICY
NEVADA MEDICAID
DRUG USE REVIEW (DUR) BOARD
PROPOSED PRIOR AUTHORIZATION CRITERIA

Therapeutic Class: Antiasthmatic Monoclonal Antibodies

Antiasthmatic monoclonal antibodies are subject to prior authorization and quantity limitations based on the Application of Standards in Section 1927 of the Social Security Act and/or approved by the DUR Board. Refer to the Nevada Medicaid and Check Up Pharmacy Manual for specific quantity limits.

1. Coverage and Limitations

Xolair® (Omalizumab)

A. The recipient will not use the requested antiasthmatic monoclonal antibody in combination with other antiasthmatic monoclonal antibodies

B. The following criteria must be met for a diagnosis of moderate to severe persistent asthma:
   1. The recipient must be age 12 years or older;
      AND
   2. The recipient must have a history of a positive skin test or Radioallergosorbent (RAST) test to a perennial aeroallergen;
      AND
   3. The prescriber must be either a pulmonologist or allergist/immunologist;
      AND
   4. The recipient must have ~~tried and failed or have a contraindication~~ had an inadequate response, adverse reaction or contraindication to inhaled oral corticosteroids;
      AND
   5. The recipient must have ~~tried and failed or have a contraindication~~ had an inadequate response, adverse reaction or contraindication to an oral second generation antihistamine;
      AND
   6. The recipient must have ~~tried and failed or have a contraindication~~ had an inadequate response, adverse reaction or contraindication to a leukotriene receptor antagonist;
      AND
   7. The recipient must have had a pretreatment serum total Immunoglobulin E (IgE) level between 30 IU/mL and 700 IU/mL;
      AND
   8. The recipient's current weight must be recorded;
      AND
   9. The requested dose is appropriate for the recipient's pre-treatment serum IgE and body weight (see Table 1 below).

C. The following criteria must be met for a diagnosis chronic idiopathic urticaria (CIU);
   1. The recipient is age 12 years or older;
      AND
   2. The recipient must have ~~tried and failed or have a contraindication~~ had an inadequate response, adverse reaction or contraindication to two different oral second generation antihistamines;
      AND
   3. The recipient must have ~~tried and failed or have a contraindication~~ had an inadequate response, adverse reaction or contraindication to an oral second generation antihistamine in combination with a leukotriene receptor antagonist;

AND

4. The prescriber must be an allergist/immunologist, dermatologist or a rheumatologist or there is documentation in the recipient's medical record that a consultation was done by an allergist/immunologist, dermatologist or a rheumatologist regarding the diagnosis and treatment recommendations.

   AND

5. The requested dose is:
   a. Initial therapy: 150 mg every four weeks or 300 mg every four weeks and clinical rational for starting therapy at 300 mg every four weeks has been provided
   b. Continuation of therapy: 150 mg or 300 mg every four weeks

Nucala® (Mepolizumab), Cinqair® (reslizumab)

A. The recipient will not use the requested antiasthmatic monoclonal antibody in combination with other antiasthmatic monoclonal antibodies;
   AND
B. The recipient must have a diagnosis severe eosinophilic-phenotype asthma;
   AND
C. Evidence of an eosinophilic phenotype (i.e. peripheral blood eosinophil count ≥ 150 cells/µL, elevated sputum eosinophils or FeNO);
   AND
D. The recipient must be an appropriate age:
   1. Mepolizumab: 12 years of age or older
   2. Reslizumab: 18 years of age or older

   AND
E. The prescriber must be either a pulmonologist or allergist/immunologist
   AND
F. The recipient must have had an inadequate response, adverse reaction or contraindication to an oral second generation antihistamine;
   AND
G. The recipient must have had an inadequate response, adverse reaction or contraindication to a leukotriene receptor antagonist;
   AND
H. The requested dose is appropriate:
   1. Mepolizumab: 100 mg subcutaneously every 4 weeks
   2. Reslizumab: 3 mg/kg via intravenous infusion of 20 to 50 minutes every 4 weeks

2. Prior Authorization Guidelines:

   Prior Authorization approval will be for 12 months.

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

3. Quantity Limits:
   - Xolair (omalizumab): 6 vials/28 days
   - Nucala (mepolizumab): 1 vial/28 days

Table 1: Dosing for Xolair® (omalizumab)[1]

Pre-treatment Serum IgE (IU/mL)	**Body Weight (kg)**			
	30-60	**>60-70**	**>70-90**	**>90-150**
≥ 30-100	150 mg	150 mg	150 mg	300 mg
> 100-200	300 mg	300 mg	300 mg	225 mg
> 200-300	300 mg	225 mg	225 mg	300 mg
> 300-400	225 mg	225 mg	300 mg	
> 400-500	300 mg	300 mg	375 mg	
> 500-600	300 mg	375 mg	**DO NOT DOSE**	
> 600-700	375 mg			
Every 2 weeks dosing				
Every 4 weeks dosing				

[1]Xolair® [package insert]. South San Francisco (CA). Genetech Inc.; 2014 March

Therapeutic Class Overview
Antiasthmatic Monoclonal Antibodies

Therapeutic Class Overview/Summary:
This review will focus on the antiasthmatic monoclonal antibodies. These agents are all used for the management of selective asthma diagnoses.[1-3] This class is subdivided into anti-immunoglobulin E (IgE) and anti-immunoglobulin G (interleukin-5 [IL-5]) monoclonal antibodies.[1-3] The IL-5 monoclonal antibodies include mepolizumab (Nucala®) and reslizumab (Cinqair®). Both are Food and Drug Administration (FDA)-approved for the add-on maintenance treatment of severe eosinophilic-phenotype asthma.[1,3] Omalizumab (Xolair®), is the only anti-IgE antibody currently available. It is FDA approved for the treatment of moderate to severe persistent asthma in patients with a positive skin test or in vitro reactivity to a perennial aeroallergen in addition to chronic idiopathic urticaria.[2] Both mepolizumab and omalizumab have been shown to be safe and effective for use in children 12 years of age and older.[1,2] There are currently no generic products available for these agents.

It is important to differentiate individuals with severe asthma based on their subgroups or phenotypes whenever possible because there is heterogeneity in this population. Some characteristics that can be used to distinguish these subtypes include, age, gender, age of asthma onset, atopic status, obesity, exacerbation frequency, aspirin exacerbated respiratory disease and glucocorticoid resistance. It should be noted, though, that there is substantial overlap that may exist between the subgroups.[4] An allergic form of asthma is found in approximately 90% of adult asthmatics.[5] Patients with allergic asthma with positive skin test reactions to a given aeroallergen tend to have exacerbations of asthma when exposed to that aeroallergen. IgE is believed to be pivotal in the pathogenesis of allergic asthma.[6] Omalizumab reduces the release of allergic response mediators by inhibiting the binding of IgE to its receptor on the surface of mast cells and basophils.[2] Although the mechanism by which treatment with omalizumab results in an improvement in the symptoms of chronic idiopathic urticaria is not fully understood, omalizumab binds to IgE and lowers free IgE levels, which down-regulates the IgE receptors on cells.[2] Another subgroup of severe asthmatics is eosinophilic asthma. Patients with severe asthma with an eosinophilic phenotype have both recurrent exacerbations and eosinophilic airway inflammation, which plays a significant part in airway remodeling, hyperresponsiveness and mucus accumulation.[4] There has been some level of tissue eosinophilia documented in 40 to 60% of patients with asthma and the intensity of eosinophilia has been correlated with asthma severity.[7] Mepolizumab and reslizumab both have high affinity and specificity for human IL-5, a key cytokine involved in the maturation, migration, activation, and survival of eosinophils. IL-5 has become a target in the inflammation pathways of asthma given that eosinophil levels have been linked to greater airway remodeling, increased asthma severity, and exacerbations. The resulting inhibition of IL-5 signaling reduces production and survival of eosinophils, as well as decreases overall eosinophil counts in patients with severe asthma. However, the exact mechanism of these agents action in asthma has not been definitively established.[1,3]

The safety and efficacy of the antiasthmatic monoclonal antibodies has been demonstrated in a number of clinical trials for their respective diagnoses.[8-29] It is important to note that these agents have been evaluated in combination with other asthma medications and are not utilized as monotherapy.[8-27] While there is a possibility that patients with severe asthma may meet criteria for treatment with both omalizumab (allergic asthma) and mepolizumab or reslizumab (eosinophilic asthma), there is currently no clinical trials evaluating combination therapy with two monoclonal antibodies..

Table 1. Current Medications Available in the Therapeutic Class[1-3]

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Mepolizumab (Nucala®)	Severe eosinophilic-phenotype asthma in adults and children 12 years of age or older	Powder for Injection (vial): 100 mg	-
Omalizumab (Xolair®)	Chronic idiopathic urticaria and moderate-to-severe persistent allergic asthma in adults and children 12 years of age or older	Powder for Injection (vial): 150 mg	-
Reslizumab (Cinqair®)	Severe eosinophilic-phenotype asthma in adults	Solution for Injection: 100 mg/10 mL	-

Evidence-based Medicine

- The Food and Drug Administration (FDA)-approval of omalizumab for the treatment of allergic asthma was based on the results of three randomized, double-blind, placebo-controlled, multicenter trials conducted in patients at least 12 years of age with moderate to severe asthma for at least one year, and a positive skin test reaction to a perennial aeroallergen. All patients were required to have a baseline immunoglobulin E (IgE) between 30 and 700 international unit (IU)/mL and body weight not more than 150 kg. Patients were treated according to a dosing table to administer at least 0.016 mg/kg/IU (IgE/mL) of omalizumab or placebo over each four-week period. Patients received omalizumab for 16 weeks with an unchanged ICS dose unless an acute exacerbation necessitated an increase. Patients then entered an ICS reduction phase of 12 (Busse et al and Solèr et al) and 16 weeks (Holgate et al) during which ICS dose reduction was attempted in a step-wise manner.[2]
    - In the first 28-week study by Busse et al (N=525), during the steroid stable phase, patients treated with omalizumab had fewer mean exacerbations/subject (0.28 vs 0.54; P=0.006) and decreased mean duration of exacerbations (7.8 vs 12.7 days; P<0.001) compared to placebo-treated patients. Similarly, during the steroid reduction phase, omalizumab was associated with fewer exacerbations/subject (0.39 vs 0.66; P=0.003), and a shorter mean duration of exacerbations (9.4 vs 12.6 days; P=0.021).[8]
    - In the second 28-week study by Solèr et al (N=546), asthma exacerbations/patient, the primary endpoint, decreased more in the omalizumab group compared to placebo during both the stable steroid (0.28 vs 0.66; P<0.001) and steroid reduction (0.36 vs 0.75; P<0.001) phases.[10]
    - In the third 32-week study by Holgate et al (N=246), the percentage reduction in ICS dose, the primary endpoint, was greater among patients treated with omalizumab than among patients treated with placebo (median, 60 vs 50%; P=0.003). The percentages of patients with at least one asthma exacerbation were similar between omalizumab and placebo groups during both the stable steroid and steroid reduction phases (P value not reported).[12]
- The asthma development program for mepolizumab included three double-blind, randomized, placebo-controlled trials: one dose-ranging and exacerbation trial and two confirmatory trials. Mepolizumab was administered every four weeks in all trials as add-on to existing asthma treatment.[1]
    - The first trial, DREAM, was a 52-week phase IIb/III trial that evaluated different doses of the intravenous (IV) formulation of mepolizumab Treatment with IV mepolizumab 75 mg, 250 mg and 750 mg, as add-on therapy, resulted in significant reductions in the frequency of clinically significant asthma exacerbations compared with placebo (48%, 39%, and 52% respectively, with corresponding P values of <0.0001, 0.0005, and <0.0001).[21]
    - The second trial, MENSA, was the 32-week, phase III trial Treatment with mepolizumab 100 mg SQ and mepolizumab 75 mg IV as add-on therapy resulted in statistically significant reductions in the annualized frequency of clinically significant asthma exacerbations compared with placebo (53% and 47%, respectively; P <0.001).[22]
    - The third trial, SIRIUS, was a 24-week, phase III trial in 135 subjects with asthma and at least a six month history of maintenance treatment with OCS and blood eosinophil levels of ≥150 cells/µL at initiation of treatment or ≥300 cells/µL in the past 12 months. Unlike the DREAM

and MENSA trials, a history of exacerbations in the prior year was not required. Treatment with mepolizumab 100 mg SQ as add-on therapy, resulted in a significantly greater percent reduction from baseline in OCS dose during weeks 20 to 24 compared with placebo (odds ratio [OR], 2.39; P=0.008).[23]

- The safety and efficacy of reslizumab was evaluated in an asthma development program which consisted of four randomized, double-blind, placebo-controlled studies (Studies I to IV) of 16 to 52 week duration and involved a total of 981 patients 12 years of age and older. Of note, all patients continued their background asthma therapy throughout the duration of the studies.[25-27]
    - Studies I and II were duplicate, 52-week, multicentre, double-blind, parallel-group, randomized, placebo-controlled phase III trials. Patients were included in the study if their asthma was inadequately controlled by medium-to-high doses of ICS and who had blood eosinophils of greater than or equal to 400 cells/µL and one or more exacerbations in the previous year. A total of 953 patients were randomly assigned (1:1) to receive either intravenous (IV) reslizumab 3 mg/kg or placebo every four weeks. Results from both trials revealed that patients receiving reslizumab had a significant reduction in the frequency of asthma exacerbations (Study I: rate ratio [RR], 0.50; 95% confidence interval [CI], 0.37 to 0.67; Study II: RR, 0.41; 95% CI, 0.28 to 0.59; both P<0.0001) compared with those receiving placebo.[25]
    - Study III was a 16-week, double-blind, multicenter, placebo-controlled, parallel-group, phase III trial of 315 patients with asthma inadequately controlled by at least a medium-dose ICS and blood eosinophils greater than or equal to 400 cells/µL at screening (within three to four weeks of dosing). Of note, patients were not allowed to be on maintenance OCS during the trial. Patients were randomized to receive reslizumab 0.3 mg/kg IV, reslizumab 3 mg/kg IV, or placebo once every four weeks. Reslizumab improved FEV_1 compared to placebo for both reslizumab treatment arms (115 mL [95% CI, 16 to 215; P=0.0237] in the 0.3 mg/kg group and 160mL [95% CI 60 to 259; P=0.0018] in the 3 mg/kg group). However, it was noted that clinically meaningful increases in forced vital capacity (FVC) and forced expiratory flow at 25 to 75% of FVC ($FEF_{25-75\%}$) were only observed with the reslizumab 3 mg/kg group.[26]
    - Lastly, Study IV was a 16-week, double-blind, multicenter, placebo-controlled, phase III trial of 496 patients with asthma inadequately controlled by at least a medium-dose ICS at screening (fluticasone propionate ≥ 440 µg/day or equivalent). Of note, patients were not allowed to be on maintenance OCS during the trial and were not tested for blood eosinophil levels prior to enrollment. Patients were randomized 4:1 to reslizumab 3 mg/kg or placebo given IV once every four weeks. There was not a statistically significant mean change in FEV_1 from baseline to week 16 (255 mL for the reslizumab group and 187 mL for the placebo group giving a between-group difference of 68 mL: standard error [SE] 49.5; P=0.17).[27]
- The FDA-approval of omalizumab for the treatment of chronic idiopathic urticaria was based on two randomized, double-blind, placebo controlled, multi-center clinical trials, ASTERIA II and GLACIAL. Both studies included patients 12 to 75 years of age with moderate to severe chronic idiopathic urticaria who remained symptomatic despite $histamine_1$ antihistamine therapy.[28,29]
    - In the ASTERIA II trial, treatment with omalizumab in doses of 150 and 300 mg every four weeks for three doses resulted in a significant reduction in itch-severity scores compared to placebo. These reductions from baseline in mean weekly itch-severity score were dose-responsive with all three omalizumab doses (75, 150 and 300 mg) and were better than placebo at the time points evaluated prior to week 12. After 12 weeks, the mean weekly itch-severity scores for all omalizumab groups increased to reach values similar to those in the placebo group but did not return to baseline values for the duration of follow-up.[28]
    - In the GLACIAL trial, treatment with omalizumab 300 mg every four weeks for six doses resulted in a significantly greater improvement in the itch-severity score from baseline to week 12 compared to placebo. This difference was sustained at week 24. After week 24 and until week 40, the mean weekly itch-severity scores in the omalizumab group gradually increased to values similar to those in the placebo group but did not return to baseline values.[29]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
    - According to current clinical guidelines for the treatment of persistent asthma, inhaled corticosteroids (ICS) are the preferred treatment option for all severities. Generally, these guidelines recommend a step-wise approach to increasing doses or adding additional agents based on asthma control or severity.[30-33]
        - Severe asthma is generally defined by those requiring high intensity therapies for asthma control or where good control is not achieved despite high intensity therapy.
        - For severe asthma, guidelines recommend an ICS plus a second controller medication, usually an inhaled long-acting β-agonist (LABA), with or without the additional use of oral corticosteroids.
        - An alternative combination that may be considered is an ICS plus a leukotriene receptor antagonist.
        - The use of the anti-IgE monoclonal antibody, omalizumab, can be considered in addition to other therapies for patients with moderate-to-severe allergic asthma with elevated serum levels of IgE.
        - Treatment and control should be reevaluated frequently and adjustments to medication regimen should be made based on current severity or control.
        - Current clinical guidelines do not address the use of anti-IL-5 monoclonal antibodies at this time.
    - Clinical guidelines for the management of chronic urticaria follow a step-wise approach.[34-36]
        - monotherapy with a non-sedating antihistamine prescribed at a normal dose is recommended first line in most situations although a sedating antihistamine may be effective when given at night.
        - Generally treatment failure with normal dose antihistamine should be followed up by increasing the antihistamine dose to that above recommended (up to four times may be useful). If the patient continues to experience symptoms on a very high dose antihistamine guidelines recommend either adding a second antihistamine or adding a leukotriene antagonist.
        - Omalizumab is considered a second- or third-line option in patients who have failed antihistamine therapy.
- Other Key Facts:
    - Both omalizumab and reslizumab carry a black box warning due to the risk of anaphylaxis. Anaphylaxis was reported as early as the first or second dose for omalizumab and reslizumab, respectively, and may continue beyond the initial doses.[2,3]
    - Mepolizumab has a potential risk of hypersensitivity, but does not have a black box warning.[1]
    - Due to the associated risks and complicated administration, all three agents must be administered by a healthcare professional. Those healthcare professionals administering omalizumab and reslizumab should be prepared to observe patients for an appropriate amount of time and the ability to manage anaphylaxis.[1-3]
    - Mepolizumab and omalizumab are subcutaneous injections and reslizumab is an intravenous injection which is given over 20 to 50 minutes. All agents are administered every four weeks; although, omalizumab may be given every two to four weeks for a diagnosis of asthma.[1-3]
    - Antiasthmatic monoclonal antibodies have not been studied when used in combination with one another. The safety and efficacy of using omalizumab in combination with mepolizumab or reslizumab have not been established.

References

1. Nucala® [package insert]. Research Triangle Park (NC): GlaxoSmithKline; 2015 Nov.
2. Xolair® [package insert]. South San Francisco (CA). Genetech Inc.; 2015 Dec.
3. Cinqair® [package insert]. Frazer (PA): Teva; 2016 Apr.
4. Wenzel S. Severe asthma phenotypes. In: Post, TW (Ed). UpToDate [database on the Internet]. Waltham (MA): UpToDate; 2016 [cited 2016 Jun 1]. Available from: http://www.uptodate.com/contents/search
5. Holt PG, Macaubas C, Stumbles PA, Sly PD. The role of allergy in the development of asthma. Nature. 1999 Nov 25;402(6760 Suppl):B12-7.
6. Rambasek TE, Lang DM, Kavuru MS. Omalizumab: where does it fit into current asthma management? Cleve Clin J Med. 2004 Mar;71(3):251-61.

7. Garcia G, Taille C, Laveneziana P, Bourdin A, Chanez P, Humbert M. Anti-interlekin-5 therapy in severe asthma. Eur Respir Rev. 2013;22(129):251-57.
8. Busse W, Corren J, Lanier BQ, McAlary M, Fowler-Taylor A, Cioppa GD, et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. J Allergy Clin Immunol. 2001 Aug;108(2):184-90.
9. Lanier BQ, Corren J, Lumry W, Liu J, Fowler-Taylor A, Gupta N. Omalizumab is effective in the long-term control of severe allergic asthma. Ann Allergy Asthma Immunol. 2003 Aug;91(2):154-9.
10. Solèr M, Matz J, Townley R, Buhl R, O'Brien J, Fox H, et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. Eur Respir J. 2001 Aug;18(2):254-61.
11. Buhl R, Solèr M, Matz J, Townley R, O'Brien J, Noga O, et al. Omalizumab provides long-term control in patients with moderate-to-severe allergic asthma. Eur Respir J. 2002 Jul;20(1):73-8.
12. Holgate ST, Chuchalin AG, Hébert J, Lötvall J, Persson GB, Chung KF, et al. Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma. Clin Exp Allergy. 2004 Apr;34(4):632-8.
13. Eisner MD, Zazzali JL, Miller MK, Bradley MS, Schatz M. Longitudinal changes in asthma control with omalizumab: 2-year interim data from the EXCELS study. Asthma. 2012;49(6):642-8.
14. Chen H, Eisner MD, Haselkorn T, Trzaskoma B. Concomitant asthma medications in moderate-to-severe allergic asthma treated with omalizumab. Respiratory Medicine. 2013;107:60-7.
15. Busse WW, Massanari M, Kianifard F, Geba GP. Effect of omalizumab on the need for rescue systemic corticosteroid treatment in patients with moderate-to-severe persistent IgE-mediated allergic asthma: a pooled analysis. Current Med Research and Opinion. 2007;23(10):2379-86.
16. Milgrom H, Berger W, Nayak A, Gupta N, Pollard S, McAlary M, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab).Pediatrics. 2001 Aug;108(2):E36.
17. Schumann C, Kropf C, Wibmer T, Rüdiger S, Stoiber KM, Thielen A, Rottbauer W and Kroegel C. Omalizumab in patients with severe asthma: the XCLUSIVE study. Clin Respir J. 2012;6:215–227.
18. Niebauer K, Dewilde S, Fox-Rushby J, Revicki DA. Impact of omalizumab on quality-of-life outcomes in patients with moderate-to-severe allergic asthma. Ann Allergy Asthma Immunol. 2006;96:316-26.
19. Chipps B, Buhl R, Beeh KM, Fox H, Thomas K, Reisner C. Improvement in quality of life with omalizumab in patients with severe allergic asthma. Current Med Research and Opinion. 2006;22(11):2201-8.
20. Normansell R, Walker S, Milan SJ, Walters EH, Nair P. Omalizumab for chronic asthma in adults and children. Cochrane Database Syst Rev. 2013 June 13;(2):CD003559.
21. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo- controlled trial (abstract). The Lancet. 2012;380(9842):651-659.
22. Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med. 2014;371(13):1198-1207.
23. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. New England Journal of Medicine. 2014;371(13):1189-1197.
24. A Study to Determine Long-term Safety of Mepolizumab in Asthmatic Subjects. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2015- [cited 2015 Dec 28]. Available from: https://clinicaltrials.gov/ct2/show/NCT01842607.
25. Castro M, Zangrilli J, Wechsler M, Bateman E, Brusselle G, Bardin P, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomized, placebo-controlled, phase 3 trials. The Lancet. 2015 May; 3(5): 355-66.
26. Bjermer L, Lemiere C, Maspero J, Weiss S, Zangrilli J and Germinaro M. Reslizumab for inadequately controlled asthma with elevated blood eosinophil levels: a randomized phase 3 study. CHEST (2016), doi: 10.1016/j.chest.2016.06.032.
27. Corrren J, Weinstein S, Janka L, Zangrilli J, and Garin M. Phase 3 study of reslizumab in patients with poorly controlled asthma: effects across a broad range of eosinophil counts. CHEST (2016), doi:10.1016/j.chest.2016.03.018.
28. Maurer M, Rosen K, Hsieh HJ, Saini S, Grattan C, Gimenez-Arnau A, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. N Engl J Med. 2013;368:924-35.
29. Kaplan A, Ledford D, Ashby M, Canvin J, Zazzali JL, Conner E, et al. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. J Allergy Clin Immunol. 2013;132(1):101-9.
30. Global Strategy for Asthma Management and Prevention. [guideline on the internet]. Bethesda (MD): Global Initiative for Asthma (GINA); 2015 [cited 2015 Dec 27]. Available from: http://www.ginasthma.org/local/uploads/files/GINA_Report_2015_Aug11.pdf.
31. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. Feb;43(2):343-73.
32. United States Department of Health and Human Services National Heart, Lung, and Blood Institute. Expert Panel Report 3: Guidelines for the diagnosis and management of asthma [guideline on the Internet]. NHLBI 2007 [cited 2010 Dec 26]. Available from: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf.
33. Bateman ED, Boulet LP, Cruz AA, FitzGerald M, Haahtela T, Levy ML, et al. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention 2012 [guideline on the internet]. 2011 Dec. [cited 2014 May 19]. Available from: http://www.ginasthma.com.
34. Powell RJ, Leech SC, Till S, Huber PA, Nasser SM, Clark AT. BSACI guideline for the management of chronic urticaria and angioedema. Clin Exp Allergy. 2015 Mar;45(3):547-65. doi: 10.1111/cea.12494.
35. Bernstein JA, Lang DM, Khan DA, Craig T, Dreyfus D, Hsieh F, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014 May;133(5):1270-7. doi: 10.1016/j.jaci.2014.02.036.
36. Zuberbier T, Asero R, Bindslev-Jensen C, Canonica GW, Church MK, Gimenez-Arnau AM, et al. EAACI/GA2LEN/EDF/WAO guideline: management of urticaria. Allergy. 2009;64:1427-43.

DIVISION OF HEALTH CARE FINANCING AND POLICY
NEVADA MEDICAID
DRUG USE REVIEW (DUR) BOARD
PROPOSED PRIOR AUTHORIZATION CRITERIA

Therapeutic Class: Hepatitis C direct-acting antivirals
Last Reviewed by the DUR Board:

1. **Coverage and limitations:**

A. All Requests must meet the following criteria:

1) Recipient has a diagnosis of chronic Hepatitis C Virus (HCV) infection

2) Recipient is 18 years of age or older

3) All of the following must be included with the PA request:
   a. Medical records and results of laboratory and diagnostic tests which support ALL of the following:
      1. HCV genotype (and subtype, if applicable)
      2. Baseline HCV RNA viral load and date drawn
      3. Hepatic fibrosis stage, including tests supporting liver disease staging (e.g. APRI, Fibroscan, Fibrosure, FIB-4)
         i Results of diagnostic tests or imaging studies that are inconclusive may require additional testing
   b. Complete treatment regimen
   c. Duration of treatment
   d. Previous treatment-experience and length of treatment, if any, including outcome (e.g. discontinued to side effects, relapsed, non-responder, null-responder)

4) Prescriber must certify that treatment will be discontinued if the viral load is detectable at week 4 of treatment and has increased by greater than 10-fold (>1 $\log_{10}$ IU/mL) on repeat testing at week 6 (or thereafter).

5) Requests for recipients with decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C) and requests for recipients who have chronic hepatitis C infection status-post liver transplant will be evaluated on a case-by-case basis.

B. Harvoni (initial requests)

1) Requested dose is one 90 mg/400 mg tablet once daily

2) Genotype 1

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, pre-treatment HCV RNA < 6 million, and the requested duration is 8 weeks
      2. No cirrhosis, pre-treatment HCV RNA ≥ 6 million, and the requested duration is 12 weeks
      3. Compensated cirrhosis (CTP class A), requested duration is 12 weeks

   b. Recipient is treatment-experienced (failed peginterferon + ribavirin) and ONE of the following is met:
      1. No cirrhosis and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and requested duration is 12 weeks

3. Compensated cirrhosis (CTP class A), documentation is provided that the recipient is unable to take ribavirin, and the requested duration is 24 weeks

c. Recipient is treatment-experienced (failed peginterferon + ribavirin + an NS3 protease inhibitor), has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir), and ONE of the following is met:
   1. No cirrhosis and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and requested duration is 12 weeks
   3. Compensated cirrhosis (CTP class A), documentation is provided that the recipient is unable to take ribavirin, and the requested duration is 24 weeks

d. Recipient is treatment-experienced (failed Olysio + Sovaldi), has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir), and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
   2. Cirrhosis (CTP class A, B, or C), will be treated with ribavirin, and the requested duration is 24 weeks

e. Recipient is treatment-experienced (failed Sovaldi + ribavirin ± peginterferon) and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
   2. Cirrhosis (CTP class A, B, or C), will be treated with ribavirin, and the requested duration is 24 weeks

3) Genotype 4,5 and 6
   a. Recipient is treatment-naïve and the requested duration is 12 weeks
   b. Recipient is treatment-experienced (failed peginterferon + ribavirin ± an NS3 protease inhibitor) and the requested duration is 12 weeks

C. Viekira Pak (initial requests)

1) Requested dose is two ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg tablets once daily (25/150/100 mg) and one dasabuvir 250 mg tablet twice daily

2) Genotype 1a

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with ribavirin and the requested duration is 12 weeks

   b. Recipient is treatment experienced (failed peginterferon + ribavirin dual therapy)
      1. No cirrhosis, recipient will be treated with ribavirin, and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the recipient was a partial responder to peginterferon and ribavirin dual therapy, and the requested duration is 12 weeks
      3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the recipient was a relapser after peginterferon and ribavirin dual therapy, and the requested duration is 24 weeks

3) Genotype 1b

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis and the requested duration is 12 weeks

2. Compensated cirrhosis (CTP class A) and the requested duration is 12 weeks

b. Recipient is treatment experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A) and the requested duration is 12 weeks

D. Technivie (initial requests)

1) Requested dose is two ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg tablets once daily (25/150/100 mg)

2) The Recipient does not have cirrhosis

3) Genotype 4

a. Recipient is treatment-naïve, will be treated with ribavirin, and the requested duration is 12 weeks

b. Recipient is treatment-naïve, documentation is provided showing that the recipient is unable to take ribavirin, and the requested duration is 12 weeks

c. Recipient is treatment-experienced (failed peginterferon and ribavirin dual therapy), will be treated with ribavirin, and the requested duration is 12 weeks

E. Daklinza (initial requests)

1) Requested dose is one of the following:
   a. 60 mg (one tablet) daily
   b. 30 mg (one tablet) and the recipient is receiving a strong CYP3A inhibitor
   c. 90 mg (one 30 mg tablet and on 60 mg tablet) daily and the recipient is receiving a concomitant moderate CYP3A inducer and clinical rational documenting medical necessity for continuing the moderate CYP3A inducer during Daklinza therapy

2) Genotype 1

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with Sovaldi and ribavirin and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with Sovaldi, the requested duration is 12 weeks and documentation has been provided showing that the recipient is unable to take ribavirin
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi ± ribavirin, and the requested duration is 12 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Sovaldi + ribavirin, and the requested duration is 24 weeks
   5. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin.

c. Recipient is treatment-experienced (failed peginterferon + ribavirin + NS3 protease inhibitor), has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir) and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin

3) Genotype 2

a. Recipient is treatment-naïve, documentation is provided showing that the recipient is unable to take ribavirin, and ONE of the following is met:
   1. No cirrhosis, will be treated with Sovaldi, and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, and the requested duration is 12 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, and the requested duration is 24 weeks

b. Recipient is treatment-experienced (failed Sovaldi + ribavirin dual therapy), documentation has been provided showing that the recipient is unable to receive peginterferon, and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
   2. No cirrhosis, will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks

4) Genotype 3

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin and showing that the recipient is unable to receive peginterferon

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy), documentation is provided showing that the recipient is unable to receive peginterferon, and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

c. Recipient is treatment-experienced (failed Sovaldi + ribavirin therapy dual therapy), documentation is provided that the recipient is unable to receive peginterferon, and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and ribavirin and the requested duration is 24 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin and the requested duration is 24 weeks

F. Olysio (initial requests)

1) Requested dose is 150 mg (one capsule) daily.

2) Genotype 1a

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, will be treated with Sovaldi and ribavirin, and the requested duration is 12 weeks
      2. No cirrhosis, will be treated with Sovaldi, the requested duration is 12 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin
      3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks, and the recipient is negative for the Q80K polymorphism
      4. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin

   b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
      1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks, and the recipient is negative for the Q80K polymorphism
      3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin

3) Genotype 1b

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, will be treated with Sovaldi, and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
      3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

   b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
      1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks
      3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

G. Sovaldi (initial requests)

1) Requested dose is 400 mg daily

2) Genotype 1

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, will be treated with Daklinza and ribavirin and the requested duration is 12 weeks

2. No cirrhosis, will be treated with Daklinza, the requested duration is 12 weeks and documentation has been provided showing the that the recipient is unable to take ribavirin
3. No cirrhosis, genotype 1a, will be treated with Olysio and ribavirin, and the requested duration is 12 weeks
4. No cirrhosis, genotype 1a, will be treated with Olysio, the requested duration is 12 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin
5. No cirrhosis, genotype 1b, will be treated with Olysio, and the requested duration is 12 weeks
6. Compensated cirrhosis (CTP class A), will be treated with Daklinza ± ribavirin, and the requested duration is 12 weeks
7. Compensated cirrhosis (CTP class A), will be treated with Daklinza + ribavirin, and the requested duration is 24 weeks
8. Compensated cirrhosis (CTP class A), will be treated with Daklinza, requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin
9. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio and ribavirin, the requested duration is 24 weeks, and the recipient is negative for the Q80K polymorphism
10. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin
11. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio and ribavirin, and the requested duration is 24 weeks
12. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio, the requested duration is 24 weeks, and documentation has been provided that the recipient is unable to take ribavirin

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with Daklinza and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with Olysio and the requested duration is 12 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, and the requested duration is 24 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza, requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin.
   5. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio and ribavirin, the requested duration is 24 weeks, and the recipient is negative for the Q80K polymorphism
   6. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin
   7. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio and ribavirin, the requested duration is 24 weeks
   8. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

c. Recipient is treatment-experienced (failed peginterferon + ribavirin + NS3 protease inhibitor), has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir) and ONE of the following:
   1. No cirrhosis, will be treated with Daklinza and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin

3) Genotype 2

a. Recipient is treatment-naïve and ONE of the following is met:
    1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
    2. No cirrhosis, will be treated with Daklinza, the requested duration is 12 weeks, and documentation is provided showing that the recipient is unable to take ribavirin
    3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and the requested duration is 16 weeks
    4. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 12 weeks, and documentation is provided showing that the recipient is unable to take ribavirin
    5. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy), and ONE of the following:
    1. No cirrhosis, will be treated with ribavirin, and the requested duration is 16 weeks
    2. No cirrhosis, will be treated with ribavirin and peginterferon and the requested duration is 12 weeks
    3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 16 weeks
    4. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 24 weeks
    5. Compensated cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks

c. Recipient is treatment-experienced (failed Sovaldi + ribavirin dual therapy) and ONE of the following:
    1. No cirrhosis, will be treated with Daklinza and ribavirin, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
    2. No cirrhosis, will be treated with Daklinza, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin and showing that the recipient is unable to receive peginterferon
    3. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
    4. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
    5. Compensated cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks

4) Genotype 3

a. Recipient is treatment-naïve and ONE of the following is met:
    1. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
    2. No cirrhosis, will be treated with ribavirin, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
    3. No cirrhosis, recipient will be treated with Daklinza and the requested duration is 12 weeks
    4. Compensated cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
    5. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 24 weeks, and documentation has been provided that the recipient is unable to receive peginterferon

6. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
7. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin and showing that the recipient is unable to receive peginterferon

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with Daklinza, and the requested duration is 12 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin and the requested duration is 24 weeks
   5. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

c. Recipient is treatment-experienced (failed Sovaldi + ribavirin therapy dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   2. No cirrhosis, recipient will be treated with Daklinza and ribavirin and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin and the requested duration is 24 weeks

5) Genotype 4

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with ribavirin and the requested duration is 24 weeks
   3. Cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
   4. Cirrhosis, will be treated with ribavirin and the requested duration is 24 weeks

b. Recipient is treatment-experienced (failed peginterferon alfa + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with ribavirin, and the requested duration is 24 weeks
   3. Cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
   4. Cirrhosis, will be treated with ribavirin, and the requested duration is 24 weeks

6) Genotype 5 and 6

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks

2. Cirrhosis, will be treated with ribavirin and peginterferon, and requested duration is 12 weeks

b. Recipient is treatment-experienced and ONE of the following:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
   2. Cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks

H. Recipients who have received previous therapy with an NS5A inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir)

1) Genotype 1
   a. One of the following:
      1. Recipient has cirrhosis
      2. Documentation which includes clinical rational for urgent retreatment have been provided

   b. Testing for resistance–associated variants (RAVs) have been done and results have been provided

   c. No NS5A RAVs detected: Harvoni + ribavirin ± peginterferon x24 weeks

   d. NS5A RAVs detected, no NS3 RAVs detected: Olysio + Sovaldi + ribavirin ± peginterferon x24 weeks

I. Requests for recertification (for treatment beyond 12 weeks) must meet ALL of the following:

1) Laboratory results for HCV RNA viral load at week 4 and week 6 (if applicable) have been submitted with the PA request

2) HCV Viral load must meet ONE of the following:
   a. Undetectable HCV RNA viral load at week 4
   b. Detectable HCV RNA viral load at treatment week 4 and HCV RNA increased by ≤10-fold (≤1 $\log_{10}$ IU/mL) on repeat testing at treatment week 6 (or thereafter)

3) Recipient is compliant on all drugs in the treatment regimen

2. **Prior Authorization Guidelines:**

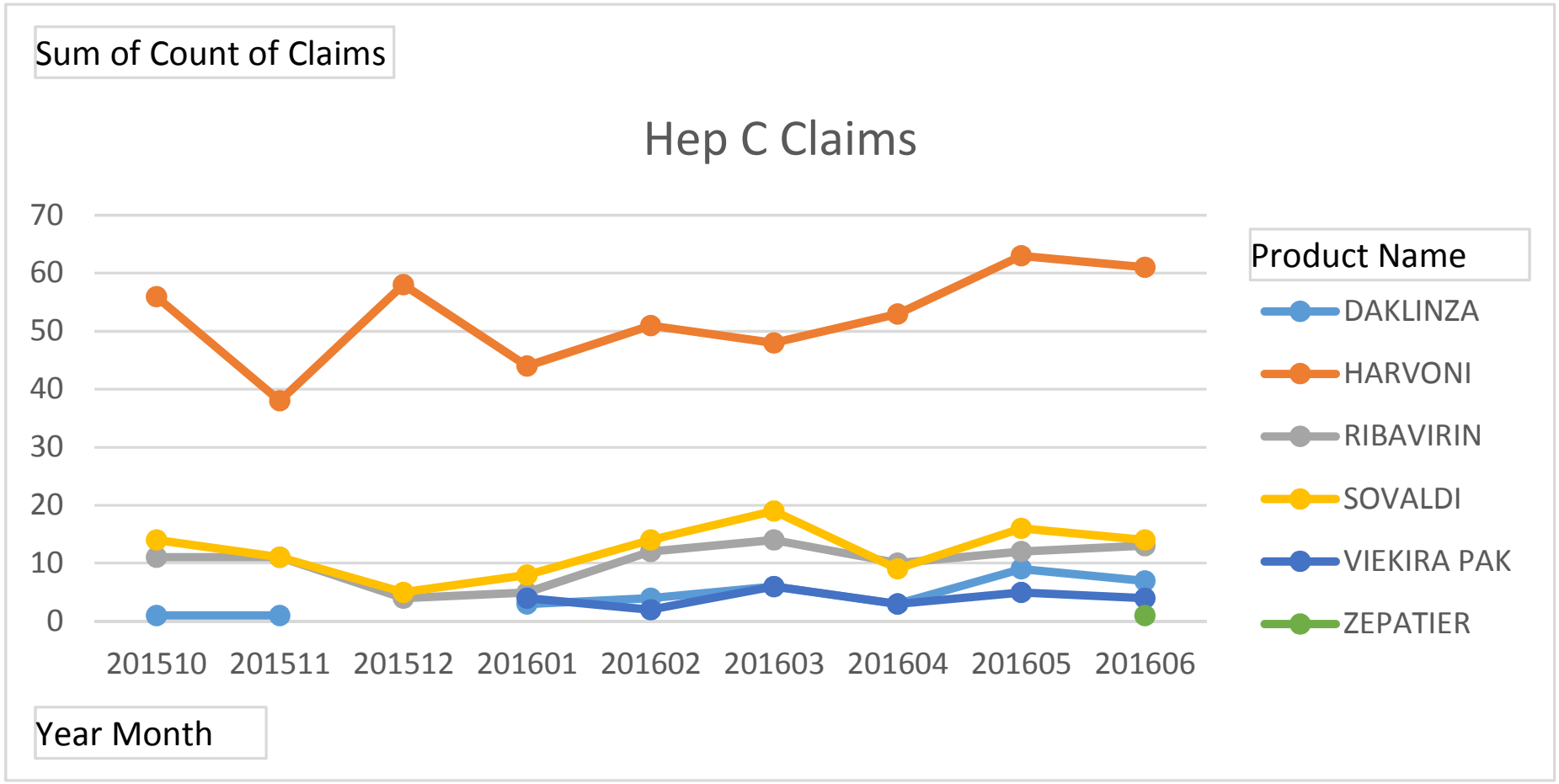
A. Prior authorization approval will be granted for a maximum of 12 weeks (unless the requested regimen is less than 12 weeks long or the remaining duration of therapy is less than 12 weeks)
B. The initial prescription will be limited to a 14-day supply; subsequent refills can be up to 34 days.

3. **Quantity Limitations**:
A. Harvoni (ledipasvir/sofosbuvir): 1 tablet/day
B. Viekira Pak (ombitasvir/paritaprevir/ritonavir/dasabuvir): 1 pack/28 days
C. Technivie (ombitasvir/paritaprevir/ritonavir): 1 tablet/day
D. Daklinza (daclatasvir): 1 tablet/day
E. Olysio (simeprevir): 1 capsule/day
F. Sovaldi (sofosbuvir): 1 tablet/day

Hep C Medications

Oct 1, 2015 - June 30, 2016

Row Labels	Sum of Claims	Sum of Members	Total Qty	Total Days Supp	Pharmacy Paid
DAKLINZA	34	28	924	924	$693,760.37
HARVONI	472	307	8218	8218	$9,063,994.00
RIBAVIRIN	92	85	13646	2606	$12,363.86
SOVALDI	110	95	2968	2968	$2,937,433.76
VIEKIRA PAK	24	14	1232	308	$300,651.45
ZEPATIER	1	1	28	28	$18,210.17
Grand Total	**733**	**530**	**27016**	**15052**	**$13,026,413.61**


Sum of Count of Claims
Hep C Claims
70
60
50
40
30
20
10
0
201510
201511
201512
201601
201602
201603
201604
201605
201606
Year Month
Product Name
DAKLINZA
HARVONI
RIBAVIRIN
SOVALDI
VIEKIRA PAK
ZEPATIER

DIVISION OF HEALTH CARE FINANCING AND POLICY
NEVADA MEDICAID
DRUG USE REVIEW (DUR) BOARD
PROPOSED PRIOR AUTHORIZATION CRITERIA

Therapeutic Class: Hepatitis C direct-acting antivirals
Last Reviewed by the DUR Board:

1. **Coverage and limitations:**

A. All Requests must meet the following criteria:

1) Recipient has a diagnosis of chronic Hepatitis C Virus (HCV) infection

2) Recipient is 18 years of age or older

3) All of the following must be included with the PA request:
   a. Medical records and results of laboratory and diagnostic tests which support ALL of the following:
      1. HCV genotype (and subtype, if applicable)
      2. Baseline HCV RNA viral load and date drawn
      3. Hepatic fibrosis stage, including tests supporting liver disease staging (e.g. APRI, Fibroscan, Fibrosure, FIB-4)
         i Results of diagnostic tests or imaging studies that are inconclusive may require additional testing
   b. Complete treatment regimen
   c. Duration of treatment
   d. Previous treatment-experience and length of treatment, if any, including outcome (e.g. discontinued due to side effects, relapsed, non-responder, null-responder)

4) Prescriber must certify that treatment will be discontinued if the viral load is detectable at week 4 of treatment and has increased by greater than 10-fold (>1 $\log_{10}$ IU/mL) on repeat testing at week 6 (or thereafter).

5) Requests for recipients with decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C) and requests for recipients who have chronic hepatitis C infection status-post liver transplant will be evaluated on a case-by-case basis.

B. Harvoni (initial requests)

1) Requested dose is one 90 mg/400 mg tablet once daily

2) Genotype 1

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, pre-treatment HCV RNA < 6 million, and the requested duration is 8 weeks
      2. No cirrhosis, pre-treatment HCV RNA ≥ 6 million, and the requested duration is 12 weeks
      3. Compensated cirrhosis (CTP class A), requested duration is 12 weeks

   b. Recipient is treatment-experienced (failed peginterferon + ribavirin) and ONE of the following is met:
      1. No cirrhosis and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and requested duration is 12 weeks

3. Compensated cirrhosis (CTP class A), documentation is provided that the recipient is unable to take ribavirin, and the requested duration is 24 weeks

c. Recipient is treatment-experienced (failed peginterferon + ribavirin + an NS3 protease inhibitor)~~, has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir),~~ and ONE of the following is met:
   1. No cirrhosis and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and requested duration is 12 weeks
   3. Compensated cirrhosis (CTP class A), documentation is provided that the recipient is unable to take ribavirin, and the requested duration is 24 weeks

~~d. Recipient is treatment-experienced (failed Olysio + Sovaldi), has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir), and ONE of the following is met:~~
   ~~1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks~~
   ~~2. Cirrhosis (CTP class A, B, or C), will be treated with ribavirin, and the requested duration is 24 weeks~~

~~e.~~d. Recipient is treatment-experienced (failed Sovaldi + ribavirin ± peginterferon) and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A~~, B, or C~~), will be treated with ribavirin, and the requested duration is 24 weeks

3) Genotype 4
   a. Recipient is treatment-naïve and ONE of the following is met
      1. No cirrhosis and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A) and the requested duration is 12 weeks
   b. Recipient is treatment-experienced (failed peginterferon + ribavirin) and ONE of the following is met:
      1. No cirrhosis and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and the requested duration is 12 weeks
      3. Compensated cirrhosis (CTP class A), documentation is provided that the recipient is unable to take ribavirin, and the requested duration is 24 weeks

4) Genotype 5 and 6
   a. Recipient is treatment-naïve and the requested duration is 12 weeks
   b. Recipient is treatment-experienced (failed peginterferon + ribavirin~~ ± an NS3 protease inhibitor~~) and the requested duration is 12 weeks

C. Viekira Pak (initial requests)

1) Requested dose is two ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg tablets once daily (25/150/100 mg) and one dasabuvir 250 mg tablet twice daily

2) Genotype 1a

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, ~~and~~ the requested duration is 24~~12~~ weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen

b. Recipient is treatment experienced (failed peginterferon + ribavirin dual therapy)
1. No cirrhosis, recipient will be treated with ribavirin, and the requested duration is 12 weeks
~~1.~~2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 24 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
~~2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the recipient was a partial responder to peginterferon and ribavirin dual therapy, and the requested duration is 12 weeks~~
~~3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the recipient was a relapser after peginterferon and ribavirin dual therapy, and the requested duration is 24 weeks~~

3) Genotype 1b

a. Recipient is treatment-naïve and ONE of the following is met:
1. No cirrhosis and the requested duration is 12 weeks
2. Compensated cirrhosis (CTP class A) and the requested duration is 12 weeks

b. Recipient is treatment experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
1. No cirrhosis and the requested duration is 12 weeks
2. Compensated cirrhosis (CTP class A) and the requested duration is 12 weeks

D. Technivie (initial requests)

1) Requested dose is two ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg tablets once daily (25/150/100 mg)

~~2) The Recipient does not have cirrhosis~~

~~3)~~2) Genotype 4

a. Recipient is treatment-naïve and ONE of the following:
1. No cirrhosis, will be treated with ribavirin and the requested duration is 12 weeks
~~1.~~2. Compensated cirrhosis (CTP class A) and the requested duration is 12 weeks

~~b. Recipient is treatment-naïve, documentation is provided showing that the recipient is unable to take ribavirin, and the requested duration is 12 weeks~~

b. Recipient is treatment-experienced (failed peginterferon and ribavirin dual therapy) and ONE of the following:
1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
~~1.~~2. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and the requested duration is 12 weeks

E. Daklinza (initial requests)

1) Requested dose is one of the following:
a. 60 mg (one tablet) daily
b. 30 mg (one tablet) and the recipient is receiving a strong CYP3A inhibitor
c. 90 mg (one ~~30 mg tablet and on 60 mg~~ tablet) daily and the recipient is receiving a concomitant moderate CYP3A inducer ~~and clinical rational documenting medical necessity for continuing the moderate CYP3A inducer during Daklinza therapy~~

2) Genotype 1

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with Sovaldi ~~and ribavirin~~ , and the requested duration is 12 weeks
   ~~2. No cirrhosis, will be treated with Sovaldi, the requested duration is 12 weeks and documentation has been provided showing that the recipient is unable to take ribavirin~~
   ~~3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi ± ribavirin, and the requested duration is 12 weeks~~
   ~~4.~~2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi + ribavirin, ~~and~~ the requested duration is 24 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   ~~5.~~3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, requested duration is 24 weeks, ~~and~~ documentation has been provided showing that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, ~~and~~ the requested duration is 24 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, requested duration is 24 weeks, ~~and~~ documentation is provided showing that the recipient is unable to take ribavirin and documentation is provided why the recipient cannot use a guideline-recommended regimen.

c. Recipient is treatment-experienced (failed peginterferon + ribavirin + NS3 protease inhibitor) ~~, has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir)~~ and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin

3) Genotype 2

a. Recipient is treatment-naïve~~, documentation is provided showing that the recipient is unable to take ribavirin,~~ and ONE of the following is met:
   1. No cirrhosis, will be treated with Sovaldi, and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, ~~and~~ the requested duration is ~~12~~16 weeks, and documentation is provided showing that the recipient is unable to take ribavirin
   ~~3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, and the requested duration is 24 weeks~~

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy), documentation is provided showing the recipient is unable to take ribavirin, and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi, and the requested 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated for Sovaldi, and the requested duration is 16 to 24 weeks

~~b.~~c. Recipient is treatment-experienced (failed Sovaldi + ribavirin dual therapy), documentation has been provided showing that the recipient is unable to receive peginterferon, and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
   2. No cirrhosis, will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
   ~~3.~~4. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

4) Genotype 3

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks~~, and documentation has been provided showing that the recipient is unable to receive peginterferon~~
      3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin~~ and showing that the recipient is unable to receive peginterferon~~

   b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy), documentation is provided showing that the recipient is unable to receive peginterferon, and ONE of the following:
      1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, ~~and~~ the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
      ~~3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin~~

   c. Recipient is treatment-experienced (failed Sovaldi + ribavirin therapy dual therapy), documentation is provided that the recipient is unable to receive peginterferon, and ONE of the following:
      1. No cirrhosis, will be treated with Sovaldi and ribavirin and the requested duration is 24 weeks
      2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin and the requested duration is 24 weeks

F. Olysio (initial requests)

1) Requested dose is 150 mg (one capsule) daily.

2) Genotype 1a

   a. Recipient is treatment-naïve and ONE of the following is met:
      1. No cirrhosis, will be treated with Sovaldi~~ and ribavirin~~, and the requested duration is 12 weeks
      ~~2. No cirrhosis, will be treated with Sovaldi, the requested duration is 12 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin~~
      ~~3.~~2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks, ~~and~~ the recipient is negative for the Q80K polymorphism, and documentation is provided why the recipient cannot use a guideline-recommended regimen

4.3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks, and the recipient is negative for the Q80K polymorphism
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin

3) Genotype 1b

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with Sovaldi, and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with Sovaldi and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Sovaldi and ribavirin, the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Sovaldi, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin

G. Sovaldi (initial requests)

1) Requested dose is 400 mg daily

2) Genotype 1

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with Daklinza and ribavirin and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with Daklinza, the requested duration is 12 weeks and documentation has been provided showing the that the recipient is unable to take ribavirin
   3.2. No cirrhosis, genotype 1a, will be treated with Olysio and ribavirin, and the requested duration is 12 weeks
   4. No cirrhosis, genotype 1a, will be treated with Olysio, the requested duration is 12 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin
   5. No cirrhosis, genotype 1b, will be treated with Olysio, and the requested duration is 12 weeks
   6. Compensated cirrhosis (CTP class A), will be treated with Daklinza ± ribavirin, and the requested duration is 12 weeks
   7.3. Compensated cirrhosis (CTP class A), will be treated with Daklinza + ribavirin, and the requested duration is 24 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen

8.4. Compensated cirrhosis (CTP class A), will be treated with Daklinza, requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen

9.5. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio and ribavirin, the requested duration is 24 weeks, and the recipient is negative for the Q80K polymorphism, and documentation is provided why the recipient cannot use a guideline-recommended regimen

10.6. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen

11.7. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio and ribavirin, and the requested duration is 24 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen

12.8. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio, the requested duration is 24 weeks, and documentation has been provided that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with Daklinza and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with Olysio and the requested duration is 12 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, and the requested duration is 24 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza, requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen.
   5. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio and ribavirin, the requested duration is 24 weeks, and the recipient is negative for the Q80K polymorphism, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   6. Compensated cirrhosis (CTP class A), genotype 1a, will be treated with Olysio, the requested duration is 24 weeks, the recipient is negative for the Q80K polymorphism, and documentation has been provided showing that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   7. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio and ribavirin, the requested duration is 24 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   8. Compensated cirrhosis (CTP class A), genotype 1b, will be treated with Olysio, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin, and documentation is provided why the recipient cannot use a guideline-recommended regimen

c. Recipient is treatment-experienced (failed peginterferon + ribavirin + NS3 protease inhibitor), has had no prior treatment with an NS5A polymerase inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir) and ONE of the following:
   1. No cirrhosis, will be treated with Daklinza and the requested duration is 12 weeks
   2. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, and the requested duration is 24 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation is provided showing that the recipient is unable to take ribavirin

3) Genotype 2

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin, and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with Daklinza, the requested duration is 12 weeks~~, and documentation is provided showing that the recipient is unable to take ribavirin~~
   3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, and the requested duration is 16 weeks to 24 weeks
   ~~4. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 12 weeks, and documentation is provided showing that the recipient is unable to take ribavirin~~
   ~~5.~~4. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is ~~24~~ 16 weeks, and documentation is provided showing that the recipient is unable to take ribavirin

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy), and ONE of the following:
   1. No cirrhosis, will be treated with ribavirin, and the requested duration is ~~16~~ 12 weeks
   ~~2. No cirrhosis, will be treated with ribavirin and peginterferon and the requested duration is 12 weeks~~
   2. No cirrhosis, will be treated with Daklinza, the requested duration is 12 weeks, and documentation is provided showing the recipient is unable to take ribavirin
   3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 16 weeks to 24 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, the requested duration is 16 weeks to 24 weeks, and documentation is provided showing the recipient is unable to take ribavirin
   5. Compensated cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, ~~and~~ the requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen

c. Recipient is treatment-experienced (failed Sovaldi + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with Daklinza and ribavirin, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
   2. No cirrhosis, will be treated with Daklinza, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin and showing that the recipient is unable to receive peginterferon
   3. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to receive peginterferon
   5. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation is been provided showing that the recipient is unable to take peginterferon and ribavirin
   ~~5.~~6. Compensated cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks

4) Genotype 3

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks

2. No cirrhosis, will be treated with ribavirin, the requested duration is 24 weeks, and documentation ~~is provided showing that the recipient is unable to receive peginterferon~~ is provided why the recipient cannot use a guideline-recommended regimen
3. No cirrhosis, recipient will be treated with Daklinza and the requested duration is 12 weeks
4. Compensated cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks
5. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 24 weeks, ~~and documentation has been provided that the recipient is unable to receive peginterferon~~ and documentation is provided why the recipient cannot use a guideline-recommended regimen
6. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, the requested duration is 24 weeks~~, and documentation has been provided showing that the recipient is unable to receive peginterferon~~
7. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin ~~and showing that the recipient is unable to receive peginterferon~~

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   2. No cirrhosis, will be treated with Daklinza, and the requested duration is 12 weeks
   3. Compensated cirrhosis (CTP class A), will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, ~~and~~ the requested duration is 24 weeks, and documentation is been provided showing that the recipient is unable to take peginterferon
   ~~5. Compensated cirrhosis (CTP class A), will be treated with Daklinza, the requested duration is 24 weeks, and documentation has been provided showing that the recipient is unable to take ribavirin~~

c. Recipient is treatment-experienced (failed Sovaldi + ribavirin therapy dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   2. No cirrhosis, recipient will be treated with Daklinza and ribavirin, ~~and~~ the requested duration is 24 weeks, and documentation is been provided showing that the recipient is unable to take peginterferon
   3. Compensated cirrhosis (CTP class A), will be treated with peginterferon and ribavirin, and the requested duration is 12 weeks
   4. Compensated cirrhosis (CTP class A), will be treated with Daklinza and ribavirin, ~~and~~ the requested duration is 24 weeks, and documentation is been provided showing that the recipient is unable to take peginterferon

5) Genotype 4

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, ~~and~~ the requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   ~~2. No cirrhosis, will be treated with ribavirin and the requested duration is 24 weeks~~
   ~~3.~~2. Compensated Cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, ~~and~~ the requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   ~~4. Cirrhosis, will be treated with ribavirin and the requested duration is 24 weeks~~

b. Recipient is treatment-experienced (failed peginterferon alfa + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, ~~and~~ the requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   ~~2. No cirrhosis, will be treated with ribavirin, and the requested duration is 24 weeks~~
   ~~3. Cirrhosis, will be treated with ribavirin and peginterferon, and the requested duration is 12 weeks~~
   ~~4.~~2. Compensated Cirrhosis (CTP class A), will be treated with ribavirin, ~~and~~ the requested duration is 24 weeks, documentation is provided why the recipient cannot take peginterferon, and documentation is provided why the recipient cannot use a guideline-recommended regimen

6) Genotype 5 and 6

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, ~~and~~ the requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   2. Compensated Cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, ~~and~~ requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen

b. Recipient is treatment-experienced (failed peginterferon alfa + ribavirin dual therapy) and ONE of the following:
   1. No cirrhosis, will be treated with ribavirin and peginterferon, ~~and~~ the requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   2. Compensated Cirrhosis (CTP class A), will be treated with ribavirin and peginterferon, ~~and~~ the requested duration is 12 weeks, and documentation is provided why the recipient cannot use a guideline-recommended regimen

H. Zepatier

1) The requested dose is one tablet (50/100 mg) daily

2) Genotype 1a

a. Recipient is treatment-naïve and ONE of the following is met:
   1. No cirrhosis, the requested duration is 12 weeks, and there are no baseline NS5A RAVs for elbasvir detected
   2. No cirrhosis, will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected, and documentation is provided why the recipient cannot use a guideline-recommended regimen
   3. Compensated cirrhosis (CTP class A), requested duration is 12 weeks, and there are no baseline NS5A RAVs for elbasvir detected
   4. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected, and documentation is provided why the recipient cannot use a guideline-recommended regimen

b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following is met:
   1. No cirrhosis, the requested duration is 12 weeks, and there are no baseline NS5A RAVs for elbasvir detected

2. No cirrhosis, will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected, and documentation is provided why the recipient cannot use a guideline-recommended regimen
3. Compensated cirrhosis (CTP class A), requested duration is 12 weeks, and there are no baseline NS5A RAVs for elbasvir detected
4. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected, and documentation is provided why the recipient cannot use a guideline-recommended regimen

c. Recipient is treatment-experienced (failed peginterferon + ribavirin + NS3 protease inhibitor) and ONE of the following is met:
1. No cirrhosis, will be treated with ribavirin, the requested duration is 12 weeks and there are no baseline NS5A RAVs for elbasvir detected
2. No cirrhosis, will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected
3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, requested duration is 12 weeks, and there are no baseline NS5A RAVs for elbasvir detected
4. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected

3) Genotype 1b
a. Recipient is treatment-naïve and ONE of the following is met:
1. No cirrhosis and the requested duration is 12 weeks
2. Compensated Cirrhosis (CTP class A) and the requested duration is 12 weeks
b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following is met:
1. No cirrhosis and the requested duration is 12 weeks
2. Compensated Cirrhosis (CTP class A) and the requested duration is 12 weeks
c. Recipient is treatment-experienced (failed peginterferon + ribavirin + NS3 protease inhibitor) and ONE of the following is met:
1. No cirrhosis, will be treated with ribavirin, the requested duration is 12 weeks and there are no baseline NS5A RAVs for elbasvir detected
2. No cirrhosis, will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected
3. Compensated cirrhosis (CTP class A), will be treated with ribavirin, requested duration is 12 weeks, and there are no baseline NS5A RAVs for elbasvir detected
4. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 16 weeks, baseline NS5A RAVs for elbasvir have been detected

4) Genotype 4
a. Recipient is treatment naïve and ONE of the following is met:
1. No cirrhosis and the requested duration is 12 weeks
2. Compensated cirrhosis (CTP class A) and the requested duration is 12 weeks
b. Recipient is treatment-experienced (failed peginterferon + ribavirin dual therapy) and ONE of the following is met:
1. No cirrhosis, the requested duration is 12 weeks, and documentation has been provided showing that the recipient experienced virologic relapse to peginterferon + ribavirin dual therapy
2. No cirrhosis, will be treated with ribavirin, the requested duration is 16 weeks, and documentation has been provided showing that the recipient experienced on-treatment virologic failure to peginterferon + ribavirin dual therapy
3. Compensated cirrhosis (CTP class A), the requested duration is 12 weeks, and documentation has been provided showing that the recipient experienced virologic relapse to peginterferon + ribavirin dual therapy

4. Compensated cirrhosis (CTP class A), will be treated with ribavirin, the requested duration is 16 weeks, and documentation has been provided showing that the recipient experienced on-treatment virologic failure to peginterferon + ribavirin dual therapy

~~H.~~I. **Recipients who have received previous therapy with an NS5A inhibitor (e.g. daclatasvir, ledipasvir, ombitasvir) or combination therapy with sofosbuvir + simeprevir**

~~1) Genotype 1~~
~~2)~~1) One of the following:
   a. Recipient has cirrhosis
   b. Documentation which includes clinical rational for urgent retreatment have been provided

2) Testing for resistance–associated variants (RAVs) have been done and results have been provided

3) Requested regimen does not include agents in which RAVs have developed

4) Requested regimen includes ribavirin or documentation has been provided that ribavirin is contraindicated

~~3) No NS5A RAVs detected: Harvoni + ribavirin ± peginterferon x24 weeks~~

~~4) NS5A RAVs detected, no NS3 RAVs detected: Olysio + Sovaldi + ribavirin ± peginterferon x24 weeks~~

~~I.~~J. **Requests for recertification (for treatment beyond 12 weeks) must meet ALL of the following**:

1) Laboratory results for HCV RNA viral load at week 4 and week 6 (if applicable) have been submitted with the PA request

2) HCV Viral load must meet ONE of the following:
   a. Undetectable HCV RNA viral load at week 4
   b. Detectable HCV RNA viral load at treatment week 4 and HCV RNA increased by ≤10-fold (≤1 $\log_{10}$ IU/mL) on repeat testing at treatment week 6 (or thereafter)

3) Recipient is compliant on all drugs in the treatment regimen

2. **Prior Authorization Guidelines:**

A. Prior authorization approval will be granted for a maximum of 12 weeks (unless the requested regimen is less than 12 weeks long or the remaining duration of therapy is less than 12 weeks)
~~**B.** The initial prescription will be limited to a 14-day supply; subsequent refills can be up to 34 days.~~

3. **Quantity Limitations**:
A. Harvoni (ledipasvir/sofosbuvir): 1 tablet/day
B. Viekira Pak (ombitasvir/paritaprevir/ritonavir/dasabuvir): 1 pack/28 days
C. Technivie (ombitasvir/paritaprevir/ritonavir): 1 tablet/day
~~**C.**~~**D.** Zepatier (elbasvir and grazoprevir): 1 tablet/day
~~**D.**~~**E.** Daklinza (daclatasvir): 1 tablet/day
~~**E.**~~**F.** Olysio (simeprevir): 1 capsule/day
~~**F.**~~**G.** Sovaldi (sofosbuvir): 1 tablet/day

Therapeutic Class Overview
Direct Acting Hepatitis C Antivirals and Combinations

Overview/Summary:
The direct acting hepatitis C antiviral and combination products are all Food and Drug Administration (FDA)-approved for the treatment of chronic hepatitis C virus (HCV) infection; although, differences in indications exist relating to use in specific genotypes, with certain combination therapies and other patient factors.[1-6] Daklinza® (daclatasvir) is a once-daily NS5A inhibitor indicated for use with an NS5B polymerase inhibitor Sovaldi® (sofosbuvir) for 12 weeks in the treatment of patients with chronic hepatitis C virus (HCV) genotype 3 infection. It is the first Food and Drug Administration (FDA)-approved all-oral regimen for the HCV genotype 3 infection that does not require co-administration of interferon or ribavirin.[1] Technivie® (ombitasvir/paritaprevir/ ritonavir) in combination with ribavirin is the first interferon-free Food and Drug Administration (FDA)-approved drug for the treatment of HCV genotype 4 infection.[6]

HCV is an enveloped ribonucleic acid virus that is transmitted through exposure with infected blood and is the most common bloodborne infection in the United States, with an estimated prevalence of 3.2 million people chronically infected. Chronic HCV develops in 70 to 85% of HCV-infected persons and is associated with significant morbidity (e.g., cirrhosis, hepatocellular carcinoma [HCC]) and is the leading cause of liver transplantation.[8,9] The average annual incidence rate of HCC in the U.S. between 2001 and 2006 was 3.0 per 100,000 people, with 48% to cases attributed to HCV.[10] These agents act via several different mechanisms of action to exert their therapeutic effect.[1-7] Daclatasvir (Daklinza) binds to the N-terminus of NS5A, a nonstructural protein encoded by HCV, and inhibits both viral ribonucleic acid (RNA) replication and virion assembly.[1] Simeprevir (Olysio®) works via inhibition of the HCV NS3/4A protease of HCV genotype 1a and 1b, thus preventing replication of HCV host cells.[2] Similarly, sofosbuvir (Sovaldi®) inhibits HCV NS5B polymerase which also prevents the replication of HCV host cells, however, it is active against multiple genotypes of HCV.[3] The three combination products that include direct acting hepatitis C antivirals include ledipasvir/sofosbuvir (Harvoni®), ombitasvir/paritaprevir/ritonavir (Technivie®), and a 4-drug regimen of ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak®). Paritaprevir and dasabuvir exert their mechanisms of action in the same was as other agents and inhibit NS3/4A protease and NS5B polymerase, respectively. Ledipasvir and Ombitasvir work along the same line as the other agents, but specifically inhibit HCV non-structural protein NS5A. Ritonavir, when used in Technivie® and Viekira Pak®, is used as a boosting agent that increases the peak and trough plasma drug concentrations of paritaprevir along with overall drug exposure; it has no direct effect on the hepatitis C virus.[4-6] Specific indications for each of the direct acting hepatitis C antiviral agents are listed in Table 1.

Efficacy of these agents have been established in multiple clinical trials with numerous clinical trials still underway.[11-33] Newly published guidelines developed by the American Association for the Study of Liver Diseases, Infectious Diseases Society of America and International Antiviral Society-USA have included all current treatments in their recommendations.[41] Generally speaking, combination regimens that include newer direct hepatis C antivirals are preferred over older pegylated interferon-based regimens (including those containing older protease inhibitors) due to a higher sustained virologic response (SVR) rate, improved side effects profile, and reduced pill burden. However, many different regimens with direct-acting agents or combinations, which may or may not also include ribavirin or pegylated interferon, are recommended based on HCV genotype, previous treatment experience and certain special populations.[41-43] Currently, there are no generic direct-acting antivirals available.

Table 1. Current Medications Available in Therapeutic Class[1-7]

Generic (Trade Name)	FDA Approved Indications	Dosage Form/Strength	Generic Availability
Single Entity Agents			
Daclatasvir (Daklinza®)	Treatment of chronic HCV genotype 3 infection in adults as part of a combination antiviral regimen	Tablet: 30 mg 60 mg	-
Simeprevir (Olysio®)	Treatment of chronic HCV genotype 1,4 infection in adults as part of a combination	Capsule: 150 mg	-

Generic (Trade Name)	FDA Approved Indications	Dosage Form/Strength	Generic Availability
	antiviral regimen		
Sofosbuvir (Sovaldi®)	Treatment of chronic HCV genotype 1, 2, 3, and 4 infection in adults as part of a combination antiviral regimen	Tablet: 400 mg	-
Combination Products			
Ledipasvir/sofosbuvir (Harvoni®)	Treatment of chronic HCV genotype 1, 4, 5, and 6 infection in adults as part of a combination antiviral regimen	Tablet: 90/400 mg	-
Ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak®)	Treatment of chronic HCV genotype 1 infection in adults as part of a combination antiviral regimen	Tablet (dasabuvir): 250 mg Tablet (ombitasvir/ paritaprevir/ ritonavir): 12.5/75/50 mg	-
Ombitasvir/paritaprevir/ ritonavir (Technivie®)	Treatment of chronic HCV genotype 4 infection in adults as part of a combination antiviral regimen	Tablet: 12.5/75/50 mg	-

FDA=Food and drug administration, HCV=hepatitis C virus

Evidence-based Medicine

- The clinical trials demonstrating the safety and efficacy of the direct acting hepatitis C antivirals are outlined in Table 4.[12-40] Overall, data from clinical trials support the FDA-approved indications and dosing recommendations for these agents.
- The FDA approval of Daklinza® (daclatasvir) was based on the results of ALLY-3, an open-label study evaluating 12 week regimen of daclatasvir 60 mg plus sofosbuvir 400 mg in treatment-naive and treatment-experienced patients with chronic HCV genotype 3 infection. The primary endpoint was the SVR at post treatment week 12 (SVR12). High SVR12 rates were observed among patients without cirrhosis: 97% (73/75) and 94% (32/34) in treatment-naïve and treatment-experienced patients, respectively. In contrast, SVR12 rates in cirrhotic patients were much lower: 58% (11/19) and 69% (9/13) in treatment-naïve and treatment-experienced patients, respectively.[32]
    - An ongoing randomized phase III study is evaluating a combination of daclatasvir, sofosbuvir and ribavirin for 12 or 16 weeks to determine whether the addition of ribavirin or extending treatment duration improved SVR rates in cirrhotic patients with HCV genotype 3 infection.[33]
- The efficacy of simeprevir (Olysio®) in patients with HCV genotype 1 infection was evaluated in several unpublished studies, including two phase III trials in treatment-naïve patients (QUEST 1 and QUEST 2), one phase III trial in patients who relapsed after prior interferon-based therapy (PROMISE).[2]
    - In the pooled analysis of QUEST 1 and QUEST 2, a greater proportion of patients in the simeprevir group achieved SVR at 12 weeks (SVR12) compared to control group (80 vs 50%; P value not reported).[2]
- The safety and efficacy of simeprevir in combination with sofosbuvir with or without ribavirin for the treatment of hepatitis C genotype 1 was evaluated in the COSMOS trial. Cohort 1 included prior null responders with METAVIR scores F0 to F2 and Cohort 2 included prior null responders and treatment-naïve patients with METAVIR scores F3 to F4.[2,26]
    - SVR at 12 weeks post therapy (SVR12) was achieved in 92% of the patients in the the intention to treat (ITT) population. SSVR12 for Cohort 1 and Cohort 2 were 90% (95% CI, 81 to 96) and 94% (95% CI, 87 to 98), respectively. The results were not significantly altered by use of ribavirin, duration of treatment, or treatment history (no P values reported). [20]

- The FDA approval of sofosbuvir was based on the results of five phase III trials (N=1,724) in HCV mono-infected patients (genotypes 1 to 6) and one unpublished phase III trial (N=223) in HCV/HIV-1 co-infected patients (HCV genotype 1, 2 or 3).[12,30,31]
    - All trials utilized SVR12 as the primary endpoint and overall, these studies showed that sofosbuvir provided a significant improvement in SVR12 compared with control in both treatment-naïve and treatment-experienced patients.[12,30,31]
    - Sofosbuvir was not specifically studied in treatment-experienced patients with HCV genotype 1 infection. According to the prescribing information, the estimated response rate in patient who previously failed treatment with peginterferon alfa and ribavirin is 71%. This is based on the observed response rate in patients from the NEUTRINO study.[12]
- The FDA-approval of Zepatier® (elbasvir/grazoprevir) was based on two placebo-controlled trials and four uncontrolled phase II and III clinical trials in 1,401 patients with genotype HCV genotype 1, 4, or 6 chronic HCV with compensated liver disease (C-EDGE TN, C-EDGE COINFECTION, C-SURFER, C-SCAPE, C-EDGE TE, and C-SALVAGE). All clinical trials evaluated SVR12 as the primary endpoint. Elbasvir/grazoprevir was administered once daily in all trials and ribavirin, if received, was dosed by weightd.[4,13-19]
    - After 12 weeks to therapy, SVR12 rates in C-EDGE TN were 91.7% (genotype 1a), 98.5% (genotype 1b), 100% (genotype 4), and 80% (genotype 6). SVR12 was achieved in 97.1% of cirrhotic patients and 93.9% (231/246) of noncirrhotic patients.[13] After 12 weeks to therapy, SVR12 rates in C-EDGE COINFECTION (HIV-coinfection) were 96.5% (genotype 1a), 95.5% (genotype 1b), 96.4% (genotype 4), and 100% (genotype 6) with 100% of cirrhotic patients. All 35 patients with cirrhosis achieved SVR12.[14] The SVR12 rate after 12 weeks of therapy in C-SURFER (chronic kidney disease) was 99.1%.[15] The overall SVR12 rate in C-SALVAGE (genotype 1, previously failed ≥4 weeks of peginterferon alfa and ribavirin combined with a protease inhibitor [boceprevir, telaprevir, or simeprevir]) was 96.2% overall, including 91.2% in patients with baseline NS3 resistance, and 94.1% (32/34) in cirrhotic patients.[16,17] C-WORTHY (N=471) was a phase II, randomized, parallel-group, multicenter, open-label study comparing grazoprevir plus elbasvir with or without ribavirin in different patient populations (20 arms total) with chronic HCV genotype 1 infection. SVR12 rates ranged from 80% to 100%.[18,19]
- The FDA approval of combination ledipasvir/sofosbuvir was based on the results of three phase III trials (N=1,518) in HCV mono-infected subjects with genotype 1 infection who had compensated liver disease. Treatment duration was fixed in each trial and was not guided by subjects' HCV RNA levels.[20,21,25]
    - ION-1 evaluated treatment-naïve patients include patients with cirrhosis; ION-2 evaluated patients with or without cirrhosis who failed previous therapy with an interferon-based regimen including those containing an HCV protease inhibitor; ION-3 evaluated non-cirrhotic, treatment-naïve patients.[20,21,25]
    - All studies showed that ledipasvir/sofosbuvir significantly improved SVR12 rate compared to control. [20,21,25]
- The FDA approval of ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira Pak®) was based on the results of six randomized, multicenter, clinical trials (N=2,308) in HCV patients with genotype 1, including one trial exclusively in patients with cirrhosis and mild hepatic impairment (Child-Pugh A). All studies included at least one treatment arm with ribavirin, while several studies included treatment arms without ribavirin.[22-24,27,28]
    - Study populations for each of the studies include treatment-naïve, non-cirrhotic adults with HCV genotype 1 infection (SAPPHIRE-I), treatment-naïve, non-cirrhotic adults with HCV genotype 1b and HCV genotype 1a infections (PEARL-III and PEARL-IV, respectively), treatment-naïve or previously treated with peginterferon alfa and ribavirin cirrhotic adults with HCV genotype 1 infection (TURQUOISE-II), noncirrhotic adults with HCV genotype 1 infection who either relapsed or were nonresponders to prior peginterferon alfa and ribavirin therapy (SAPPHIRE-II) and finally, non-cirrhotic adults with HCV genotype 1b infection who either relapsed or were nonresponders to prior peginterferon alfa and ribavirin therapy (PEARL-II).[22-24,27,28]
    - Overall, SVR12 rates were high and significantly improved compared with control after 12 weeks of therapy.[22-24,27,28] Only TURQUOISE-II evaluated patients beyond 12 weeks of

therapy and found there was no difference between 12 weeks of therapy compared with 24 weeks of therapy (P=0.09).[24]

- The FDA-approval of Technivie® (ombitasvir/paritaprevir/ritonavir) in the treatment of HCV genotype 4 was based on the results of an open-label, randomized, multicenter phase IIb PEARL-I study, which evaluated ombitasvir/paritaprevir/ritonavir with or without ribavirin and no cirrhosis. Patients were either treatment-naïve or treatment experienced (prior failure of peginterferon alfa and ribavirin). In treatment-naive patients, the SVR12s were 100% (42/42) in the ribavirin-containing regimen and 90.9% (40/44) in the ribavirin-free regimen. In the treatment-naive group without ribavirin, on-treatment virologic breakthrough was reported in one patient (2%), two patients (5%) experienced post-treatment relapse, and one patient (2%) was lost to follow-up. All 49 treatment-experienced patients in the ribavirin-containing group achieved SVR12.[34]
    - AGATE-I is an ongoing phase III study evaluating ombitasvir/paritaprevir/ritonavir with ribavirin for 12, 16 or 24 weeks in cirrhotic patients with HCV genotype 4 infection, including treatment-naïve patients and those who have failed peginterferon alfa and ribavirin or sofosbuvir-containing regimens.[35]
    - TURQUOISE-CPB is another ongoing phase III study evaluating ombitasvir/paritaprevir/ritonavir with ribavirin for 24 weeks in patients with HCV genotype 4 infection and decompensated cirrhosis.[36]
    - Several other studies are planned or recruiting patients to evaluate ombitasvir/paritaprevir/ritonavir with or without ribavirin in less well studied subpopulations with HCV genotype 4 infection, including severe renal disease, children (three to 17 years old), and status post successful treatment of early stage hepatocellular carcinoma.[37-40]

Key Points within the Medication Class

- American Association for the Study of Liver Diseases, Infectious Diseases Society of America and International Antiviral Society-USA have included all current treatments in their guideline.[41]
- Old standards of therapy, including pegylated interferon alfa and ribavirin dual therapy and pegylated interferon alfa, ribavirin along with a protease inhibitor triple therapy are no longer recommended.
- Current, first-line therapies recommended in the new guidelines include all-oral combination therapies, each of which generally has at least one polymerase inhibitor and one other direct-acting agent that acts via a different mechanism of action.
- Each of the new HCV direct acting antivirals are recommended as part of a first-line regimen for at least one genotype and/or patient population.[41]
- Depending on genotype, previous treatment-experience and special populations, the recommended regimens and durations of treatment vary due to differences in efficacy provided by clinical trials.
    - For genotype 1, five regimens with similar efficacy are recommended. Duration and addition of ribavirin depend on cirrhosis status and/or previous treatment failures.
        - Daclatasvir 60 mg daily (QD) + sofosbuvir 400 mg QD ± ribavirin for 12 to 24 weeks
        - Ledipasvir/sofosbuvir 90/400 mg QD ± ribavirin for 12 to 24 weeks
        - Paritaprevir/ritonavir/ombitasvir 150/100/25 mg QD + dasabuvir 250 mg twice-daily (BID) ± ribavirin for 12 to 24 weeks
        - Sofosbuvir 400 mg QD + simeprevir 150 mg QD for 12 weeks
        - Elbasvir/grazoprevir 50/100 mg QD 12.5/75/50 mg ± ribavirin for 12 to 16 weeks
    - For genotype 2:
        - sofosbuvir 400 mg QD + ribavirin for 12 weeks (16 to 24 weeks with cirrhosis)
        - Daclatasvir 60 mg QD + sofosbuvir (4000 mg) for 12 weeks
    - For genotype 3:
        - Daclatasvir (60 mg) and sofosbuvir (400 mg) ± ribavirin for 12 weeks
        - sofosbuvir 400 mg QD + ribavirin + weekly peginterferon for 12 weeks
    - For Genotype 4:
        - Ledipasvir/sofosbuvir 90/400 mg QD ± ribavirin for 12 weeks to 24 weeks
        - Paritaprevir/ritonavir/ombitasvir 150/100/25 QD + ribavirin for 12 weeks
        - Elbasvir/grazoprevir 50/100 mg QD 12.5/75/50 mg ± ribavirin for 12 to 16 weeks
    - Genotype 5 and 6:
        - Ledipasvir/sofosbuvir 90/400 mg QD for 12 weeks

  - In patients that fail a sofosbuvir, daclatasvir, ledipasvir/sofosbuvir, or paritaprevir/ritonavir/ombitasvir plus dasabuvir, it is recommended to defer therapy if they have minimal liver disease; guidelines do not offer a specific regimen for recipients with extensive liver disease, but recommend resistance-testing. They recommend treatment for at least 24 weeks with ribavirin, if not contraindicated.[4]

- Other Key Facts:
  - There are also disparities between the FDA-approved indications and first-line recommendations according to the AASLD-IDSA guidelines.[1-7,33]
  - Prior to initiating therapy with simeprevir (in combination with sofosbuvir) in cirrhotic patients with genotype 1a, they should be screened for the presence of NS3 Q80K polymorphism. Alternative therapy should be considered if this polymorphism is present.[2]
  - When prescribing ombitasvir/paritaprevir/ritonavir (Technivie®) or ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak®), screening for drugs that should not be coadministered is recommended due to many, often severe, drug interactions.[5,6]
  - Dose of daclatasvir must be adjusted when given with strong CYP3A inhibitors (30 mg QD) and moderate CYP3A inducers (90 mg QD).[1]
  - Testing for NS5A-associated resistance is recommended prior to treatment with elbasvir/grazoprevir for several patient populations with genotype 1. Treatment length must be extended if the patient has resistance to elbasvir.[4]

References

1. Daklinza® [package insert]. Princeton (NJ): Bristol-Myers Squibb Company; 2016 Apr.
2. Olysio® [package insert]. Titusville (NJ): Janssen Therapeutics; 2016 May.
3. Sovaldi® [package insert]. Foster City (CA): Gilead Sciences, Inc.; 2015 Aug.
4. Zepatier® [package insert on the internet]. Whitehouse Station (NJ): Merck and Co., Inc; 2016 January [cited 2016 Jan 29]. Available from: http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf.
5. Harvoni® [package insert]. Foster City (CA): Gilead Sciences, Inc.; 2016 Feb.
6. Viekira Pak® [package insert]. North Chicago (IL): AbbVie; 2016 Apr.
7. Technivie® [package insert on the internet]. North Chicago (IL): AbbVie; 2016 Jan.
8. Micromedex® 2.0 [database on the Internet]. Greenwood Village (CO): Truven Health Analytics; Updated periodically [cited 2015 Nov 25]. Available from http://www.micromedexsolutions.com/.
9. Workowski KA, Berman S; Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep. 2010 Dec 17;59(RR-12):1-110.
10. Ghany MG, Strader DB, Thomas DL, Seeff LB; American Association for the Study of Liver Diseases. Diagnosis, Management and treatment of hepatitis C; An Update. 2009. Hepatology 2009; 49(4):1-40.
11. Ng J, Wu J. Hepatitis B- and hepatitis C-related hepatocellular carcinomas in the United States: similarities and differences. Hepat Mon. 2012 Oct;12(10 HCC):e7635.
12. Lawitz E, Mangia A, Wyles D, Rodriguez-Torres M, Hassanein T, Gordon SC, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med. 2013 May 16;368(20):1878-87.
13. Zeuzem S, Ghalib R, Reddy KR, Pockros PJ, Ben Ari Z, Zhao Y, et al. Grazoprevir-Elbasvir Combination Therapy for Treatment-Naive Cirrhotic and Noncirrhotic Patients With Chronic Hepatitis C Virus Genotype 1, 4, or 6 Infection: A Randomized Trial. Ann Intern Med. 2015 Jul 7;163(1):1-13.
14. Rockstroh JK, Nelson M, Katlama C, Lalezari J, Mallolas J, Bloch M, et al. Efficacy and safety of grazoprevir (MK-5172) and elbasvir (MK-8742) in patients with hepatitis C virus and HIV co-infection (C-EDGE COINFECTION): a non-randomised, open-label trial. Lancet HIV. 2015 Aug;2(8):e319-27.
15. Roth D, Nelson DR, Bruchfeld A, Liapakis A, Silva M, Monsour H Jr, et al. Grazoprevir plus elbasvir in treatment-naive and treatment-experienced patients with hepatitis C virus genotype 1 infection and stage 4-5 chronic kidney disease (the C-SURFER study): a combination phase 3 study. Lancet. 2015 Oct 17;386(10003):1537-45.
16. Forns X, Gordon SC, Zuckerman E, Lawitz E, Calleja JL, Hofer H, et al. Grazoprevir and elbasvir plus ribavirin for chronic HCV genotype-1 infection after failure of combination therapy containing a direct-acting antiviral agent. J Hepatol. 2015 Sep;63(3):564-72.
17. Buti M, Gordon SC, Zuckerman E, Lawitz E, Calleja JL, Hofer H, et al. Grazoprevir, Elbasvir, and Ribavirin for Chronic Hepatitis C Virus Genotype 1 Infection After Failure of Pegylated Interferon and Ribavirin With an Earlier-Generation Protease Inhibitor: Final 24-Week Results From C-SALVAGE. Clin Infect Dis. 2016 Jan 1;62(1):32-6.
18. Lawitz E, Gane E, Pearlman B, Tam E, Ghesquiere W, Guyader D, et al. Efficacy and safety of 12 weeks versus 18 weeks of treatment with grazoprevir (MK-5172) and elbasvir (MK-8742) with or without ribavirin for hepatitis C virus genotype 1 infection in previously untreated patients with cirrhosis and patients with previous null response with or without cirrhosis (C-WORTHY): a randomised, open-label phase 2 trial. Lancet. 2015 Mar 21;385(9973):1075-86.
19. Sulkowski M, Hezode C, Gerstoft J, Vierling JM, Mallolas J, Pol S, et al. Efficacy and safety of 8 weeks versus 12 weeks of treatment with grazoprevir (MK-5172) and elbasvir (MK-8742) with or without ribavirin in patients with hepatitis C virus genotype 1 mono-infection and HIV/hepatitis C virus co-infection (C-WORTHY): a randomised, open-label phase 2 trial. Lancet. 2015 Mar 21;385(9973):1087-97.
20. Afdhal N, Zeuzem S, Kwo P, Chojkier M, Gitlin N, Puoti M, et al. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. N Engl J Med. 2014 May 15;370(20):1889-98.

21. Kowdley KV, Gordon SC, Reddy KR, Rossaro L, Bernstein DE, Lawitz E, et al. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. N Engl J Med. 2014 May 15;370(20):1879-88.
22. Feld JJ, Kowdley KV, Coakley E, Sigal S, Nelson DR, Crawford D, et al. Treatment of HCV with ABT-450/r-ombitasvir and dasabuvir with ribavirin. N Engl J Med. 2014 Apr 24;370(17):1594-603.
23. Ferenci P, Bernstein D, Lalezari J, Cohen D, Luo Y, Cooper C, et al. ABT-450/r-ombitasvir and dasabuvir with or without ribavirin for HCV. N Engl J Med. 2014 May 22;370(21):1983-92.
24. Poordad F, Hezode C, Trinh R, Kowdley KV, Zeuzem S, Agarwal K, et al. ABT-450/r-ombitasvir and dasabuvir with ribavirin for hepatitis C with cirrhosis. N Engl J Med. 2014 May 22;370(21):1973-82.
25. Afdhal N, Reddy KR, Nelson DR, Lawitz E, Gordon SC, Schiff E, et al. Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. N Engl J Med. 2014 Apr 17;370(16):1483-93.
26. Lawitz E, Sulkowski MS, Ghalib R, Rodriguez-Torres M, Younossi ZM, Corregidor A, et al. Simeprevir plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naive patients: the COSMOS randomised study. Lancet. 2014 Jul 26. pii: S0140-6736(14)61036-9.
27. Zeuzem S, Jacobson IM, Baykal T, Marinho RT, Poordad F, Bourlière M, et al. Retreatment of HCV with ABT-450/r-ombitasvir and dasabuvir with ribavirin. N Engl J Med. 2014 Apr 24;370(17):1604-14.
28. Andreone P, Colombo MG, Enejosa JV, Koksal I, Ferenci P, Maieron A, et al. ABT-450, Ritonavir, Ombitasvir, and Dasabuvir Achieves 97% and 100% Sustained Virologic Response With or Without Ribavirin in Treatment-Experienced Patients With HCV Genotype 1b Infection. Gastroenterology. 2014 May 9.
29. Kwo PY, Mantry PS, Coakley E, Te HS, Vargas HE, Brown R Jr, et al. An interferon-free antiviral regimen for HCV after liver transplantation. N Engl J Med. 2014 Dec 18;371(25):2375-82.
30. Jacobson IM, Gordon SC, Kowdley KV, Yoshida EM, Rodriguez-Torres M, Sulkowski MS, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013 May 16;368(20):1867-77.
31. Zeuzem S, Dusheiko GM, Salupere R, Mangia A, Flisiak R, Hyland RH, et al. Sofosbuvir and ribavirin in HCV genotypes
32. Nelson DR, Cooper JN, Lalezari JP, Lawitz E, Pockros PJ, Gitlin N, et al. All-oral 12-week treatment with daclatasvir plus sofosbuvir in patients with hepatitis C virus genotype 3 infection: ALLY-3 phase III study. Hepatology. 2015 Apr;61(4):1127-35.
33. Bristol-Myers Squibb. Safety and Efficacy Study of Daclatasvir 60mg, Sofosbuvir 400mg, and Ribavirin (Dosed Based Upon Weight) in Subjects With Chronic Genotype 3 Hepatitis C Infection With or Without Prior Treatment Experience and Compensated Advanced Cirrhosis for 12 or 16 Weeks. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Aug 5]. Available https://clinicaltrials.gov/ct2/show/NCT02319031 NLM Identifier: NCT02319031.
34. Hézode C, Asselah T, Reddy KR, Hassanein T, Berenguer M, Fleischer-Stepniewska K, et al. Ombitasvir plus paritaprevir plus ritonavir with or without ribavirin in treatment-naive and treatment-experienced patients with genotype 4 chronic hepatitis C virus infection (PEARL-I): a randomised, open-label trial. Lancet. 2015 Jun 20;385(9986):2502-9.
35. AbbVie. A Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Ombitasvir/ABT-450/Ritonavir Co-administered With Ribavirin (RBV) in Adults With Genotype 4 Chronic Hepatitis C Virus (HCV) Infection and Cirrhosis (AGATE-1). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Aug 5]. Available https://clinicaltrials.gov/ct2/show/NCT02265237 NLM Identifier: NCT02265237.
36. AbbVie. A Study to Evaluate the Safety and Efficacy of Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir with Ribavirin in Adults with Genotype 1 and Ombitasvir/Paritaprevir/Ritonavir with Ribavirin in Adults with Genotype 4 Chronic Hepatitis C Virus Infection and Decompensated Cirrhosis (TURQUOISE-CPB). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Aug 5]. Available https://clinicaltrials.gov/ct2/show/NCT02219477 NLM Identifier: NCT02219477.
37. AbbVie. Ombitasvir/Paritaprevir/Ritonavir with or without Dasabuvir in Adults with Genotype 1a or Genotype 4 Chronic Hepatitis C Virus (HCV) Infection, with Severe Kidney Impairment or End Stage Kidney Disease. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Aug 5]. Available https://clinicaltrials.gov/ct2/show/NCT02487199 NLM Identifier: NCT02487199.
38. AbbVie. Ombitasvir/Paritaprevir/Ritonavir with or without Dasabuvir in Adults with Genotype 1a or Genotype 4 Chronic Hepatitis C Virus (HCV) Infection, With Severe Kidney Impairment or End Stage Kidney Disease. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Aug 5]. Available https://clinicaltrials.gov/ct2/show/NCT02487199 NLM Identifier: NCT02487199.
39. AbbVie. A Study to Evaluate Treatment of Hepatitis C Virus Infection in Pediatric Subjects (Zircon). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Aug 5]. Available https://clinicaltrials.gov/ct2/show/NCT02486406 NLM Identifier: NCT02486406.
40. AbbVie. A Study to Evaluate the Safety and Efficacy of Ombitasvir/Paritaprevir/r with or without Dasabuvir and with Ribavirin in Chronic Hepatitis C Virus Genotype 1 or 4 Infected Adults with Successfully Treated Early Stage Hepatocellular Carcinoma. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Aug 5]. Available https://clinicaltrials.gov/ct2/show/NCT02504099 NLM Identifier: NCT02504099.
41. American Association for the Study of Liver Diseases (AASLD), Infectious Diseases Society of America (IDSA), International Antiviral Society-USA (IAS-USA). Recommendations for testing, managing, and treating hepatitis C [guideline on the Internet]. Alexandria (VA): AASLD/IDSA/IAS-USA 2015 Dec [cited 2016 Jan 29]. Available at: http://www.hcvguidelines.org.
42. Department of Veteran Affairs National Hepatitis C Resource Center Program and the Office of Public Health. Chronic hepatitis C Virus (HCV) infection: Treatment considerations [guideline on the Internet]. Washington (DC): VA 2015 July [cited 2015 July 31]. Available at: http://www.hepatitis.va.gov/pdf/treatment-considerations-2015-07.pdf.
43. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2015. J Hepatol. 2015 Jul;63(1):199-236.

Product Counts

April 1, 2016 - June 30, 2016

Count of Products	Count of Members
2	2308
3	339
4	49
5	5
6	3
Grand Total	**2704**

Products:

HYDROCODONE/ACETAMINOPHEN
OXYCODONE HCL
OXYCODONE/ACETAMINOPHEN

Top 25 Short Acting Opioids by Total Qty

Solid Oral Dosage Forms Only

October 1, 2015 - June 30, 2016

Short or Long acting	Short Acting
Dosage Form	(Multiple Items)

Row Labels	Claim count	Member Count	Total Qty	Days Supply	Pharmacy Paid
HYDROCODONE/ACETAMINOPHEN	51,056	47,372	3,733,869	987,689	$ 1,178,043.81
OXYCODONE HCL	18,094	16,500	1,959,645	462,384	$ 678,554.71
OXYCODONE/ACETAMINOPHEN	24,029	21,997	1,903,937	481,368	$ 1,286,394.63
TRAMADOL HCL	12,835	11,989	920,869	243,500	$ 139,555.01
HYDROMORPHONE HCL	1,742	1,517	148,868	35,848	$ 37,789.60
MORPHINE SULFATE	1,167	1,065	103,252	29,883	$ 32,455.03
ACETAMINOPHEN/CODEINE #3	1,703	1,592	54,594	14,683	$ 22,472.05
ACETAMINOPHEN/CODEINE PHO	1,520	1,459	52,399	14,181	$ 20,040.56
SUBOXONE	1,475	928	37,146	24,140	$ 274,532.14
ACETAMINOPHEN/CODEINE	419	360	35,317	8,201	$ 11,381.27
BUTALBITAL/ACETAMINOPHEN/	502	424	28,490	7,505	$ 74,900.41
OXYMORPHONE HYDROCHLORIDE	241	229	24,042	7,048	$ 52,503.27
ENDOCET	231	228	21,918	5,703	$ 15,631.90
TRAMADOL HYDROCHLORIDE/AC	396	386	21,456	5,329	$ 8,113.75
HYDROCODONE/IBUPROFEN	212	200	15,167	3,793	$ 11,343.89
HYDROCODONE BITARTRATE/AC	191	188	10,156	2,816	$ 14,870.22
VICODIN HP	102	92	9,149	2,474	$ 16,947.78
NUCYNTA	96	81	8,988	2,390	$ 48,281.42
BUTALBITAL/ASPIRIN/CAFFEI	88	66	5,490	1,232	$ 8,273.55
PRIMLEV	34	33	3,237	938	$ 48,830.96
VICODIN	95	94	2,847	649	$ 3,789.44
VICODIN ES	48	45	2,373	726	$ 3,270.87
ACETAMINOPHEN/CODEINE #4	27	26	2,170	670	$ 694.38
ASCOMP/CODEINE	35	23	1,585	369	$ 2,492.88
MEPERIDINE HCL	39	37	1,490	452	$ 940.43
Grand Total	**116,377**	**106,931**	**9,108,454**	**2,343,971**	**$ 3,992,103.96**

Hepatitis C - Therapy Compliance

October 1, 2015 - May 31, 2016

Encrypted ID	Sum of Total Qty	Sum of Days Supply	Sum of Amt Paid
22227301654	**14**	**14**	**$ 16,069.76**
HARVONI	**14**	**14**	**$ 16,069.76**
201510	14	14	$ 16,069.76
77779725229	**14**	**14**	**$ 15,356.84**
HARVONI	**14**	**14**	**$ 15,356.84**
201605	14	14	$ 15,356.84
44444523297	**14**	**14**	**$ 16,069.76**
HARVONI	**14**	**14**	**$ 16,069.76**
201510	14	14	$ 16,069.76
11114250566	**14**	**14**	**$ 16,069.76**
HARVONI	**14**	**14**	**$ 16,069.76**
201510	14	14	$ 16,069.76
53996966667	**14**	**14**	**$ 15,356.84**
HARVONI	**14**	**14**	**$ 15,356.84**
201605	14	14	$ 15,356.84
22222392668	**14**	**14**	**$ 15,356.84**
HARVONI	**14**	**14**	**$ 15,356.84**
201605	14	14	$ 15,356.84
55554631448	**14**	**14**	**$ 15,356.84**
HARVONI	**14**	**14**	**$ 15,356.84**
201605	14	14	$ 15,356.84
11117236082	**56**	**14**	**$ 13,648.10**
VIEKIRA PAK	**56**	**14**	**$ 13,648.10**
201605	56	14	$ 13,648.10
66660759953	**14**	**14**	**$ 15,356.84**
HARVONI	**14**	**14**	**$ 15,356.84**
201605	14	14	$ 15,356.84
00006006350	**14**	**14**	**$ 15,356.84**
HARVONI	**14**	**14**	**$ 15,356.84**
201605	14	14	$ 15,356.84
66662741437	**14**	**14**	**$ 16,069.76**
HARVONI	**14**	**14**	**$ 16,069.76**
201510	14	14	$ 16,069.76
44447586330	**28**	**28**	**$ 32,134.76**
HARVONI	**28**	**28**	**$ 32,134.76**
201510	28	28	$ 32,134.76
55558672368	**28**	**28**	**$ 30,713.68**
HARVONI	**28**	**28**	**$ 30,713.68**
201602	28	28	$ 30,713.68
21744366667	**28**	**28**	**$ 30,713.68**
HARVONI	**28**	**28**	**$ 30,713.68**
201512	28	28	$ 30,713.68
00007196520	**28**	**28**	**$ 32,134.76**
HARVONI	**28**	**28**	**$ 32,134.76**

Encrypted ID	Sum of Total Qty	Sum of Days Supply	Sum of Amt Paid
201510	28	28	$ 32,134.76
05597144445	**140**	**28**	**$ 278.52**
RIBAVIRIN	**140**	**28**	**$ 278.52**
201510	140	28	$ 278.52
99995064944	**28**	**28**	**$ 32,139.52**
HARVONI	**28**	**28**	**$ 32,139.52**
201510	28	28	$ 32,139.52
33331453399	**28**	**28**	**$ 30,713.68**
HARVONI	**28**	**28**	**$ 30,713.68**
201605	28	28	$ 30,713.68
42105388889	**28**	**28**	**$ 32,134.76**
HARVONI	**28**	**28**	**$ 32,134.76**
201510	28	28	$ 32,134.76
11117238701	**28**	**28**	**$ 32,134.76**
HARVONI	**28**	**28**	**$ 32,134.76**
201510	28	28	$ 32,134.76
00001165845	**28**	**28**	**$ 28,569.52**
SOVALDI	**28**	**28**	**$ 28,569.52**
201510	28	28	$ 28,569.52
77777840124	**28**	**28**	**$ 30,713.68**
HARVONI	**28**	**28**	**$ 30,713.68**
201512	28	28	$ 30,713.68
00003132975	**28**	**28**	**$ 31,426.60**
HARVONI	**28**	**28**	**$ 31,426.60**
201510	14	14	$ 16,069.76
201511	14	14	$ 15,356.84
77778737407	**168**	**28**	**$ 113.07**
RIBAVIRIN	**168**	**28**	**$ 113.07**
201604	168	28	$ 113.07
55555768545	**28**	**28**	**$ 30,713.68**
HARVONI	**28**	**28**	**$ 30,713.68**
201605	28	28	$ 30,713.68
11113186406	**28**	**28**	**$ 31,426.60**
HARVONI	**28**	**28**	**$ 31,426.60**
201510	14	14	$ 16,069.76
201511	14	14	$ 15,356.84
55552685135	**28**	**28**	**$ 32,139.52**
HARVONI	**28**	**28**	**$ 32,139.52**
201510	28	28	$ 32,139.52
17508777778	**28**	**28**	**$ 30,713.68**
HARVONI	**28**	**28**	**$ 30,713.68**
201605	28	28	$ 30,713.68
88888073592	**28**	**28**	**$ 30,713.68**
HARVONI	**28**	**28**	**$ 30,713.68**
201605	28	28	$ 30,713.68
88420833334	**28**	**28**	**$ 32,139.52**

Encrypted ID	Sum of Total Qty	Sum of Days Supply	Sum of Amt Paid
HARVONI	**28**	**28**	**$ 32,139.52**
201510	28	28	$ 32,139.52
33339347777	**60**	**30**	**$ 86.40**
RIBAVIRIN	**60**	**30**	**$ 86.40**
201510	60	30	$ 86.40
88884829498	**150**	**30**	**$ 298.07**
RIBAVIRIN	**150**	**30**	**$ 298.07**
201510	150	30	$ 298.07
11111169065	**224**	**42**	**$ 13,804.98**
RIBAVIRIN	**168**	**28**	**$ 156.88**
201605	168	28	$ 156.88
VIEKIRA PAK	**56**	**14**	**$ 13,648.10**
201605	56	14	$ 13,648.10
88885925184	**42**	**42**	**$ 48,204.52**
HARVONI	**42**	**42**	**$ 48,204.52**
201510	42	42	$ 48,204.52
88888067634	**42**	**42**	**$ 46,070.52**
HARVONI	**42**	**42**	**$ 46,070.52**
201604	14	14	$ 15,356.84
201605	28	28	$ 30,713.68
55555612088	**42**	**42**	**$ 46,060.35**
HARVONI	**42**	**42**	**$ 46,060.35**
201605	42	42	$ 46,060.35
77514344445	**154**	**42**	**$ 15,489.27**
HARVONI	**14**	**14**	**$ 15,356.84**
201605	14	14	$ 15,356.84
RIBAVIRIN	**140**	**28**	**$ 132.43**
201605	140	28	$ 132.43
88880991915	**42**	**42**	**$ 46,070.52**
HARVONI	**42**	**42**	**$ 46,070.52**
201604	14	14	$ 15,356.84
201605	28	28	$ 30,713.68
11113216457	**42**	**42**	**$ 46,060.35**
HARVONI	**42**	**42**	**$ 46,060.35**
201604	28	28	$ 30,703.51
201605	14	14	$ 15,356.84
Grand Total	**1778**	**1040**	**$ 963,980.83**

Members With Steroid and Rescue Inhaler

April 1, 2016 - June 30, 2016

Count of Members	Column Labels								
Row Labels	ALBUTEROL SULFATE	LEVALBUTEROL HCL	PROAIR HFA	PROVENTIL HFA	VENTOLIN HFA	XOPENEX	XOPENEX CONCENTRATE	XOPENEX HFA	Grand Total
ADVAIR DISKUS	209	6	502	203	15	4	1	5	945
ADVAIR HFA	15		45	16					76
AEROSPAN	7		8						15
ALVESCO				1					1
ASMANEX HFA	9		11	3					23
ASMANEX TWISTHALER 120 ME	2		3	1					6
ASMANEX TWISTHALER 30 MET	19		22	6				1	48
ASMANEX TWISTHALER 60 MET	7		10	6	1				24
BREO ELLIPTA	9		14	2	3	1	1		30
BUDESONIDE	159	3	23	5	2	8		1	201
DULERA	36		72	24	3	1		3	139
FLOVENT DISKUS	4		15	1					20
FLOVENT HFA	70		147	49	3	3	1	1	274
PULMICORT FLEXHALER	18	1	31	7		1			58
QVAR	127		274	76	2				479
SYMBICORT	186		403	138	16	3		9	755
Grand Total	**877**	**10**	**1580**	**538**	**45**	**21**	**3**	**20**	**3094**

Claims for Short-Acting Without Long Acting

April 1, 2016 - June 30, 2016

Row Labels	Sum of Claims	Count of Enc ID	Sum of Qty	Sum of Days	Sum of Paid
ALBUTEROL SULFATE	2,317	1,736	366,715	31,387	$39,030.80
ALBUTEROL SULFATE ER	5	2	300	150	$436.71
LEVALBUTEROL	1	1	1	1	$5.25
LEVALBUTEROL HCL	22	17	1,806	164	$1,477.93
PROAIR HFA	5,542	3,700	50,754	122,356	$360,296.54
PROAIR RESPICLICK	4	2	4	67	$178.98
PROVENTIL HFA	1,705	1,076	12,335	39,947	$142,844.13
VENTOLIN HFA	229	198	4,212	4,730	$3,492.86
XOPENEX	15	11	3,459	314	$9,083.92
XOPENEX HFA	71	35	1,155	1,796	$5,091.04
Grand Total	**9,911**	**6,778**	**440,740**	**200,912**	**$561,938.16**

Short-Acting Insulin without Long-Acting

October 1, 2015 - June 30, 2016

Row Labels	Count of Me	Sum of Claims	Sum of Qty	Sum of Days	Sum of Paid
APIDRA INJ SOLOSTAR	12	15	255	565	$ 7,503.10
APIDRA INJ U-100	16	50	1,190	1,668	$ 27,409.66
HUMALOG INJ 100/ML	73	233	5,340	7,588	$ 125,624.49
HUMALOG KWIK INJ 100/ML	72	144	2,418	4,887	$ 72,492.90
HUMULIN R INJ U-100	22	37	520	1,192	$ 6,764.78
HUMULIN R INJ U-500	14	56	2,460	1,821	$ 153,718.71
NOVOLIN R INJ RELION	4	4	50	115	$ 124.40
NOVOLIN R INJ U-100	6	16	260	542	$ 3,376.45
NOVOLOG INJ 100/ML	64	187	5,150	5,822	$ 118,924.44
NOVOLOG INJ FLEXPEN	60	106	1,953	4,227	$ 58,706.97
Grand Total	**343**	**848**	**19,596**	**28,427**	**$ 574,645.90**

Long-Acting Insulins without a Short-Acting

October 1, 2015 - June 30, 2016

Row Labels	Count of Me	Sum of Claims	Sum of Qty	Sum of Days	Sum of Paid
HUMULIN N INJ U-100	15	39	593	1,278	$ 7,796.52
HUMULIN N INJ U-100KWP	7	14	240	495	$ 6,529.77
LANTUS INJ 100/ML	269	834	13,350	26,607	$ 326,490.80
LANTUS INJ SOLOSTAR	627	1,932	33,576	73,288	$ 828,329.41
LEVEMIR INJ	59	153	2,700	5,019	$ 68,657.69
LEVEMIR INJ FLEXPEN	2	2	45	190	$ 1,064.37
LEVEMIR INJ FLEXTOUC	195	546	9,672	20,754	$ 260,293.16
NOVOLIN N INJ RELION	17	35	570	1,293	$ 1,418.16
NOVOLIN N INJ U-100	16	41	610	1,501	$ 7,823.95
TOUJEO SOLO INJ 300IU/ML	11	36	216	987	$ 16,090.81
TRESIBA FLEX INJ 200UNIT	1	1	18	28	$ 1,033.66
Grand Total	**1,219**	**3,633**	**61,590**	**131,440**	**$ 1,525,528.30**

Long-Acting Insulins

October 1, 2015 - June 30, 2016

Row Labels	Count of ID	Sum of Claims	Sum of Qty	Sum of Days	Sum of Paid
HUMULIN N INJ U-100	55	158	2,813	4,972	$ 36,441.50
HUMULIN N INJ U-100KWP	15	35	675	1,170	$ 18,248.34
LANTUS INJ 100/ML	674	2,257	38,240	68,608	$ 930,789.00
LANTUS INJ SOLOSTAR	1,458	4,973	90,390	181,422	$ 2,227,387.18
LEVEMIR INJ	171	452	7,080	13,969	$ 184,682.33
LEVEMIR INJ FLEXPEN	4	4	75	330	$ 1,750.95
LEVEMIR INJ FLEXTOUC	483	1,570	30,330	56,197	$ 813,347.12
NOVOLIN N INJ RELION	34	68	1,220	2,299	$ 5,470.84
NOVOLIN N INJ U-100	39	99	1,860	3,560	$ 23,309.28
TOUJEO SOLO INJ 300IU/ML	33	86	575	2,519	$ 42,918.94
TRESIBA FLEX INJ 100UNIT	2	3	45	85	$ 1,311.30
TRESIBA FLEX INJ 200UNIT	3	5	126	142	$ 7,215.28
Grand Total	**2,971**	**9,710**	**173,429**	**335,273**	**$ 4,292,872.06**

Short-Acting Insulins

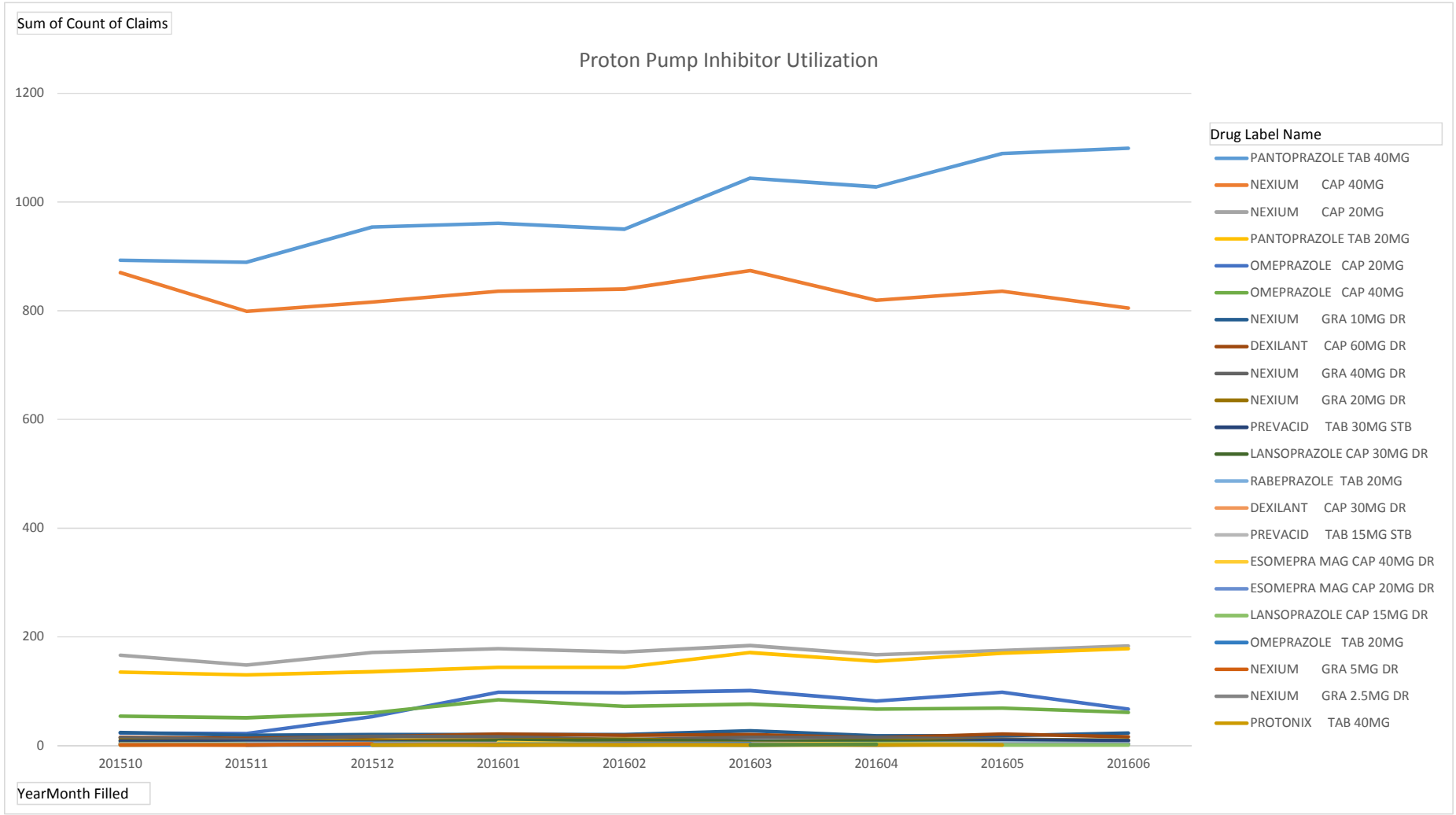
October 1, 2015 - June 30, 2016

Row Labels	Count of ID	Sum of Claims	Sum of Qty	Sum of Days	Sum of Paid
AFREZZA POW 4& 8UNIT	1	2	180	60	$ 525.00
AFREZZA POW 8&12UNIT	1	2	180	60	$ 653.86
APIDRA INJ SOLOSTAR	82	232	4,473	8,224	$ 132,533.17
APIDRA INJ U-100	39	125	2,330	3,877	$ 53,972.45
HUMALOG INJ 100/ML	366	1,084	20,711	34,261	$ 483,958.11
HUMALOG KWIK INJ 100/ML	609	1,939	36,753	67,598	$ 1,092,513.60
HUMALOG KWIK INJ 200/ML	6	9	180	252	$ 10,982.83
HUMULIN R INJ U-100	119	290	4,548	9,017	$ 58,648.33
HUMULIN R INJ U-500	18	63	2,578	2,136	$ 161,356.84
NOVOLIN R INJ RELION	28	59	930	1,769	$ 3,552.12
NOVOLIN R INJ U-100	51	127	1,580	3,953	$ 20,341.78
NOVOLOG INJ 100/ML	239	738	15,640	23,680	$ 359,347.63
NOVOLOG INJ FLEXPEN	522	1,735	32,334	59,976	$ 966,583.66
NOVOLOG INJ PENFILL	10	40	720	1,173	$ 20,611.38
Grand Total	**2,091**	**6,445**	**123,137**	**216,036**	**$ 3,365,580.76**

Proton Pump Inhibitor Utilization

October 1, 2015 - June 30, 2016

Row Labels	Count of Member	Sum of Claims	Sum of Qty	Sum of Days Supply	Sum of Amt Paid
DEXILANT CAP 30MG DR	7	24	720	720	$ 5,552.40
DEXILANT CAP 60MG DR	24	118	3,522	3,522	$ 27,015.27
ESOMEPRA MAG CAP 20MG DR	2	10	300	300	$ 1,374.55
FIRST-OMEPRA SUS 2MG/ML	1	2	600	60	$ 158.74
LANSOPRAZOLE CAP 15MG DR	4	12	600	360	$ 579.27
LANSOPRAZOLE CAP 30MG DR	8	40	1,200	1,200	$ 1,074.64
LANSOPRAZOLE SUS 3MG/ML	1	2	300	60	$ 125.02
NEXIUM CAP 20MG	448	1,623	49,058	48,158	$ 400,173.32
NEXIUM CAP 40MG	1,601	7,627	237,053	227,990	$ 1,977,759.54
NEXIUM GRA 10MG DR	60	185	5,640	5,520	$ 47,921.79
NEXIUM GRA 2.5MG DR	4	7	210	210	$ 1,784.59
NEXIUM GRA 20MG DR	34	90	2,700	2,700	$ 22,688.84
NEXIUM GRA 40MG DR	25	101	3,030	3,030	$ 25,725.18
NEXIUM GRA 5MG DR	6	9	390	270	$ 3,266.77
OMEPRA/BICAR CAP 40-1100	2	10	300	300	$ 4,092.60
OMEPRAZOLE CAP 10MG	1	2	60	60	$ 37.43
OMEPRAZOLE CAP 20MG	54	216	7,803	6,423	$ 2,622.93
OMEPRAZOLE CAP 40MG	95	323	9,945	9,645	$ 4,559.97
PANTOPRAZOLE TAB 20MG	493	1,381	41,768	40,906	$ 17,662.59
PANTOPRAZOLE TAB 40MG	2,669	8,336	254,723	248,317	$ 102,599.40
PREVACID TAB 15MG STB	7	22	720	660	$ 9,081.86
PREVACID TAB 30MG STB	11	69	2,366	2,051	$ 29,676.54
PROTONIX INJ 40MG	1	4	56	28	$ 304.64
PROTONIX PAK	1	1	30	30	$ 284.35
PROTONIX TAB 40MG	1	11	450	225	$ 3,602.39
RABEPRAZOLE TAB 20MG	5	30	1,320	900	$ 1,286.14
Grand Total	**5,565**	**20,255**	**624,864**	**603,645**	**$ 2,691,010.76**


Sum of Count of Claims
Proton Pump Inhibitor Utilization
1200
1000
800
600
400
200
0
201510
201511
201512
201601
201602
201603
201604
201605
201606
YearMonth Filled
Drug Label Name
PANTOPRAZOLE TAB 40MG
NEXIUM CAP 40MG
NEXIUM CAP 20MG
PANTOPRAZOLE TAB 20MG
OMEPRAZOLE CAP 20MG
OMEPRAZOLE CAP 40MG
NEXIUM GRA 10MG DR
DEXILANT CAP 60MG DR
NEXIUM GRA 40MG DR
NEXIUM GRA 20MG DR
PREVACID TAB 30MG STB
LANSOPRAZOLE CAP 30MG DR
RABEPRAZOLE TAB 20MG
DEXILANT CAP 30MG DR
PREVACID TAB 15MG STB
ESOMEPRA MAG CAP 40MG DR
ESOMEPRA MAG CAP 20MG DR
LANSOPRAZOLE CAP 15MG DR
OMEPRAZOLE TAB 20MG
NEXIUM GRA 5MG DR
NEXIUM GRA 2.5MG DR
PROTONIX TAB 40MG

Opioid Utilization - By Days Supply

March 1, 2016 - June 30, 2016

Row Labels	Count of Member	Sum of Claims	Sum of Qty	Sum of Days Supp	Sum of Paid Amt
HYDROCODONE/ACETAMINOPHEN	10,457	21,761	1,608,002	426,924	$ 515,226.04
OXYCODONE/ACETAMINOPHEN	4,569	10,115	829,704	212,312	$ 571,636.96
OXYCODONE HCL	2,622	7,967	870,662	207,636	$ 300,857.39
MORPHINE SULFATE ER	1,245	3,888	245,790	111,814	$ 240,290.79
TRAMADOL HCL	3,353	5,724	409,401	108,775	$ 64,747.76
METHADONE HCL	286	987	139,683	27,543	$ 28,711.90
FENTANYL	191	608	6,131	17,227	$ 50,457.97
HYDROMORPHONE HCL	293	664	61,284	15,326	$ 15,208.33
MORPHINE SULFATE	210	532	51,015	13,707	$ 17,329.05
SUBOXONE	195	757	18,256	12,354	$ 137,814.23
OXYCONTIN	124	398	25,731	11,361	$ 219,403.50
ACETAMINOPHEN/CODEINE #3	582	723	23,984	6,779	$ 10,249.17
ACETAMINOPHEN/CODEINE PHO	552	677	23,199	6,234	$ 9,749.60
OXYMORPHONE HYDROCHLORIDE	64	200	16,152	5,880	$ 53,872.86
ACETAMINOPHEN/CODEINE	341	462	52,848	5,638	$ 8,218.00
OPANA ER (CRUSH RESISTANT	54	163	9,797	4,756	$ 89,349.71
HYDROCODONE BITARTRATE/AC	341	408	106,326	3,948	$ 21,476.98
BUTALBITAL/ACETAMINOPHEN/	98	223	12,818	3,405	$ 33,858.18
OXYCODONE HCL ER	37	113	7,320	3,310	$ 65,630.76
EMBEDA	41	77	3,194	2,182	$ 35,016.28
TRAMADOL HYDROCHLORIDE/AC	126	162	8,646	2,152	$ 3,389.08
ENDOCET	52	68	5,908	1,618	$ 4,261.97
HYDROCODONE/IBUPROFEN	46	86	6,671	1,551	$ 5,497.37
NUCYNTA	13	42	3,986	1,071	$ 21,844.97
VICODIN HP	14	40	3,874	975	$ 6,833.87
NUCYNTA ER	12	30	1,746	888	$ 17,748.20
TRAMADOL HCL ER	9	25	810	750	$ 2,815.09
BUTRANS	12	26	104	736	$ 10,281.81
PRIMLEV	11	25	2,607	708	$ 39,977.95
HYDROMORPHONE HCL ER	9	24	990	705	$ 33,711.23
BUTALBITAL/ASPIRIN/CAFFEI	16	37	2,220	586	$ 3,414.76
HYSINGLA ER	5	16	480	480	$ 5,678.57
VICODIN ES	13	21	1,317	442	$ 1,834.07
BUTORPHANOL TARTRATE	6	20	70	420	$ 1,183.22
SUBSYS	7	15	1,800	330	$ 148,071.91
ACETAMINOPHEN/CODEINE #4	5	10	810	280	$ 274.58
NALBUPHINE HCL	2	9	170	253	$ 828.35
ZUBSOLV	7	12	608	237	$ 4,980.51
BUNAVAIL	3	8	367	217	$ 4,036.06
BUPRENORPHINE HCL/NALOXON	4	8	337	199	$ 1,668.98
MEPERIDINE HCL	15	17	666	190	$ 460.96
VICODIN	32	34	899	184	$ 1,231.49
LORTAB	17	20	7,786	174	$ 3,207.41
ASCOMP/CODEINE	10	21	877	165	$ 1,413.91
DURAGESIC	1	5	50	150	$ 4,949.65
KADIAN	2	5	300	150	$ 15,116.65
PENTAZOCINE/NALOXONE HCL	2	8	630	120	$ 1,356.47

Row Labels	Count of Member	Sum of Claims	Sum of Qty	Sum of Days Supp	Sum of Paid Amt
ZOHYDRO ER	3	4	240	120	$ 1,667.43
ACETAMINOPHEN/CAFFEINE/DI	4	5	460	114	$ 1,338.77
FENTANYL CITRATE ORAL TRA	1	3	360	90	$ 4,350.41
OXYCODONE/IBUPROFEN	1	3	180	68	$ 221.55
LEVORPHANOL TARTRATE	1	2	180	60	$ 6,995.34
BUPRENORPHINE HCL	2	4	73	56	$ 167.72
EXALGO	1	1	30	30	$ 770.83
LAZANDA	1	1	8	30	$ 3,638.17
CODEINE SULFATE	1	1	30	15	$ 22.01
ZAMICET	1	1	420	7	$ 173.15
OXYCODONE/ASPIRIN	1	2	15	2	$ 26.58
Grand Total	**26,123**	**57,268**	**4,578,022**	**1,223,434**	**$ 2,854,546.51**

Top 10 Drug Group by Paid Amt

Q4 2015

Class	Drug Class Name	Count of Claims	Pharmacy Paid
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	28,529	$ 8,459,355.17
12	ANTIVIRALS*	4,350	$ 6,786,933.47
85	HEMATOLOGICAL AGENTS - MISC.*	3,468	$ 6,040,891.59
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	41,016	$ 4,252,191.38
27	ANTIDIABETICS*	25,693	$ 4,119,924.90
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	3,839	$ 3,318,535.62
72	ANTICONVULSANTS*	42,061	$ 3,032,148.17
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	6,736	$ 2,312,280.28
65	ANALGESICS - OPIOID*	61,918	$ 2,264,637.31
61	ADHD/ANTI-NARCOLEPSY/ANTI-OBESITY/ANOREX	10,364	$ 1,992,241.63

Q1 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,674	$ 8,547,529.77
12	ANTIVIRALS*	5,953	$ 7,908,302.65
85	HEMATOLOGICAL AGENTS - MISC.*	3,884	$ 6,076,059.01
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	47,005	$ 4,644,538.82
27	ANTIDIABETICS*	29,459	$ 4,390,716.80
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	3,926	$ 3,420,878.79
72	ANTICONVULSANTS*	45,563	$ 3,352,827.10
65	ANALGESICS - OPIOID*	65,228	$ 2,318,478.19
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	4,070	$ 2,245,267.23
61	ADHD/ANTI-NARCOLEPSY/ANTI-OBESITY/ANOREX	10,669	$ 2,231,944.62

Q2 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
85	HEMATOLOGICAL AGENTS - MISC.*	3,970	$ 9,497,316.28
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,573	$ 8,642,955.08
12	ANTIVIRALS*	4,621	$ 8,447,604.50
27	ANTIDIABETICS*	29,216	$ 4,509,734.45
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	42,939	$ 4,448,011.15
72	ANTICONVULSANTS*	45,833	$ 3,494,343.07
21	ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	3,908	$ 3,471,390.82
30	ENDOCRINE AND METABOLIC AGENTS - MISC.*	4,096	$ 2,518,757.46
65	ANALGESICS - OPIOID*	63,977	$ 2,340,525.75
61	ADHD/ANTI-NARCOLEPSY/ANTI-OBESITY/ANOREX	10,463	$ 2,191,365.76

Top 10 Drug Group by Claim Count

Q4 2015

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	61,918	$ 2,264,637.31
72	ANTICONVULSANTS*	42,061	$ 3,032,148.17
58	ANTIDEPRESSANTS*	41,113	$ 1,028,273.96
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	41,016	$ 4,252,191.38
36	ANTIHYPERTENSIVES*	33,205	$ 346,303.03
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	28,529	$ 8,459,355.17
39	ANTIHYPERLIPIDEMICS*	26,047	$ 893,740.49
27	ANTIDIABETICS*	25,693	$ 4,119,924.90
57	ANTIANXIETY AGENTS*	24,862	$ 256,278.70
66	ANALGESICS - ANTI-INFLAMMATORY*	23,819	$ 1,343,991.15

Q1 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	65,228	$ 2,318,478.19
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	47,005	$ 4,644,538.82
72	ANTICONVULSANTS*	45,563	$ 3,352,827.10
58	ANTIDEPRESSANTS*	44,597	$ 811,842.98
36	ANTIHYPERTENSIVES*	36,373	$ 395,972.40
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,674	$ 8,547,529.77
27	ANTIDIABETICS*	29,459	$ 4,390,716.80
39	ANTIHYPERLIPIDEMICS*	28,268	$ 920,798.52
57	ANTIANXIETY AGENTS*	26,426	$ 292,794.40
49	ULCER DRUGS*	25,554	$ 1,228,607.26

Q2 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
65	ANALGESICS - OPIOID*	63,977	$ 2,340,525.75
72	ANTICONVULSANTS*	45,833	$ 3,494,343.07
58	ANTIDEPRESSANTS*	44,834	$ 865,277.92
44	ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	42,939	$ 4,448,011.15
36	ANTIHYPERTENSIVES*	36,743	$ 462,472.16
59	ANTIPSYCHOTICS/ANTIMANIC AGENTS*	30,573	$ 8,642,955.08
27	ANTIDIABETICS*	29,216	$ 4,509,734.45
39	ANTIHYPERLIPIDEMICS*	28,413	$ 846,948.15
57	ANTIANXIETY AGENTS*	26,447	$ 291,807.39
66	ANALGESICS - ANTI-INFLAMMATORY*	25,907	$ 1,645,980.08

Top 10 Drug Classes by Paid Amt

Q4 2015

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	97	$ 5,443,221.59
5925	QUINOLINONE DERIVATIVES**	4,102	$ 3,932,817.79
1235	HEPATITIS AGENTS**	253	$ 3,826,362.18
2710	INSULIN**	7,946	$ 2,896,856.96
1210	ANTIRETROVIRALS**	2,445	$ 2,810,481.30
4420	SYMPATHOMIMETICS**	27,801	$ 2,544,387.58
7260	ANTICONVULSANTS - MISC.**	30,082	$ 2,010,100.97
5907	BENZISOXAZOLES**	6,776	$ 1,780,266.62
5940	ANTIPSYCHOTICS - MISC.**	2,988	$ 1,348,488.13
6240	MULTIPLE SCLEROSIS AGENTS**	280	$ 1,314,127.63

Q1 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	74	$ 5,475,106.43
1235	HEPATITIS AGENTS**	322	$ 4,572,228.22
5925	QUINOLINONE DERIVATIVES**	4,528	$ 3,961,801.73
2710	INSULIN**	9,395	$ 3,055,847.55
1210	ANTIRETROVIRALS**	2,863	$ 3,052,764.94
4420	SYMPATHOMIMETICS**	32,133	$ 2,895,178.76
7260	ANTICONVULSANTS - MISC.**	32,718	$ 2,272,715.37
5907	BENZISOXAZOLES**	7,418	$ 1,834,626.45
6240	MULTIPLE SCLEROSIS AGENTS**	321	$ 1,564,217.26
1950	MONOCLONAL ANTIBODIES**	542	$ 1,418,671.43

Q2 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
8510	ANTIHEMOPHILIC PRODUCTS**	99	$ 9,008,974.49
1235	HEPATITIS AGENTS**	342	$ 5,084,281.21
5925	QUINOLINONE DERIVATIVES**	4,573	$ 4,001,103.93
1210	ANTIRETROVIRALS**	2,497	$ 3,227,888.06
2710	INSULIN**	9,234	$ 3,056,550.88
4420	SYMPATHOMIMETICS**	28,418	$ 2,787,047.21
7260	ANTICONVULSANTS - MISC.**	33,351	$ 2,383,324.38
5907	BENZISOXAZOLES**	7,411	$ 1,918,837.07
6240	MULTIPLE SCLEROSIS AGENTS**	330	$ 1,616,694.40
5940	ANTIPSYCHOTICS - MISC.**	3,027	$ 1,335,640.83

Top 10 Drug Classes by Claim Count

Q4 2015

Class	Drug Class Name	Count of Claims	Pharmacy Paid
6599	OPIOID COMBINATIONS**	35,803	$ 996,454.99
7260	ANTICONVULSANTS - MISC.**	30,082	$ 2,010,100.97
4420	SYMPATHOMIMETICS**	27,801	$ 2,544,387.58
6510	OPIOID AGONISTS**	25,457	$ 1,131,255.26
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	23,390	$ 298,980.25
3940	HMG COA REDUCTASE INHIBITORS**	21,017	$ 421,916.07
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	20,779	$ 222,712.81
5710	BENZODIAZEPINES**	18,941	$ 174,588.21
7510	CENTRAL MUSCLE RELAXANTS**	15,606	$ 268,767.99
3610	ACE INHIBITORS**	14,965	$ 121,863.94

Q1 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
6599	OPIOID COMBINATIONS**	37,390	$ 985,741.99
7260	ANTICONVULSANTS - MISC.**	32,718	$ 2,272,715.37
4420	SYMPATHOMIMETICS**	32,133	$ 2,895,178.76
6510	OPIOID AGONISTS**	27,049	$ 1,186,411.51
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	24,954	$ 309,221.51
3940	HMG COA REDUCTASE INHIBITORS**	23,051	$ 463,760.83
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	21,955	$ 249,389.83
5710	BENZODIAZEPINES**	19,959	$ 200,155.97
7510	CENTRAL MUSCLE RELAXANTS**	16,521	$ 281,338.19
3610	ACE INHIBITORS**	16,246	$ 139,454.49

Q2 2016

Class	Drug Class Name	Count of Claims	Pharmacy Paid
6599	OPIOID COMBINATIONS**	36,031	$ 998,619.78
7260	ANTICONVULSANTS - MISC.**	33,351	$ 2,383,324.38
4420	SYMPATHOMIMETICS**	28,418	$ 2,787,047.21
6510	OPIOID AGONISTS**	27,084	$ 1,189,543.00
6610	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)*	25,434	$ 324,302.91
3940	HMG COA REDUCTASE INHIBITORS**	23,247	$ 451,276.52
5816	SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**	22,291	$ 270,261.54
5710	BENZODIAZEPINES**	19,589	$ 194,569.28
7510	CENTRAL MUSCLE RELAXANTS**	16,282	$ 313,046.01
3610	ACE INHIBITORS**	16,266	$ 144,716.12

Top 50 Drugs by Amount - Q4 2015

Drug Code	Drug Name	Claim Count		Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
5925001500	ARIPIPRAZOLE	4,022	$	3,867,527.48	14	13
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	27	$	3,398,650.44	56,363	12
1235990240	LEDIPASVIR-SOFOSBUVIR	170	$	2,952,849.45	8	8
5940002310	LURASIDONE HCL	1,370	$	1,251,574.38	17	15
1950206000	PALIVIZUMAB	480	$	1,243,714.46	1	25
2710400300	INSULIN GLARGINE	3,195	$	1,157,470.04	12	25
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	12	$	1,132,174.00	42,544	16
5907005010	PALIPERIDONE PALMITATE	552	$	1,012,117.39	1	22
4420101010	ALBUTEROL SULFATE	19,448	$	896,498.42	40	16
5915307010	QUETIAPINE FUMARATE	7,342	$	865,615.27	30	20
4927002510	ESOMEPRAZOLE MAGNESIUM	3,903	$	865,012.65	19	19
4420990270	FLUTICASONE-SALMETEROL	3,042	$	863,832.87	42	22
1235308000	SOFOSBUVIR	30	$	811,221.36	12	12
9410003000	GLUCOSE BLOOD	6,179	$	782,286.76	71	22
7260005700	PREGABALIN	2,314	$	685,093.63	47	20
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	2,426	$	598,153.16	24	25
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	466	$	569,117.35	22	22
2710400500	INSULIN LISPRO (HUMAN)	1,240	$	514,339.23	11	20
2710400200	INSULIN ASPART	1,327	$	503,976.23	12	21
6510007510	OXYCODONE HCL	8,415	$	493,152.03	71	17
6240552500	DIMETHYL FUMARATE	83	$	484,779.31	17	9
3010002000	SOMATROPIN	168	$	482,754.90	2	11
6135303010	GUANFACINE HCL (ADHD)	1,705	$	481,811.95	18	16
6627001500	ADALIMUMAB	131	$	471,183.52	1	12
6599000220	OXYCODONE W/ ACETAMINOPHEN	10,776	$	470,103.55	55	14
6599170210	HYDROCODONE-ACETAMINOPHEN	22,773	$	468,091.98	58	14
8580005000	ECULIZUMAB	24	$	467,735.94	95	1
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2,275	$	452,802.94	8	24
6629003000	ETANERCEPT	133	$	447,680.16	2	12
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	33	$	421,684.03	6,202	10
8240157000	PEGFILGRASTIM	94	$	420,198.04	1	1
4530402000	DORNASE ALFA	142	$	413,540.34	46	16
5907005000	PALIPERIDONE	397	$	394,100.26	17	13
3030001000	CORTICOTROPIN	10	$	378,532.73	1	2
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,709	$	377,956.58	24	23
6140002010	METHYLPHENIDATE HCL	2,434	$	370,507.54	33	18
2710400600	INSULIN DETEMIR	1,072	$	369,006.07	11	22
1210990430	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR	161	$	364,726.02	19	19
3090685000	IDURSULFASE	18	$	364,409.39	20	10
7210000700	CLOBAZAM	311	$	352,816.68	61	14
5818002510	DULOXETINE HCL	1,812	$	348,531.54	22	17
7260003600	LACOSAMIDE	718	$	337,059.03	52	13
9085006000	LIDOCAINE	1,050	$	336,191.53	40	13
8510002840	COAGULATION FACTOR IX (RECOMB) FC FUSION PROTEIN (RFIXFC)	11	$	333,021.10	6,091	11
0700007000	TOBRAMYCIN	78	$	323,496.07	99	10
1210990330	EFAVIRENZ-EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	141	$	299,813.71	19	19
2153253000	EVEROLIMUS	24	$	296,646.43	15	13
1910002010	IMMUNE GLOBULIN (HUMAN) IV	107	$	288,994.97	270	2
2135307000	TRASTUZUMAB	93	$	287,888.47	1	2
4530990230	LUMACAFTOR-IVACAFTOR	16	$	286,041.81	31	8

Top 50 Drugs by Amount - Q1 2016

Drug Code	Drug Name	Claim Count		Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
5925001500	ARIPIPRAZOLE	4,405.00	$	3,852,937.00	16	14
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	21.00	$	3,622,683.07	61,108	12
1235990240	LEDIPASVIR-SOFOSBUVIR	166.00	$	3,009,536.99	11	11
1950206000	PALIVIZUMAB	542.00	$	1,418,671.43	1	23
5940002310	LURASIDONE HCL	1,489.00	$	1,286,669.28	18	15
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	16.00	$	1,185,398.20	25,202	12
2710400300	INSULIN GLARGINE	3,793.00	$	1,170,681.26	13	26
1235308000	SOFOSBUVIR	45.00	$	1,143,425.94	11	11
5907005010	PALIPERIDONE PALMITATE	736.00	$	1,113,590.75	1	21
4420101010	ALBUTEROL SULFATE	22,212.00	$	1,046,449.01	39	15
4420990270	FLUTICASONE-SALMETEROL	3,364.00	$	951,085.87	43	22
4927002510	ESOMEPRAZOLE MAGNESIUM	4,227.00	$	911,697.72	21	21
5915307010	QUETIAPINE FUMARATE	7,960.00	$	880,748.27	30	20
9410003000	GLUCOSE BLOOD	6,659.00	$	852,605.25	73	22
7260005700	PREGABALIN	2,759.00	$	787,891.79	51	22
6627001500	ADALIMUMAB	171.00	$	615,796.47	1	10
2710400500	INSULIN LISPRO (HUMAN)	1,567.00	$	602,978.70	11	19
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	2,643.00	$	584,694.74	23	24
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	516.00	$	584,273.89	18	18
3010002000	SOMATROPIN	177.00	$	560,191.64	2	10
6240552500	DIMETHYL FUMARATE	91.00	$	536,158.33	16	8
2710400200	INSULIN ASPART	1,507.00	$	528,552.94	12	22
6135303010	GUANFACINE HCL (ADHD)	1,776.00	$	520,769.95	21	18
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2,713.00	$	510,708.49	8	24
4530402000	DORNASE ALFA	163.00	$	507,218.18	35	12
6510007510	OXYCODONE HCL	9,172.00	$	502,934.38	75	18
6629003000	ETANERCEPT	148.00	$	489,584.23	2	16
8580005000	ECULIZUMAB	24.00	$	488,061.00	99	1
6599000220	OXYCODONE W/ ACETAMINOPHEN	11,281.00	$	469,731.39	55	14
6599170210	HYDROCODONE-ACETAMINOPHEN	23,683.00	$	454,257.48	61	15
6140002010	METHYLPHENIDATE HCL	2,522.00	$	419,548.14	35	19
6110002510	LISDEXAMFETAMINE DIMESYLATE	1,762.00	$	417,516.20	22	22
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	23.00	$	397,224.88	6,873	10
8240157000	PEGFILGRASTIM	85.00	$	394,614.55	1	4
2710400600	INSULIN DETEMIR	1,323.00	$	390,902.73	12	24
7260003600	LACOSAMIDE	810.00	$	383,958.69	52	14
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	2,865.00	$	380,568.64	26	19
3090685000	IDURSULFASE	17.00	$	367,917.86	19	9
9085006000	LIDOCAINE	1,262.00	$	358,800.33	45	14
0700007000	TOBRAMYCIN	94.00	$	351,977.31	104	11
5907005000	PALIPERIDONE	440.00	$	350,497.01	22	17
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	157.00	$	349,135.56	19	19
3030001000	CORTICOTROPIN	9.00	$	340,431.53	2	7
7210000700	CLOBAZAM	322.00	$	336,061.13	65	14
2153253000	EVEROLIMUS	27.00	$	334,854.46	13	11
4530990230	LUMACAFTOR-IVACAFTOR	19.00	$	319,007.96	28	7
1210990330	EFAVIRENZ-EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	188.00	$	308,601.09	18	18
3090404500	NITISINONE	6.00	$	300,025.77	90	18
1210990430	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR	143.00	$	297,544.08	19	19
2755007010	SITAGLIPTIN PHOSPHATE	1,242.00	$	290,035.32	26	25

Top 50 Drugs by Amount - Q2 2016

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
5925001500	ARIPIPRAZOLE	4417	$ 3,854,833.09	16	14
1235990240	LEDIPASVIR-SOFOSBUVIR	186	$ 3,404,424.58	12	12
8510002620	COAGULATION FACTOR VIIA (RECOMBINANT)	8	$ 3,360,081.36	84,000	12
8510001025	ANTIHEMOPHILIC FACTOR RAHF-PFM	19	$ 3,284,427.56	51,151	8
8510001020	ANTIHEMOPHILIC FACTOR (RECOMBINANT)	18	$ 1,456,732.86	26,116	11
5907005010	PALIPERIDONE PALMITATE	689	$ 1,236,613.21	1	23
5940002310	LURASIDONE HCL	1335	$ 1,208,399.22	17	15
2710400300	INSULIN GLARGINE	3645	$ 1,148,802.37	12	25
1235308000	SOFOSBUVIR	42	$ 1,065,448.17	16	16
4420101010	ALBUTEROL SULFATE	18843	$ 936,892.60	39	16
4420990270	FLUTICASONE-SALMETEROL	3231	$ 923,339.19	43	23
9410003000	GLUCOSE BLOOD	6801	$ 889,235.77	73	22
5915307010	QUETIAPINE FUMARATE	8077	$ 887,795.66	30	20
4927002510	ESOMEPRAZOLE MAGNESIUM	4106	$ 887,238.62	22	21
7260005700	PREGABALIN	2706	$ 821,939.73	50	21
6627001500	ADALIMUMAB	172	$ 687,474.44	1	11
3010002000	SOMATROPIN	199	$ 655,153.30	2	10
2710400500	INSULIN LISPRO (HUMAN)	1582	$ 608,629.11	12	21
4410008010	TIOTROPIUM BROMIDE MONOHYDRATE	2505	$ 582,110.41	22	24
1210990230	EMTRICITABINE-TENOFOVIR DISOPROXIL FUMARATE	441	$ 562,451.65	19	19
1210990429	ELVITEGRAVIR-COBICISTAT-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	237	$ 560,798.67	21	21
6135303010	GUANFACINE HCL (ADHD)	1795	$ 515,554.36	19	17
8240157000	PEGFILGRASTIM	107	$ 513,767.22	0	2
3030001000	CORTICOTROPIN	14	$ 510,652.38	2	4
2710400200	INSULIN ASPART	1425	$ 506,495.12	13	23
6599000220	OXYCODONE W/ ACETAMINOPHEN	10990	$ 505,528.33	57	15
6240552500	DIMETHYL FUMARATE	82	$ 504,215.94	18	9
4420990241	BUDESONIDE-FORMOTEROL FUMARATE DIHYDRATE	2621	$ 501,408.20	8	24
4530402000	DORNASE ALFA	151	$ 468,673.93	50	16
6510007510	OXYCODONE HCL	8937	$ 466,578.08	75	18
6629003000	ETANERCEPT	125	$ 435,921.20	2	14
6599170210	HYDROCODONE-ACETAMINOPHEN	22754	$ 431,734.80	61	15
9085006000	LIDOCAINE	1442	$ 431,439.52	52	15
6110002510	LISDEXAMFETAMINE DIMESYLATE	1764	$ 419,650.59	23	22
6140002010	METHYLPHENIDATE HCL	2432	$ 414,104.32	35	19
2710400600	INSULIN DETEMIR	1312	$ 402,484.48	12	23
7260003600	LACOSAMIDE	860	$ 401,287.06	55	15
1235302510	DACLATASVIR DIHYDROCHLORIDE	19	$ 399,193.23	21	21
8580005000	ECULIZUMAB	19	$ 381,738.00	96	1
6110990210	AMPHETAMINE-DEXTROAMPHETAMINE	2788	$ 370,641.92	28	19
3090685000	IDURSULFASE	19	$ 367,917.86	19	10
7210000700	CLOBAZAM	309	$ 349,134.39	57	13
6240306045	INTERFERON BETA-1A	69	$ 343,222.89	2	12
2153253000	EVEROLIMUS	24	$ 342,388.05	17	13
8510001510	ANTIHEMOPHILIC FACTOR/VON WILLEBRAND FACTOR COMPLEX (HUMAN)	31	$ 337,045.09	4,085	8
5907005000	PALIPERIDONE	401	$ 331,055.84	22	17
1910002010	IMMUNE GLOBULIN (HUMAN) IV	85	$ 330,297.64	426	2
9340002010	NALOXONE HCL	129	$ 313,349.90	0	6
9310002500	DEFERASIROX	57	$ 310,015.52	19	10
2755007010	SITAGLIPTIN PHOSPHATE	1288	$ 307,716.67	27	26

Top 50 Drugs by Claim Count - Q4 2015

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
6599170210	HYDROCODONE-ACETAMINOPHEN	22773	$ 468,091.98	58	14
4420101010	ALBUTEROL SULFATE	19448	$ 896,498.42	40	16
3610003000	LISINOPRIL	13319	$ 93,292.79	32	29
7260003000	GABAPENTIN	12018	$ 195,863.75	72	23
6610002000	IBUPROFEN	11057	$ 90,551.47	46	13
6599000220	OXYCODONE W/ ACETAMINOPHEN	10776	$ 470,103.55	55	14
5710001000	ALPRAZOLAM	10521	$ 102,635.29	52	22
3400000310	AMLODIPINE BESYLATE	10058	$ 69,524.96	26	25
2810001010	LEVOTHYROXINE SODIUM	9641	$ 121,900.62	29	29
2725005000	METFORMIN HCL	9599	$ 139,225.65	53	26
3940001010	ATORVASTATIN CALCIUM	9015	$ 100,346.33	25	25
6510007510	OXYCODONE HCL	8415	$ 493,152.03	71	17
5915307010	QUETIAPINE FUMARATE	7342	$ 865,615.27	30	20
0120001010	AMOXICILLIN	7309	$ 68,780.45	57	6
5812008010	TRAZODONE HCL	7209	$ 62,342.84	31	23
5025006505	ONDANSETRON HCL	6603	$ 42,017.41	5	2
4220003230	FLUTICASONE PROPIONATE (NASAL)	6453	$ 103,616.79	11	21
3940007500	SIMVASTATIN	6440	$ 47,333.64	28	28
6510005510	MORPHINE SULFATE	6415	$ 234,561.32	29	12
5816007010	SERTRALINE HCL	6376	$ 64,709.69	29	23
3320003010	METOPROLOL TARTRATE	6349	$ 41,652.63	42	22
4450505010	MONTELUKAST SODIUM	6251	$ 128,184.02	23	23
9410003000	GLUCOSE BLOOD	6179	$ 782,286.76	71	22
0340001000	AZITHROMYCIN	6117	$ 81,739.97	7	4
6410001000	ASPIRIN	5695	$ 27,959.95	23	23
6510009510	TRAMADOL HCL	5618	$ 50,575.58	55	15
5907007000	RISPERIDONE	5511	$ 99,224.11	32	19
7510005010	CYCLOBENZAPRINE HCL	5474	$ 53,332.81	46	20
6020408010	ZOLPIDEM TARTRATE	5346	$ 49,820.40	23	23
4920002010	RANITIDINE HCL	5303	$ 62,856.06	45	22
7210001000	CLONAZEPAM	5230	$ 47,241.72	45	21
4927007010	PANTOPRAZOLE SODIUM	5038	$ 45,366.61	16	16
5816002010	CITALOPRAM HYDROBROMIDE	5034	$ 37,404.44	26	24
3720003000	FUROSEMIDE	4999	$ 30,518.29	32	25
2210004500	PREDNISONE	4982	$ 35,598.29	18	9
7720203200	CHOLECALCIFEROL	4868	$ 31,401.40	24	21
4155003000	LORATADINE	4843	$ 44,127.56	35	22
5816004000	FLUOXETINE HCL	4798	$ 66,528.05	30	23
7250001010	DIVALPROEX SODIUM	4470	$ 263,462.19	58	20
3620101010	CLONIDINE HCL	4434	$ 58,687.86	38	21
3615004020	LOSARTAN POTASSIUM	4299	$ 34,370.74	30	28
5710006000	LORAZEPAM	4228	$ 38,781.91	25	11
3330000700	CARVEDILOL	4078	$ 30,256.13	42	21
5925001500	ARIPIPRAZOLE	4022	$ 3,867,527.48	14	13
5710004000	DIAZEPAM	3930	$ 30,108.20	40	18
4927002510	ESOMEPRAZOLE MAGNESIUM	3903	$ 865,012.65	19	19
3760004000	HYDROCHLOROTHIAZIDE	3876	$ 24,077.70	28	27
7260004000	LAMOTRIGINE	3866	$ 192,209.00	43	21
5025006500	ONDANSETRON	3841	$ 53,257.13	10	4
6610005200	MELOXICAM	3783	$ 26,708.85	26	23

Top 50 Drugs by Claim Count - Q1 2016

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
6599170210	HYDROCODONE-ACETAMINOPHEN	23683	$ 454,257.48	61	15
4420101010	ALBUTEROL SULFATE	22212	$ 1,046,449.01	39	15
3610003000	LISINOPRIL	14523	$ 109,858.33	31	28
7260003000	GABAPENTIN	13329	$ 196,123.31	72	23
6610002000	IBUPROFEN	12403	$ 112,002.83	45	12
6599000220	OXYCODONE W/ ACETAMINOPHEN	11281	$ 469,731.39	55	14
5710001000	ALPRAZOLAM	11174	$ 116,293.90	52	22
3400000310	AMLODIPINE BESYLATE	10924	$ 82,987.16	28	27
2725005000	METFORMIN HCL	10663	$ 133,577.21	56	28
2810001010	LEVOTHYROXINE SODIUM	10584	$ 136,665.47	29	29
3940001010	ATORVASTATIN CALCIUM	10212	$ 106,651.31	25	25
6510007510	OXYCODONE HCL	9172	$ 502,934.38	75	18
0120001010	AMOXICILLIN	9166	$ 94,787.59	61	6
5812008010	TRAZODONE HCL	8002	$ 78,287.90	32	23
5915307010	QUETIAPINE FUMARATE	7960	$ 880,748.27	30	20
0340001000	AZITHROMYCIN	7725	$ 110,858.13	8	4
4220003230	FLUTICASONE PROPIONATE (NASAL)	7701	$ 93,007.64	12	23
4450505010	MONTELUKAST SODIUM	7128	$ 130,210.12	24	24
6510005510	MORPHINE SULFATE	6904	$ 236,726.68	28	12
3320003010	METOPROLOL TARTRATE	6848	$ 50,288.41	43	23
3940007500	SIMVASTATIN	6800	$ 52,085.48	29	29
5816007010	SERTRALINE HCL	6703	$ 71,254.33	29	23
9410003000	GLUCOSE BLOOD	6659	$ 852,605.25	73	22
6410001000	ASPIRIN	5946	$ 32,355.33	23	23
2210004500	PREDNISONE	5940	$ 46,262.17	17	9
6510009510	TRAMADOL HCL	5871	$ 57,977.32	60	16
5907007000	RISPERIDONE	5849	$ 95,908.74	34	20
5025006505	ONDANSETRON HCL	5793	$ 43,309.71	6	2
4920002010	RANITIDINE HCL	5747	$ 69,533.43	44	22
6020408010	ZOLPIDEM TARTRATE	5702	$ 55,141.49	23	23
7210001000	CLONAZEPAM	5635	$ 56,129.73	45	22
7510005010	CYCLOBENZAPRINE HCL	5601	$ 58,548.15	45	20
3720003000	FUROSEMIDE	5541	$ 36,941.48	31	25
4927007010	PANTOPRAZOLE SODIUM	5442	$ 53,656.04	18	18
4155003000	LORATADINE	5401	$ 56,125.54	35	21
5816004000	FLUOXETINE HCL	5315	$ 74,945.66	31	24
5816002010	CITALOPRAM HYDROBROMIDE	5165	$ 43,890.76	25	23
7720203200	CHOLECALCIFEROL	5054	$ 36,410.94	25	22
3615004020	LOSARTAN POTASSIUM	4905	$ 40,552.37	29	28
7250001010	DIVALPROEX SODIUM	4858	$ 269,202.22	58	20
3620101010	CLONIDINE HCL	4737	$ 62,477.77	38	21
3330000700	CARVEDILOL	4538	$ 33,406.92	47	24
5925001500	ARIPIPRAZOLE	4405	$ 3,852,937.00	16	14
5710006000	LORAZEPAM	4336	$ 44,327.56	27	12
5025006500	ONDANSETRON	4303	$ 60,454.42	11	4
4927002510	ESOMEPRAZOLE MAGNESIUM	4227	$ 911,697.72	21	21
3760004000	HYDROCHLOROTHIAZIDE	4218	$ 28,194.28	28	28
7260004000	LAMOTRIGINE	4198	$ 253,297.19	45	21
0199000220	AMOXICILLIN & POT CLAVULANATE	4188	$ 89,886.40	34	7
5710004000	DIAZEPAM	4187	$ 36,241.54	41	19

Top 50 Drugs by Claim Count - Q2 2016

Drug Code	Drug Name	Claim Count	Pharmacy Paid	Avg Qty/Rx	Avg Day Supply
6599170210	HYDROCODONE-ACETAMINOPHEN	22754	$ 431,734.80	61	15
4420101010	ALBUTEROL SULFATE	18843	$ 936,892.60	39	16
3610003000	LISINOPRIL	14561	$ 112,101.83	29	26
7260003000	GABAPENTIN	13819	$ 198,000.62	73	23
6610002000	IBUPROFEN	12078	$ 109,340.87	46	14
3400000310	AMLODIPINE BESYLATE	11096	$ 84,518.70	28	27
6599000220	OXYCODONE W/ ACETAMINOPHEN	10990	$ 505,528.33	57	15
3940001010	ATORVASTATIN CALCIUM	10885	$ 114,367.32	26	25
5710001000	ALPRAZOLAM	10873	$ 113,655.57	51	22
2725005000	METFORMIN HCL	10552	$ 154,378.99	52	25
2810001010	LEVOTHYROXINE SODIUM	10520	$ 151,985.98	29	29
6510007510	OXYCODONE HCL	8937	$ 466,578.08	75	18
5915307010	QUETIAPINE FUMARATE	8077	$ 887,795.66	30	20
5812008010	TRAZODONE HCL	8024	$ 81,416.15	29	21
4220003230	FLUTICASONE PROPIONATE (NASAL)	7427	$ 89,313.11	12	23
4450505010	MONTELUKAST SODIUM	7395	$ 129,844.81	23	22
5025006505	ONDANSETRON HCL	7143	$ 41,494.87	4	2
3320003010	METOPROLOL TARTRATE	7098	$ 51,804.42	43	23
6510005510	MORPHINE SULFATE	7034	$ 223,738.82	26	11
5816007010	SERTRALINE HCL	6896	$ 75,840.60	29	24
9410003000	GLUCOSE BLOOD	6801	$ 889,235.77	73	22
0120001010	AMOXICILLIN	6788	$ 69,996.82	55	6
3940007500	SIMVASTATIN	6556	$ 51,184.29	27	27
6410001000	ASPIRIN	6344	$ 34,488.04	23	22
5907007000	RISPERIDONE	6000	$ 96,284.57	35	21
6510009510	TRAMADOL HCL	5921	$ 57,772.67	56	16
3720003000	FUROSEMIDE	5803	$ 38,981.34	32	25
4920002010	RANITIDINE HCL	5752	$ 71,757.86	45	22
4155003000	LORATADINE	5652	$ 59,469.52	34	21
4927007010	PANTOPRAZOLE SODIUM	5625	$ 58,969.63	21	20
7720203200	CHOLECALCIFEROL	5440	$ 39,744.33	25	22
7210001000	CLONAZEPAM	5429	$ 55,461.22	45	22
5816004000	FLUOXETINE HCL	5382	$ 88,036.05	30	23
7510005010	CYCLOBENZAPRINE HCL	5372	$ 60,912.33	46	20
5816002010	CITALOPRAM HYDROBROMIDE	5088	$ 45,052.54	26	24
3615004020	LOSARTAN POTASSIUM	5034	$ 42,280.31	30	28
2210004500	PREDNISONE	5027	$ 45,841.60	18	9
3620101010	CLONIDINE HCL	4811	$ 62,298.47	38	22
7250001010	DIVALPROEX SODIUM	4746	$ 253,211.27	57	20
7720203000	ERGOCALCIFEROL	4503	$ 48,029.08	4	22
5710006000	LORAZEPAM	4501	$ 42,800.81	23	10
3330000700	CARVEDILOL	4477	$ 32,648.88	49	25
4155002010	CETIRIZINE HCL	4445	$ 46,247.02	43	20
0340001000	AZITHROMYCIN	4418	$ 60,953.03	7	4
5925001500	ARIPIPRAZOLE	4417	$ 3,854,833.09	16	14
3760004000	HYDROCHLOROTHIAZIDE	4335	$ 30,314.72	28	28
6020408010	ZOLPIDEM TARTRATE	4304	$ 41,894.72	23	23
7260004000	LAMOTRIGINE	4235	$ 237,991.43	44	21
7975001000	SODIUM CHLORIDE	4118	$ 11,397.59	445	1
6610005200	MELOXICAM	4106	$ 36,800.19	27	24

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between Oct 1, 2015 and Dec 31, 2015

Jan 14, 2016
3:23:18 PM

Claims Summary:

RxCLAIM Status	Total Rxs	% of Total Rxs	Total Plan Paid	Total Member Paid
Paid	728,709	62.5%	$68,309,265.55	$0.00
Rejected	348,704	29.9%	$46,365,673.67	$0.00
Reversed	88,886	7.6%	-$17,169,152.91	$0.00
Totals	1,166,299	100%	$97,505,786.31	$0.00

DUR Information Summary:

		Total DURs		DURs on Paid Rxs		DURs on Rejected Rxs		DURs on Reversed Rxs	
DUR Type	Clinical Level	Count	% of All DURs	Count	% of DUR Type	Count	% of DUR Type	Count	% of DUR Type
LR - Underuse Precaution	0 - NS	61,890	23.1%	55,662	89.9%	0	0.0%	6,228	10.1%
TD - Therapeutic Duplication	0 - NS	54,957	20.5%	40,307	73.3%	7,027	12.8%	7,623	13.9%
ID - Ingredient Duplication	2 - Mod	50,935	19.0%	12,178	23.9%	35,353	69.4%	3,404	6.7%
DD - Drug-Drug Interaction	1 - Maj	36,668	13.7%	30,102	82.1%	3,203	8.7%	3,363	9.2%
LD - Low Dose Alert	0 - NS	26,988	10.1%	22,878	84.8%	0	0.0%	4,110	15.2%
HD - High Dose Alert	0 - NS	20,687	7.7%	18,648	90.1%	165	0.8%	1,874	9.1%
MN - Insufficnt Duration Alert	0 - NS	10,859	4.0%	8,302	76.5%	0	0.0%	2,557	23.5%
MX - Excessive Duration Alert	0 - NS	5,353	2.0%	4,934	92.2%	0	0.0%	419	7.8%
PA - Drug-Age Precaution	1 - Maj	45	0.0%	42	93.3%	0	0.0%	3	6.7%
Total All DURs		268,382	100.0%	193,053	71.9%	45,748	17.0%	29,581	11.0%

* DUR Information Summary results are sorted by Total DUR count in descending order
* Some Rx claims could have multiple DUR messages. And there could be multiple instances of the same DUR message on a Rx claim
* The Count and % of DUR Type for Paid, Rejected and Reversed Rxs are based on DUR Type totals for each row

DD - Drug-Drug Interaction

Rank	Top Drug Drug Interaction	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	CARISOPRODOL - ALPRAZOLAM	Message Only	611	$5,957.90	$9.75	$0.00	29.1	80.4	71	23	$190.17
2	TRAZODONE HCL - QUETIAPINE	Message Only	430	$3,870.03	$9.00	$0.00	27.1	39.5	35	29	$653.83
3	SIMVASTATIN - FENOFIBRATE	Message Only	390	$7,260.74	$18.62	$0.00	31.8	32.3	46	18	$302.62
4	SPIRONOLACT - LISINOPRIL	Message Only	355	$2,626.36	$7.40	$0.00	34.1	40.0	44	23	$90.80
5	TRAZODONE - QUETIAPINE FUMARATE	Message Only	370	$6,407.66	$17.32	$0.00	27.2	44.4	18	20	$290.62
6	TRAZODONE HCL - CITALOPRAM	Message Only	332	$2,686.88	$8.09	$0.00	30.2	39.3	34	19	$175.68
7	SPIRONOLACTONE - LISINOPRIL	Message Only	309	$3,120.78	$10.10	$0.00	36.8	41.6	31	18	$196.36
8	DIVALPROEX - CLONAZEPAM	Message Only	304	$2,625.84	$8.64	$0.00	26.9	57.9	27	22	$147.52
9	TRAZODONE - CITALOPRAM HYDROBROMIDE	Message Only	281	$1,980.52	$7.05	$0.00	31.3	34.6	23	18	$142.53
10	SERTRALINE - CYCLOBENZAPRINE HCL	Message Only	284	$2,538.12	$8.94	$0.00	25.3	58.1	28	6	$45.27
All Others			26,436	$2,775,417.80	$104.99	$0.00	24.9	46.1	2,846	3,167	$535,835.27
DD - Drug-Drug Interaction			30,102	$2,814,492.63	$93.50	$0.00	25.5	46.4	3,203	3,363	$538,070.67

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

HD - High Dose Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	HECTOROL	GERIATRIC MAX DLY = 1.28UN	Message Only	1,088	$15,034.94	$13.82	$0.00	1.0	2.2	0	0	$0.00
2	HYDROCODONE/ ACETAMINOPHEN	ADULT MAX DLY = 6.00 UN	Message Only	544	$17,927.72	$32.96	$0.00	16.2	127.2	0	22	$912.69
3	KETOROLAC TROMETHAMINE	GERIATRIC MAX DLY = 2.00UN	Message Only	458	$2,951.51	$6.44	$0.00	1.0	4.3	0	36	$220.31
4	FLUZONE QUADRIVALENT 2015	GERIATRIC MAX DLY = .50UN	Message Only	396	$8,966.75	$22.64	$0.00	1.0	16.3	0	3	$108.54
5	ZOLPIDEM TARTRATE	GERIATRIC MAX DLY = .50UN	Message Only	352	$1,798.05	$5.11	$0.00	29.6	29.6	0	11	$56.10
6	PREVNAR 13	GERIATRIC MAX DLY = .50UN	Message Only	300	$19,836.73	$66.12	$0.00	1.0	9.4	0	1	$0.00
7	FLUVIRIN 2015-2016	GERIATRIC MAX DLY = .50UN	Message Only	293	$6,567.49	$22.41	$0.00	1.0	2.9	0	1	$28.58
8	DEXAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 2.60UN	Message Only	207	$3,418.57	$16.51	$0.00	1.0	12.0	0	5	$35.39
9	ADACEL	GERIATRIC MAX DLY = .50UN	Message Only	193	$14,049.24	$72.79	$0.00	1.0	1.2	0	13	$1,223.26
10	KENALOG-40	GERIATRIC MAX DLY = 2.00UN	Message Only	200	$6,575.67	$32.88	$0.00	1.0	6.1	0	2	$65.78
All Others				14,617	$3,707,540.99	$253.65	$0.00	13.9	106.2	165	1,780	$737,405.69
HD - High Dose Alert				18,648	$3,804,667.66	$204.03	$0.00	12.1	88.5	165	1,874	$740,056.34

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

ID - Ingredient Duplication

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	EPOGEN	EPOGEN INJ 10000/ML	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	2,864	0	$0.00
2	HYDROCODONE/ ACETAMINOPHEN	HYDROCO/APAP TAB 10-325MG	Hard Reject	5	$81.41	$16.28	$0.00	8.4	36.0	947	0	$0.00
3	SODIUM CHLORIDE	SOD CHLORIDE INJ 0.9%	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	593	0	$0.00
4	OXYCODONE/ ACETAMINOPHEN	OXYCOD/APAP TAB 10-325MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	514	0	$0.00
5	ALPRAZOLAM	ALPRAZOLAM TAB 1MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	402	0	$0.00
6	PROAIR HFA	PROAIR HFA AER	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	393	0	$0.00
7	ZOLPIDEM TARTRATE	ZOLPIDEM TAB 10MG	Hard Reject	2	$11.56	$5.78	$0.00	30.0	30.0	362	0	$0.00
8	GABAPENTIN	GABAPENTIN CAP 300MG	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	348	0	$0.00
9	HECTOROL	HECTOROL INJ 4MCG/2ML	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	330	0	$0.00
10	TRAMADOL HCL	TRAMADOL HCL TAB 50MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	327	0	$0.00
All Others				12,171	$1,723,968.11	$141.65	$0.00	27.0	95.4	28,273	3,404	$889,757.44
ID - Ingredient Duplication				12,178	$1,724,061.08	$141.57	$0.00	27.0	95.4	35,353	3,404	$889,757.44

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

LD - Low Dose Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	ONDANSETRON HCL	GERIATRIC MIN DLY = 2.00UN	Message Only	957	$532.32	$0.56	$0.00	1.4	1.4	0	584	$179.80
2	ONDANSETRON ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	575	$351.70	$0.61	$0.00	1.5	1.5	0	187	$103.04
3	IPRATROPIUM BROMIDE/ALBUT	GERIATRIC MIN DLY = 12.00UN	Message Only	439	$1,019.90	$2.32	$0.00	3.0	19.7	0	147	$132.98
4	METFORMIN HCL	ADULT MIN DLY = 1.70 UN	Message Only	541	$3,835.50	$7.09	$0.00	34.2	34.0	0	39	$277.67
5	ZOFRAN ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	356	$7,433.56	$20.88	$0.00	1.0	1.0	0	164	$3,437.42
6	VITAMIN D	ADULT MIN DLY = .14 UN	Message Only	481	$3,960.70	$8.23	$0.00	30.8	3.1	0	33	$244.55
7	HECTOROL	GERIATRIC MIN DLY = .85UN	Message Only	501	$1,568.13	$3.13	$0.00	1.0	0.5	0	0	$0.00
8	GABAPENTIN	ADULT MIN DLY = 3.00 UN	Message Only	380	$3,702.75	$9.74	$0.00	31.6	52.4	0	19	$199.73
9	CITALOPRAM HYDROBROMIDE	ADULT MIN DLY = 2.00 UN	Message Only	343	$3,003.11	$8.76	$0.00	30.3	30.1	0	36	$266.15
10	ALBUTEROL SULFATE	GERIATRIC MIN DLY = 9.00UN	Message Only	306	$255.13	$0.83	$0.00	2.7	13.6	0	72	$24.27
All Others				17,999	$1,951,701.08	$108.43	$0.00	24.4	56.4	0	2,829	$371,599.63
LD - Low Dose Alert				22,878	$1,977,363.88	$86.43	$0.00	21.9	47.2	0	4,110	$376,465.24

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

LR - Underuse Precaution

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	LISINOPRIL	7 DAYS LATE REFILLING	Message Only	88	$599.49	$6.81	$0.00	30.0	32.0	0	5	$35.18
2	LEVOTHYROXINE SODIUM	7 DAYS LATE REFILLING	Message Only	87	$775.85	$8.92	$0.00	30.5	30.1	0	4	$52.38
3	AMLODIPINE BESYLATE	7 DAYS LATE REFILLING	Message Only	69	$490.63	$7.11	$0.00	30.0	30.0	0	10	$71.05
4	AMLODIPINE BESYLATE	8 DAYS LATE REFILLING	Message Only	71	$525.81	$7.41	$0.00	30.9	31.3	0	2	$19.57
5	PROAIR HFA	11 DAYS LATE REFILLING	Message Only	68	$3,792.56	$55.77	$0.00	20.2	9.1	0	3	$166.18
6	LISINOPRIL	9 DAYS LATE REFILLING	Message Only	61	$461.31	$7.56	$0.00	29.6	32.6	0	3	$16.05
7	LEVOTHYROXINE SODIUM	8 DAYS LATE REFILLING	Message Only	58	$520.28	$8.97	$0.00	29.3	29.8	0	4	$22.09
8	LISINOPRIL	8 DAYS LATE REFILLING	Message Only	57	$381.66	$6.70	$0.00	29.6	33.8	0	3	$20.43
9	PROAIR HFA	10 DAYS LATE REFILLING	Message Only	54	$3,039.14	$56.28	$0.00	21.7	9.3	0	2	$114.36
9	MONTELUKAST SODIUM	7 DAYS LATE REFILLING	Message Only	51	$902.74	$17.70	$0.00	30.0	30.0	0	5	$328.83
All Others				54,998	$5,192,140.81	$94.41	$0.00	28.5	48.9	0	6,187	$911,162.82
LR - Underuse Precaution				55,662	$5,203,630.28	$93.49	$0.00	28.5	48.6	0	6,228	$912,008.94

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

MN - Insufficnt Duration Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	CALCITRIOL	MIN. DAYS THERAPY = 7	Message Only	662	$721.51	$1.09	$0.00	1.0	1.9	0	5	$2.81
2	HECTOROL	MIN. DAYS THERAPY = 7	Message Only	618	$3,863.15	$6.25	$0.00	1.0	1.0	0	0	$0.00
3	PANTOPRAZOLE SODIUM	MIN. DAYS THERAPY = 7	Message Only	317	$92.68	$0.29	$0.00	1.1	1.2	0	223	$40.04
4	IPRATROPIUM BROMIDE/ALBUT	MIN. DAYS THERAPY = 30	Message Only	396	$8,421.26	$21.27	$0.00	9.1	143.7	0	61	$937.35
5	LISINOPRIL	MIN. DAYS THERAPY = 7	Message Only	231	$44.59	$0.19	$0.00	1.1	1.7	0	140	$28.57
6	LEVETIRACETAM	MIN. DAYS THERAPY = 14	Message Only	330	$3,334.00	$10.10	$0.00	6.0	40.6	0	37	$103.29
7	CLONIDINE HCL	MIN. DAYS THERAPY = 7	Message Only	240	$401.73	$1.67	$0.00	1.7	5.3	0	79	$33.66
8	METOPROLOL TARTRATE	MIN. DAYS THERAPY = 7	Message Only	187	$138.84	$0.74	$0.00	1.4	2.0	0	89	$13.61
9	SULFAMETHOXAZOLE/ TRIMETHO	MIN. DAYS THERAPY = 5	Message Only	179	$1,073.99	$6.00	$0.00	1.9	8.0	0	36	$38.41
9	ATORVASTATIN CALCIUM	MIN. DAYS THERAPY = 7	Message Only	146	$292.65	$2.00	$0.00	1.8	1.9	0	69	$55.71
All Others				4,996	$310,869.56	$62.22	$0.00	3.1	17.3	0	1,818	$55,880.23
MN - Insufficnt Duration Alert				8,302	$329,253.96	$39.66	$0.00	2.9	19.6	0	2,557	$57,133.68

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

MX - Excessive Duration Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	2,490	$22,568.56	$9.06	$0.00	30.1	65.4	0	119	$1,047.72
2	AZITHROMYCIN	MAX DAYS THERAPY = 5	Message Only	268	$5,753.48	$21.47	$0.00	10.3	19.7	0	13	$290.83
3	FLUCONAZOLE	MAX DAYS THERAPY = 1	Message Only	200	$2,441.57	$12.21	$0.00	3.0	3.0	0	21	$415.66
4	MAPAP	MAX DAYS THERAPY = 10	Message Only	149	$1,215.70	$8.16	$0.00	26.9	102.8	0	9	$74.59
5	EPIPEN 2-PAK	MAX DAYS THERAPY = 1	Message Only	125	$62,735.41	$501.88	$0.00	2.3	2.3	0	17	$10,074.96
6	POLYETHYLENE GLYCOL 3350	MAX DAYS THERAPY = 14	Message Only	110	$4,112.50	$37.39	$0.00	30.4	30.4	0	28	$1,134.66
7	DIPHENOXYLATE/ ATROPINE	MAX DAYS THERAPY = 14	Message Only	126	$3,206.03	$25.44	$0.00	26.5	112.1	0	4	$55.82
8	SENEXON-S	MAX DAYS THERAPY = 14	Message Only	91	$777.81	$8.55	$0.00	27.9	52.9	0	6	$45.78
9	CEFDINIR	MAX DAYS THERAPY = 10	Message Only	82	$3,721.76	$45.39	$0.00	15.8	72.8	0	6	$221.39
10	TRAMADOL HYDROCHLORIDE/AC	MAX DAYS THERAPY = 5	Message Only	78	$1,321.37	$16.94	$0.00	19.5	72.7	0	9	$169.01
All Others				1,215	$197,431.97	$162.50	$0.00	26.8	74.5	0	187	$67,995.15
MX - Excessive Duration Alert				4,934	$305,286.16	$61.87	$0.00	25.8	62.6	0	419	$81,525.57

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

PA - Drug-Age Precaution

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	PROMETHAZINE/ DEXTROMETHOR	AGE LESS THAN 4	Message Only	17	$126.43	$7.44	$0.00	11.8	89.7	0	2	$11.38
2	PROMETHAZINE-DM	AGE LESS THAN 4	Message Only	15	$109.20	$7.28	$0.00	12.8	93.6	0	0	$0.00
3	PROMETHAZINE HCL PLAIN	AGE LESS THAN 4	Message Only	4	$20.89	$5.22	$0.00	9.5	105.0	0	0	$0.00
4	PROMETHAZINE HCL	AGE LESS THAN 4	Message Only	2	$26.60	$13.30	$0.00	7.5	122.0	0	1	$8.35
5	PROMETHAZINE/CODEINE	AGE LESS THAN 4	Message Only	2	$13.39	$6.70	$0.00	5.5	40.0	0	0	$0.00
6	PROMETHAZINE VC/CODEINE	AGE LESS THAN 4	Message Only	1	$18.33	$18.33	$0.00	7.0	30.0	0	0	$0.00
6	PROMETHEGAN	AGE LESS THAN 4	Message Only	1	$13.05	$13.05	$0.00	3.0	3.0	0	0	$0.00
PA - Drug-Age Precaution				42	$327.89	$7.81	$0.00	11.1	88.2	0	3	$19.73

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

TD - Therapeutic Duplication

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	HYDROCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,327	$22,866.41	$17.23	$0.00	16.7	65.3	0	186	$1,372.06
2	HYDROMORPHONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	900	$4,869.55	$5.41	$0.00	4.6	16.3	0	484	$1,280.02
3	MORPHINE SULFATE	SHORT ACTING NARCOTIC ANALGESI	Message Only	827	$4,341.73	$5.25	$0.00	4.7	15.3	0	491	$1,293.25
4	OXYCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,073	$37,847.53	$35.27	$0.00	14.4	58.6	0	193	$1,898.24
5	QUETIAPINE FUMARATE	ORAL ANTIPSYCHOTICS	Message Only	1,142	$20,315.44	$17.79	$0.00	27.4	40.1	0	103	$1,196.85
6	OXYCODONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	952	$32,655.02	$34.30	$0.00	22.6	102.2	0	93	$1,754.34
7	RISPERIDONE	ORAL ANTIPSYCHOTICS	Message Only	842	$11,120.73	$13.21	$0.00	27.6	45.8	0	75	$915.38
8	TRAMADOL HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	715	$6,751.12	$9.44	$0.00	21.6	88.8	0	70	$427.63
9	ALPRAZOLAM	BENZODIAZEPINES	Message Only	666	$5,958.00	$8.95	$0.00	25.3	62.4	0	88	$375.53
10	LISINOPRIL	ANGIOTENSIN BLOCKERS	Message Only	540	$3,248.41	$6.02	$0.00	34.8	39.1	0	123	$418.81
All Others				31,323	$4,229,601.89	$135.03	$0.00	24.1	54.9	7,027	5,717	$765,683.36
TD - Therapeutic Duplication				40,307	$4,379,575.83	$108.66	$0.00	23.0	54.7	7,027	7,623	$776,615.47

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

Selected Filters

Client(s): Nevada Medicaid - HPES

Carrier(s): NVM-NEVADA MEDICAID

Account(s): ALL

Group(s): ALL

Date Type:	Date Filled Submitted
Primary Start Date:	Oct 1, 2015
Primary End Date:	Dec 31, 2015
Relative Date Description:	N/A
Select Report Group By:	Product
Top Values Displayed:	10
Display Report Description:	Yes

Report Description

Report overview:

This report will be used to track concurrent DURs. The subsequent information will also be used to assist clients in managing Hard Rejects, Soft Rejects as well as Message Only edits. Reversals are also included in the report.

Detail Line Description:

Column Name	Description
Summary Page:	
Claims Summary:	
RxCLAIM Status	The claims status associated with the RxCLAIM transaction. For this reoprt, a claim Status can be any one of the following values: P = Paid Status, X = Reversal Status, R = Rejected Status.
Total Rxs	The total number of Rxs.
% of Total Rxs	The percentage of the total number of Rxs.

Total Plan Paid	The Client Total Amount Due.
Total Member Paid	The Client Total Patient Pay Amount. The patient pay would include copays and all other charges paid by the member.

DUR Information Summary:

DUR Type	DUR Reason for Service Code and Description
Clinical Level	DUR (Drug Utilization Review). Indicates how significant the first conflict is. This field reflects the significance that the originating database assigned to it. 0 = Not specified, 1 = Major, 2 = Moderate, 3 = Minor
Total DURs	
Count	Total count of DUR edits. An Rx claim may have more than 1 DUR edit.
% of All DURs	The percentage is based on the total number of each unique DUR Type divided by the total number of all DUR Types.
DURs on Paid Rxs	
Count	Total count of DUR edits on paid Rx claims. A paid Rx claim may have more than 1 DUR edit.
% of DUR Type	The percentage is based on the total number of each unique DUR Type divided by the total number of all DUR Types on Paid Rx claims.
DURs on Rejected Rxs	
Count	Total count of DUR edits on rejected Rx claims. A rejected Rx claim may have more than 1 DUR edit.
% of DUR Type	The percentage is based on the total number of each unique DUR Type divided by the total number of all DUR Types on Rejected Rx claims.
DURs on Reversed Rxs	
Count	Total count of DUR edits on reversed Rx claims. A reversed Rx claim may have more than 1 DUR edit.
% of DUR Type	The percentage is based on the total number of each unique DUR Type divided by the total number of all DUR Types on Reversed Rx claims.

DUR Tabs:

Rank	Ranking is based on total number of Rxs (Paid + Rjected + Reversal) in descending order. A gap in sequence may occur if two or more rows tie (known as Olympic ranking).
Top Drug-Drug Interaction (DD Only)	Drug combination with a DD DUR code
Top Drug	Product Name
Therapy / Reason	DUR Free Text Message
DUR Response	DUR Responses are categorized as: H = Hard Reject, S = Soft Reject, any other code = Message Only
Total Paid Rxs	The total number of paid Rxs.
Total Plan Paid	The Client total amount due.
Avg Plan Paid / Rx	The average plan cost per Rx.

Avg Member Paid / Rx	The average member cost per Rx.
Avg Days Supply / Rx	The average days supply per Rx.
Avg Quantity / Rx	The average quantity per Rx.
Total Rejected Rxs	The total number of rejected Rxs.
Total Reversed Rxs	The total number of reversed Rxs.
Total Reversed Amount	The total amount of reversed Rxs.

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between Jan 1, 2016 and Mar 31, 2016

Apr 19, 2016
11:39:49 AM

Claims Summary:

RxCLAIM Status	Total Rxs	% of Total Rxs	Total Plan Paid	Total Member Paid
Paid	788,252	61.3%	$71,987,212.63	$0.00
Rejected	402,093	31.3%	$57,052,700.28	$0.00
Reversed	94,747	7.4%	-$17,976,944.80	$0.00
Totals	1,285,092	100%	$111,062,968.11	$0.00

DUR Information Summary:

		Total DURs		DURs on Paid Rxs		DURs on Rejected Rxs		DURs on Reversed Rxs	
DUR Type	Clinical Level	Count	% of All DURs	Count	% of DUR Type	Count	% of DUR Type	Count	% of DUR Type
LR - Underuse Precaution	0 - NS	63,841	22.8%	57,667	90.3%	0	0.0%	6,174	9.7%
TD - Therapeutic Duplication	0 - NS	60,506	21.6%	44,395	73.4%	7,775	12.8%	8,336	13.8%
ID - Ingredient Duplication	2 - Mod	50,063	17.9%	13,624	27.2%	32,745	65.4%	3,694	7.4%
DD - Drug-Drug Interaction	1 - Maj	40,153	14.3%	32,767	81.6%	3,742	9.3%	3,644	9.1%
LD - Low Dose Alert	0 - NS	28,546	10.2%	24,050	84.2%	0	0.0%	4,496	15.8%
HD - High Dose Alert	0 - NS	19,809	7.1%	17,342	87.5%	170	0.9%	2,297	11.6%
MN - Insufficnt Duration Alert	0 - NS	11,358	4.1%	8,100	71.3%	0	0.0%	3,258	28.7%
MX - Excessive Duration Alert	0 - NS	5,691	2.0%	5,278	92.7%	0	0.0%	413	7.3%
PA - Drug-Age Precaution	1 - Maj	79	0.0%	73	92.4%	0	0.0%	6	7.6%
Total All DURs		280,046	100.0%	203,296	72.6%	44,432	15.9%	32,318	11.5%

* DUR Information Summary results are sorted by Total DUR count in descending order
* Some Rx claims could have multiple DUR messages. And there could be multiple instances of the same DUR message on a Rx claim
* The Count and % of DUR Type for Paid, Rejected and Reversed Rxs are based on DUR Type totals for each row

DD - Drug-Drug Interaction

Rank	Top Drug Drug Interaction	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	CARISOPRODOL - ALPRAZOLAM	Message Only	587	$5,888.20	$10.03	$0.00	28.3	78.5	64	30	$147.53
2	TRAZODONE HCL - QUETIAPINE	Message Only	467	$4,764.48	$10.20	$0.00	28.5	41.7	41	53	$228.41
3	SIMVASTATIN - FENOFIBRATE	Message Only	441	$6,960.96	$15.78	$0.00	32.1	32.2	48	17	$273.67
4	TRAZODONE - QUETIAPINE FUMARATE	Message Only	396	$6,176.60	$15.60	$0.00	28.2	45.6	39	57	$380.02
5	TRAZODONE HCL - CITALOPRAM	Message Only	387	$3,668.48	$9.48	$0.00	29.7	39.6	42	16	$161.98
6	SPIRONOLACTONE - LISINOPRIL	Message Only	353	$3,665.70	$10.38	$0.00	35.8	38.9	55	26	$179.71
7	SPIRONOLACT - LISINOPRIL	Message Only	369	$3,044.07	$8.25	$0.00	36.2	43.7	30	31	$141.85
8	TRAZODONE - CITALOPRAM HYDROBROMIDE	Message Only	330	$2,637.86	$7.99	$0.00	30.2	33.4	30	18	$145.69
9	DIVALPROEX - CLONAZEPAM	Message Only	327	$3,096.65	$9.47	$0.00	26.7	56.6	26	15	$104.83
10	VOLTAREN - METFORMIN	Message Only	303	$24,070.17	$79.44	$0.00	24.6	224.4	43	14	$1,080.93
All Others			28,807	$2,877,658.69	$99.89	$0.00	25.4	46.0	3,324	3,367	$604,370.99
DD - Drug-Drug Interaction			32,767	$2,941,631.86	$89.77	$0.00	25.9	47.8	3,742	3,644	$607,215.61

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

HD - High Dose Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	HYDROCODONE/ ACETAMINOPHEN	ADULT MAX DLY = 6.00 UN	Message Only	494	$15,784.93	$31.95	$0.00	16.2	126.2	0	19	$670.21
2	ZOLPIDEM TARTRATE	GERIATRIC MAX DLY = .50UN	Message Only	426	$1,746.78	$4.10	$0.00	30.0	30.0	0	21	$103.43
3	KETOROLAC TROMETHAMINE	GERIATRIC MAX DLY = 2.00UN	Message Only	424	$2,680.57	$6.32	$0.00	1.0	4.7	0	21	$142.79
4	DEXAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 2.60UN	Message Only	241	$4,216.38	$17.50	$0.00	1.0	12.7	0	9	$107.83
5	KENALOG-40	GERIATRIC MAX DLY = 2.00UN	Message Only	227	$7,569.76	$33.35	$0.00	1.0	5.8	0	15	$315.91
6	PROMETHAZINE/ CODEINE	ADULT MAX DLY = 30.00 UN	Message Only	223	$2,660.16	$11.93	$0.00	2.9	130.6	0	8	$91.21
7	GRANISETRON HCL	GERIATRIC MAX DLY = .85UN	Message Only	215	$5,416.43	$25.19	$0.00	1.0	1.6	0	6	$389.50
8	MIDAZOLAM HCL	GERIATRIC MAX DLY = 3.50UN	Message Only	158	$295.42	$1.87	$0.00	1.0	5.3	0	52	$98.19
9	VITAMIN D3	ADULT MAX DLY = 1.00 UN	Message Only	195	$1,702.04	$8.73	$0.00	28.8	65.8	0	11	$82.75
10	INVEGA SUSTENNA	ADULT MAX DLY = .05 UN	Message Only	198	$320,493.71	$1,618.66	$0.00	26.4	1.5	0	6	$10,311.90
All Others				14,541	$3,788,680.16	$260.55	$0.00	15.0	117.1	170	2,129	$883,394.62
HD - High Dose Alert				17,342	$4,151,246.34	$239.38	$0.00	14.5	105.4	170	2,297	$895,708.34

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

ID - Ingredient Duplication

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	HYDROCODONE/ ACETAMINOPHEN	HYDROCO/APAP TAB 10-325MG	Hard Reject	1	$14.62	$14.62	$0.00	7.0	21.0	891	0	$0.00
2	SODIUM CHLORIDE	SOD CHLORIDE INJ 0.9%	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	588	0	$0.00
3	OXYCODONE/ ACETAMINOPHEN	OXYCOD/APAP TAB 10-325MG	Hard Reject	2	$46.81	$23.40	$0.00	7.0	21.0	489	0	$0.00
4	PROAIR HFA	PROAIR HFA AER	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	419	0	$0.00
5	ALPRAZOLAM	ALPRAZOLAM TAB 1MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	411	0	$0.00
6	ZOLPIDEM TARTRATE	ZOLPIDEM TAB 10MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	404	0	$0.00
7	GABAPENTIN	GABAPENTIN CAP 300MG	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	371	0	$0.00
8	ALPRAZOLAM	ALPRAZOLAM TAB 2MG	Hard Reject	1	$13.43	$13.43	$0.00	30.0	60.0	368	0	$0.00
9	TRAMADOL HCL	TRAMADOL HCL TAB 50MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	311	0	$0.00
10	CLONAZEPAM	CLONAZEPAM TAB 1MG	Hard Reject	2	$22.23	$11.12	$0.00	20.0	30.0	276	0	$0.00
All Others				13,618	$2,077,676.07	$152.57	$0.00	27.4	99.1	28,217	3,694	$612,675.71
ID - Ingredient Duplication				13,624	$2,077,773.16	$152.51	$0.00	27.4	99.1	32,745	3,694	$612,675.71

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

LD - Low Dose Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	ONDANSETRON HCL	GERIATRIC MIN DLY = 2.00UN	Message Only	723	$281.80	$0.39	$0.00	1.5	1.5	0	461	$120.14
2	ONDANSETRON ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	659	$333.89	$0.51	$0.00	1.3	1.3	0	275	$114.45
3	IPRATROPIUM BROMIDE/ALBUT	GERIATRIC MIN DLY = 12.00UN	Message Only	590	$854.34	$1.45	$0.00	2.7	15.9	0	273	$216.15
4	METFORMIN HCL	ADULT MIN DLY = 1.70 UN	Message Only	575	$4,633.08	$8.06	$0.00	34.8	34.5	0	46	$401.21
5	VITAMIN D	ADULT MIN DLY = .14 UN	Message Only	499	$4,703.60	$9.43	$0.00	30.2	3.0	0	22	$188.82
6	ALBUTEROL SULFATE	GERIATRIC MIN DLY = 9.00UN	Message Only	386	$525.74	$1.36	$0.00	3.5	18.0	0	111	$104.10
7	GABAPENTIN	ADULT MIN DLY = 3.00 UN	Message Only	441	$4,710.65	$10.68	$0.00	32.0	51.8	0	29	$296.81
8	CITALOPRAM HYDROBROMIDE	ADULT MIN DLY = 2.00 UN	Message Only	323	$3,335.64	$10.33	$0.00	29.1	29.2	0	38	$406.20
9	PROPRANOLOL HCL	ADULT MIN DLY = 3.00 UN	Message Only	312	$3,666.21	$11.75	$0.00	30.2	53.6	0	43	$522.31
10	ONDANSETRON HCL	ADULT MIN DLY = 2.00 UN	Message Only	323	$3,760.19	$11.64	$0.00	19.0	12.0	0	22	$266.04
All Others				19,219	$2,039,169.61	$106.10	$0.00	24.2	52.7	0	3,176	$440,680.45
LD - Low Dose Alert				24,050	$2,065,974.75	$85.90	$0.00	22.6	46.0	0	4,496	$443,316.68

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

LR - Underuse Precaution

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	LISINOPRIL	7 DAYS LATE REFILLING	Message Only	79	$589.32	$7.46	$0.00	30.0	32.3	0	9	$66.00
2	LEVOTHYROXINE SODIUM	7 DAYS LATE REFILLING	Message Only	75	$734.08	$9.79	$0.00	29.8	29.4	0	0	$0.00
3	AMLODIPINE BESYLATE	7 DAYS LATE REFILLING	Message Only	72	$630.06	$8.75	$0.00	29.7	30.1	0	1	$10.93
4	ATORVASTATIN CALCIUM	8 DAYS LATE REFILLING	Message Only	67	$773.67	$11.55	$0.00	29.5	29.8	0	3	$27.25
5	ATORVASTATIN CALCIUM	7 DAYS LATE REFILLING	Message Only	64	$724.27	$11.32	$0.00	30.0	30.5	0	4	$43.98
6	PROAIR HFA	11 DAYS LATE REFILLING	Message Only	63	$3,192.04	$50.67	$0.00	19.9	8.9	0	2	$120.07
6	LISINOPRIL	8 DAYS LATE REFILLING	Message Only	62	$450.39	$7.26	$0.00	29.4	31.6	0	3	$25.54
8	AMLODIPINE BESYLATE	8 DAYS LATE REFILLING	Message Only	57	$447.59	$7.85	$0.00	30.0	31.6	0	4	$33.76
8	GABAPENTIN	8 DAYS LATE REFILLING	Message Only	53	$691.73	$13.05	$0.00	28.2	97.3	0	8	$125.08
10	LISINOPRIL	9 DAYS LATE REFILLING	Message Only	53	$406.83	$7.68	$0.00	29.6	33.0	0	3	$18.91
All Others				57,022	$5,520,860.25	$96.82	$0.00	28.8	49.1	0	6,137	$1,037,297.01
LR - Underuse Precaution				57,667	$5,529,500.23	$95.89	$0.00	28.8	48.9	0	6,174	$1,037,768.53

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

MN - Insufficnt Duration Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	IPRATROPIUM BROMIDE/ALBUT	MIN. DAYS THERAPY = 30	Message Only	542	$9,551.67	$17.62	$0.00	9.3	145.2	0	105	$1,176.72
2	LISINOPRIL	MIN. DAYS THERAPY = 7	Message Only	338	$252.28	$0.75	$0.00	1.3	1.6	0	223	$11.51
3	PANTOPRAZOLE SODIUM	MIN. DAYS THERAPY = 7	Message Only	292	$155.96	$0.53	$0.00	1.2	1.3	0	200	$30.07
4	METOPROLOL TARTRATE	MIN. DAYS THERAPY = 7	Message Only	228	$69.38	$0.30	$0.00	1.1	1.6	0	162	$5.68
5	CLONIDINE HCL	MIN. DAYS THERAPY = 7	Message Only	240	$393.66	$1.64	$0.00	1.6	5.5	0	110	$44.30
6	LEVETIRACETAM	MIN. DAYS THERAPY = 14	Message Only	313	$3,390.76	$10.83	$0.00	5.8	49.0	0	35	$177.76
7	LIPITOR	MIN. DAYS THERAPY = 7	Message Only	170	$2,399.45	$14.11	$0.00	1.0	1.5	0	135	$1,836.53
8	SULFAMETHOXAZOLE/ TRIMETHO	MIN. DAYS THERAPY = 5	Message Only	210	$1,020.72	$4.86	$0.00	2.0	8.8	0	42	$112.96
9	FERROUS SULFATE	MIN. DAYS THERAPY = 30	Message Only	179	$998.08	$5.58	$0.00	12.3	22.9	0	60	$41.37
10	BROMPHEN/ PSEUDOEPHEDRINE	MIN. DAYS THERAPY = 7	Message Only	221	$6,006.92	$27.18	$0.00	4.7	112.2	0	16	$435.52
All Others				5,367	$238,319.39	$44.40	$0.00	2.5	17.4	0	2,170	$70,638.97
MN - Insufficnt Duration Alert				8,100	$262,558.27	$32.41	$0.00	3.2	27.3	0	3,258	$74,511.39

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

MX - Excessive Duration Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	2,519	$25,673.52	$10.19	$0.00	30.1	65.3	0	140	$2,164.02
2	AZITHROMYCIN	MAX DAYS THERAPY = 5	Message Only	321	$7,211.59	$22.47	$0.00	11.0	20.7	0	15	$314.35
3	FLUCONAZOLE	MAX DAYS THERAPY = 1	Message Only	204	$2,843.12	$13.94	$0.00	3.1	3.3	0	13	$304.86
4	EPIPEN 2-PAK	MAX DAYS THERAPY = 1	Message Only	152	$82,423.18	$542.26	$0.00	2.2	2.2	0	20	$9,956.65
5	MAPAP	MAX DAYS THERAPY = 10	Message Only	161	$1,522.89	$9.46	$0.00	26.9	101.1	0	9	$88.57
6	DIPHENOXYLATE/ ATROPINE	MAX DAYS THERAPY = 14	Message Only	146	$3,267.95	$22.38	$0.00	26.9	104.7	0	16	$320.58
7	POLYETHYLENE GLYCOL 3350	MAX DAYS THERAPY = 14	Message Only	111	$3,378.78	$30.44	$0.00	29.5	29.5	0	19	$505.14
8	SENEXON-S	MAX DAYS THERAPY = 14	Message Only	112	$1,085.73	$9.69	$0.00	29.5	58.3	0	6	$51.01
9	TRAMADOL HYDROCHLORIDE/AC	MAX DAYS THERAPY = 5	Message Only	106	$1,710.22	$16.13	$0.00	21.1	73.5	0	9	$153.59
10	CEFDINIR	MAX DAYS THERAPY = 10	Message Only	104	$4,459.59	$42.88	$0.00	15.7	70.1	0	2	$75.27
All Others				1,342	$201,446.32	$150.11	$0.00	26.3	74.4	0	164	$44,849.12
MX - Excessive Duration Alert				5,278	$335,022.89	$63.48	$0.00	25.5	62.2	0	413	$58,783.16

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

PA - Drug-Age Precaution

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	PROMETHAZINE-DM	AGE LESS THAN 4	Message Only	29	$218.50	$7.53	$0.00	10.1	86.4	0	1	$7.05
2	PROMETHAZINE/ DEXTROMETHOR	AGE LESS THAN 4	Message Only	19	$149.23	$7.85	$0.00	9.5	96.3	0	0	$0.00
3	PROMETHAZINE HCL PLAIN	AGE LESS THAN 4	Message Only	12	$87.77	$7.31	$0.00	9.3	114.4	0	1	$11.99
4	PROMETHAZINE HCL	AGE LESS THAN 4	Message Only	6	$62.68	$10.45	$0.00	10.0	114.2	0	2	$22.16
5	PROMETHAZINE/CODEINE	AGE LESS THAN 4	Message Only	4	$38.97	$9.74	$0.00	13.8	82.5	0	1	$12.41
6	PROMETHAZINE VC/CODEINE	AGE LESS THAN 4	Message Only	2	$80.35	$40.18	$0.00	20.0	102.5	0	0	$0.00
6	PROMETHEGAN	AGE LESS THAN 4	Message Only	1	$19.78	$19.78	$0.00	2.0	10.0	0	1	$19.78
PA - Drug-Age Precaution				73	$657.28	$9.00	$0.00	10.2	95.0	0	6	$73.39

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

TD - Therapeutic Duplication

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	MORPHINE SULFATE	SHORT ACTING NARCOTIC ANALGESI	Message Only	969	$4,815.23	$4.97	$0.00	3.8	12.6	0	656	$1,778.56
2	HYDROCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,262	$21,591.36	$17.11	$0.00	16.4	66.0	0	188	$1,097.22
3	QUETIAPINE FUMARATE	ORAL ANTIPSYCHOTICS	Message Only	1,318	$19,845.33	$15.06	$0.00	26.8	38.8	0	101	$939.53
4	HYDROMORPHONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	876	$4,680.25	$5.34	$0.00	4.7	16.3	0	458	$1,328.77
5	OXYCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,074	$32,960.98	$30.69	$0.00	13.4	54.0	0	229	$2,095.21
6	RISPERIDONE	ORAL ANTIPSYCHOTICS	Message Only	963	$11,541.98	$11.99	$0.00	27.6	46.7	0	99	$997.04
7	OXYCODONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	959	$29,472.73	$30.73	$0.00	22.6	103.4	0	87	$1,132.45
8	TRAMADOL HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	750	$7,348.00	$9.80	$0.00	21.2	85.3	0	48	$338.60
9	LISINOPRIL	ANGIOTENSIN BLOCKERS	Message Only	646	$4,007.48	$6.20	$0.00	32.6	35.8	0	141	$391.82
10	ALPRAZOLAM	BENZODIAZEPINES	Message Only	707	$6,704.52	$9.48	$0.00	24.9	62.1	0	62	$314.85
All Others				34,871	$4,233,948.17	$121.42	$0.00	24.4	52.8	7,775	6,267	$809,768.65
TD - Therapeutic Duplication				44,395	$4,376,916.03	$98.59	$0.00	23.2	52.6	7,775	8,336	$820,182.70

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

Selected Filters

Client(s): Nevada Medicaid - HPES

Carrier(s): NVM-NEVADA MEDICAID

Account(s): ALL

Group(s): ALL

Date Type:	Date Filled Submitted
Primary Start Date:	Jan 1, 2016
Primary End Date:	Mar 31, 2016
Relative Date Description:	N/A
Select Report Group By:	Product
Top Values Displayed:	10
Display Report Description:	No

CONFIDENTIAL

RXT6050D - Summarized DUR Activity Report

Between Apr 1, 2016 and Jun 30, 2016

Jul 19, 2016
12:52:37 PM

Claims Summary:

RxCLAIM Status	Total Rxs	% of Total Rxs	Total Plan Paid	Total Member Paid
Paid	770,262	61.0%	$75,375,612.97	$0.00
Rejected	394,885	31.3%	$52,173,684.05	$0.00
Reversed	97,038	7.7%	-$18,841,737.47	$0.00
Totals	1,262,185	100%	$108,707,559.55	$0.00

DUR Information Summary:

		Total DURs		DURs on Paid Rxs		DURs on Rejected Rxs		DURs on Reversed Rxs	
DUR Type	Clinical Level	Count	% of All DURs	Count	% of DUR Type	Count	% of DUR Type	Count	% of DUR Type
LR - Underuse Precaution	0 - NS	64,269	23.2%	57,951	90.2%	0	0.0%	6,318	9.8%
TD - Therapeutic Duplication	0 - NS	60,772	22.0%	43,711	71.9%	8,259	13.6%	8,802	14.5%
ID - Ingredient Duplication	2 - Mod	49,689	18.0%	13,782	27.7%	32,115	64.6%	3,792	7.6%
DD - Drug-Drug Interaction	1 - Maj	39,572	14.3%	32,013	80.9%	3,864	9.8%	3,695	9.3%
LD - Low Dose Alert	0 - NS	28,464	10.3%	23,623	83.0%	0	0.0%	4,841	17.0%
HD - High Dose Alert	0 - NS	17,638	6.4%	15,482	87.8%	194	1.1%	1,962	11.1%
MN - Insufficnt Duration Alert	0 - NS	10,871	3.9%	7,876	72.4%	0	0.0%	2,995	27.6%
MX - Excessive Duration Alert	0 - NS	5,382	1.9%	4,978	92.5%	0	0.0%	404	7.5%
PA - Drug-Age Precaution	1 - Maj	26	0.0%	24	92.3%	0	0.0%	2	7.7%
Total All DURs		276,683	100.0%	199,440	72.1%	44,432	16.1%	32,811	11.9%

* DUR Information Summary results are sorted by Total DUR count in descending order
* Some Rx claims could have multiple DUR messages. And there could be multiple instances of the same DUR message on a Rx claim
* The Count and % of DUR Type for Paid, Rejected and Reversed Rxs are based on DUR Type totals for each row

DD - Drug-Drug Interaction

Rank	Top Drug Drug Interaction	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	CARISOPRODOL - ALPRAZOLAM	Message Only	461	$5,103.26	$11.07	$0.00	28.6	80.7	57	31	$227.09
2	TRAZODONE HCL - QUETIAPINE	Message Only	442	$5,081.38	$11.50	$0.00	28.7	40.9	37	38	$579.19
3	SIMVASTATIN - FENOFIBRATE	Message Only	407	$6,202.83	$15.24	$0.00	32.9	33.1	56	31	$542.55
4	TRAZODONE HCL - CITALOPRAM	Message Only	404	$3,904.07	$9.66	$0.00	29.8	40.0	34	25	$238.02
5	TRAZODONE - QUETIAPINE FUMARATE	Message Only	377	$6,190.00	$16.42	$0.00	28.0	43.8	49	22	$290.24
6	SPIRONOLACT - LISINOPRIL	Message Only	360	$3,017.86	$8.38	$0.00	36.2	43.2	37	35	$222.29
7	SPIRONOLACTONE - LISINOPRIL	Message Only	364	$3,674.34	$10.09	$0.00	36.3	40.5	47	15	$125.62
8	TRAZODONE - CITALOPRAM HYDROBROMIDE	Message Only	354	$2,760.09	$7.80	$0.00	29.4	30.4	37	18	$90.96
9	DIVALPROEX - CLONAZEPAM	Message Only	364	$3,378.64	$9.28	$0.00	25.5	52.6	29	15	$122.93
10	FENOFIBRATE - ATORVASTATIN CALCIUM	Message Only	333	$3,795.01	$11.40	$0.00	32.1	32.1	49	15	$108.58
All Others			28,147	$2,943,661.42	$104.58	$0.00	25.2	49.2	3,432	3,450	$511,681.12
DD - Drug-Drug Interaction			32,013	$2,986,768.90	$93.30	$0.00	25.8	48.6	3,864	3,695	$514,228.59

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

HD - High Dose Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	HYDROCODONE/ ACETAMINOPHEN	ADULT MAX DLY = 6.00 UN	Message Only	473	$14,603.13	$30.87	$0.00	15.8	122.3	0	21	$511.14
2	KETOROLAC TROMETHAMINE	GERIATRIC MAX DLY = 2.00UN	Message Only	385	$3,037.50	$7.89	$0.00	1.0	5.2	0	28	$176.18
3	ZOLPIDEM TARTRATE	GERIATRIC MAX DLY = .50UN	Message Only	333	$1,625.92	$4.88	$0.00	29.6	29.6	0	18	$46.09
4	DEXAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 2.60UN	Message Only	266	$4,467.86	$16.80	$0.00	1.0	12.8	0	18	$234.00
5	MIDAZOLAM HCL	GERIATRIC MAX DLY = 3.50UN	Message Only	199	$335.06	$1.68	$0.00	1.0	5.1	0	52	$92.27
6	GRANISETRON HCL	GERIATRIC MAX DLY = .85UN	Message Only	222	$5,858.81	$26.39	$0.00	1.0	1.8	0	9	$67.50
7	IBUPROFEN	ADULT MAX DLY = 4.00 UN	Message Only	202	$2,047.97	$10.14	$0.00	6.9	32.4	0	8	$94.60
8	KENALOG-40	GERIATRIC MAX DLY = 2.00UN	Message Only	200	$7,083.10	$35.42	$0.00	1.0	6.0	0	3	$127.18
9	INVEGA SUSTENNA	ADULT MAX DLY = .05 UN	Message Only	188	$344,373.93	$1,831.78	$0.00	26.0	1.5	0	6	$12,369.96
10	BETAMETHASONE SODIUM PHOS	GERIATRIC MAX DLY = 1.50UN	Message Only	183	$4,482.35	$24.49	$0.00	1.0	5.2	0	10	$236.49
All Others				12,831	$3,772,254.27	$294.00	$0.00	16.0	363.3	194	1,789	$695,810.92
HD - High Dose Alert				15,482	$4,160,169.90	$268.71	$0.00	14.9	306.5	194	1,962	$709,766.33

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

ID - Ingredient Duplication

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	HYDROCODONE/ ACETAMINOPHEN	HYDROCO/APAP TAB 10-325MG	Hard Reject	2	$32.03	$16.02	$0.00	9.0	30.0	734	0	$0.00
2	SODIUM CHLORIDE	SOD CHLORIDE INJ 0.9%	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	678	0	$0.00
3	OXYCODONE/ ACETAMINOPHEN	OXYCOD/APAP TAB 10-325MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	470	0	$0.00
4	PROAIR HFA	PROAIR HFA AER	Soft Reject	0	$0.00	$0.00	$0.00	0.00	0.00	392	0	$0.00
5	GABAPENTIN	GABAPENTIN CAP 300MG	Soft Reject	1	$10.46	$10.46	$0.00	7.0	7.0	385	0	$0.00
6	ALPRAZOLAM	ALPRAZOLAM TAB 2MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	367	0	$0.00
7	ALPRAZOLAM	ALPRAZOLAM TAB 1MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	363	0	$0.00
8	GABAPENTIN	GABAPENTIN CAP 300MG	Message Only	271	$3,495.96	$12.90	$0.00	30.6	98.7	0	43	$519.73
9	ZOLPIDEM TARTRATE	ZOLPIDEM TAB 10MG	Hard Reject	0	$0.00	$0.00	$0.00	0.00	0.00	272	0	$0.00
10	TRAMADOL HCL	TRAMADOL HCL TAB 50MG	Hard Reject	1	$12.72	$12.72	$0.00	30.0	120.0	268	0	$0.00
All Others				13,507	$1,909,203.87	$141.35	$0.00	27.4	90.7	28,186	3,749	$779,869.93
ID - Ingredient Duplication				13,782	$1,912,755.04	$138.79	$0.00	27.5	90.8	32,115	3,792	$780,389.66

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

LD - Low Dose Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	ONDANSETRON HCL	GERIATRIC MIN DLY = 2.00UN	Message Only	1,339	$486.63	$0.36	$0.00	1.3	1.3	0	951	$223.87
2	ONDANSETRON ODT	GERIATRIC MIN DLY = 2.00UN	Message Only	680	$398.04	$0.59	$0.00	1.6	1.5	0	271	$133.88
3	IPRATROPIUM BROMIDE/ALBUT	GERIATRIC MIN DLY = 12.00UN	Message Only	468	$832.63	$1.78	$0.00	2.9	18.7	0	179	$161.49
4	METFORMIN HCL	ADULT MIN DLY = 1.70 UN	Message Only	498	$3,996.69	$8.03	$0.00	35.1	34.8	0	63	$577.16
5	VITAMIN D	ADULT MIN DLY = .14 UN	Message Only	510	$4,961.75	$9.73	$0.00	30.4	3.0	0	35	$357.37
6	HEPARIN SODIUM	GERIATRIC MIN DLY = 4.00UN	Message Only	332	$1,225.32	$3.69	$0.00	1.5	3.0	0	203	$480.93
7	GABAPENTIN	ADULT MIN DLY = 3.00 UN	Message Only	447	$4,672.94	$10.45	$0.00	32.8	53.7	0	30	$319.61
8	ALBUTEROL SULFATE	GERIATRIC MIN DLY = 9.00UN	Message Only	320	$516.23	$1.61	$0.00	3.7	19.0	0	84	$74.84
9	METFORMIN HCL	GERIATRIC MIN DLY = 1.70UN	Message Only	307	$1,065.72	$3.47	$0.00	36.9	36.4	0	42	$101.88
10	ONDANSETRON HCL	ADULT MIN DLY = 2.00 UN	Message Only	300	$3,366.38	$11.22	$0.00	18.6	11.5	0	34	$378.92
All Others				18,422	$1,614,904.12	$87.66	$0.00	24.5	54.3	0	2,949	$371,959.91
LD - Low Dose Alert				23,623	$1,636,426.45	$69.27	$0.00	22.1	45.6	0	4,841	$374,769.86

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

LR - Underuse Precaution

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	LISINOPRIL	7 DAYS LATE REFILLING	Message Only	98	$756.93	$7.72	$0.00	30.0	34.3	0	6	$59.07
2	ATORVASTATIN CALCIUM	7 DAYS LATE REFILLING	Message Only	79	$868.13	$10.99	$0.00	29.4	29.6	0	2	$27.40
3	ATORVASTATIN CALCIUM	8 DAYS LATE REFILLING	Message Only	73	$797.42	$10.92	$0.00	29.7	29.7	0	1	$1.20
4	AMLODIPINE BESYLATE	7 DAYS LATE REFILLING	Message Only	66	$580.34	$8.79	$0.00	30.4	31.5	0	3	$22.78
4	GABAPENTIN	7 DAYS LATE REFILLING	Message Only	62	$856.27	$13.81	$0.00	29.6	92.7	0	7	$102.00
6	LISINOPRIL	8 DAYS LATE REFILLING	Message Only	63	$437.19	$6.94	$0.00	29.8	33.6	0	4	$14.53
7	MONTELUKAST SODIUM	7 DAYS LATE REFILLING	Message Only	56	$1,071.47	$19.13	$0.00	30.0	30.0	0	8	$111.05
7	METFORMIN HCL	8 DAYS LATE REFILLING	Message Only	54	$416.10	$7.71	$0.00	30.8	67.8	0	10	$86.63
9	LISINOPRIL	9 DAYS LATE REFILLING	Message Only	57	$435.19	$7.63	$0.00	30.0	32.6	0	6	$37.17
10	LEVOTHYROXINE SODIUM	8 DAYS LATE REFILLING	Message Only	55	$660.29	$12.01	$0.00	29.6	30.1	0	5	$70.58
All Others				57,288	$5,698,666.21	$99.47	$0.00	28.6	49.7	0	6,266	$982,731.40
LR - Underuse Precaution				57,951	$5,705,545.54	$98.45	$0.00	28.6	49.5	0	6,318	$983,263.81

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

MN - Insufficnt Duration Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	LISINOPRIL	MIN. DAYS THERAPY = 7	Message Only	343	$73.88	$0.22	$0.00	1.1	1.5	0	205	$28.22
2	IPRATROPIUM BROMIDE/ALBUT	MIN. DAYS THERAPY = 30	Message Only	475	$9,278.23	$19.53	$0.00	9.0	139.7	0	57	$821.12
3	METOPROLOL TARTRATE	MIN. DAYS THERAPY = 7	Message Only	305	$102.53	$0.34	$0.00	1.2	1.6	0	187	$6.33
4	CLONIDINE HCL	MIN. DAYS THERAPY = 7	Message Only	290	$644.47	$2.22	$0.00	1.6	3.7	0	111	$10.44
5	LEVETIRACETAM	MIN. DAYS THERAPY = 14	Message Only	289	$3,422.14	$11.84	$0.00	6.1	56.4	0	41	$268.00
6	ATORVASTATIN CALCIUM	MIN. DAYS THERAPY = 7	Message Only	202	$164.47	$0.81	$0.00	1.3	1.4	0	111	$38.48
7	AMLODIPINE BESYLATE	MIN. DAYS THERAPY = 7	Message Only	189	$72.30	$0.38	$0.00	1.2	1.3	0	100	$2.32
8	NICOTINE TRANSDERMAL SYST	MIN. DAYS THERAPY = 7	Message Only	135	$220.39	$1.63	$0.00	1.0	1.0	0	103	$231.48
9	FERROUS SULFATE	MIN. DAYS THERAPY = 30	Message Only	180	$953.98	$5.30	$0.00	13.0	26.2	0	56	$41.97
10	SULFAMETHOXAZOLE/ TRIMETHO	MIN. DAYS THERAPY = 5	Message Only	198	$1,008.81	$5.10	$0.00	2.2	6.4	0	33	$135.52
All Others				5,270	$288,879.37	$54.82	$0.00	2.4	19.5	0	1,991	$146,425.59
MN - Insufficnt Duration Alert				7,876	$304,820.57	$38.70	$0.00	2.9	24.6	0	2,995	$148,009.47

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

MX - Excessive Duration Alert

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	CYCLOBENZAPRINE HCL	MAX DAYS THERAPY = 21	Message Only	2,460	$25,841.79	$10.50	$0.00	30.2	65.3	0	112	$1,131.07
2	EPIPEN 2-PAK	MAX DAYS THERAPY = 1	Message Only	186	$103,507.30	$556.49	$0.00	2.3	2.3	0	33	$20,954.80
2	AZITHROMYCIN	MAX DAYS THERAPY = 5	Message Only	203	$4,575.14	$22.54	$0.00	12.6	21.3	0	16	$322.28
4	FLUCONAZOLE	MAX DAYS THERAPY = 1	Message Only	190	$2,699.96	$14.21	$0.00	3.4	3.5	0	13	$142.06
5	MAPAP	MAX DAYS THERAPY = 10	Message Only	174	$1,647.00	$9.47	$0.00	26.7	107.3	0	2	$15.72
6	DIPHENOXYLATE/ ATROPINE	MAX DAYS THERAPY = 14	Message Only	160	$5,103.63	$31.90	$0.00	26.8	108.2	0	9	$330.32
7	SENEXON-S	MAX DAYS THERAPY = 14	Message Only	122	$1,219.82	$10.00	$0.00	30.4	60.2	0	6	$46.35
8	POLYETHYLENE GLYCOL 3350	MAX DAYS THERAPY = 14	Message Only	93	$2,624.90	$28.22	$0.00	29.3	29.3	0	20	$672.85
9	LOPERAMIDE HCL	MAX DAYS THERAPY = 14	Message Only	87	$2,684.72	$30.86	$0.00	26.5	108.0	0	4	$108.37
10	TRAMADOL HYDROCHLORIDE/AC	MAX DAYS THERAPY = 5	Message Only	68	$896.71	$13.19	$0.00	22.3	74.7	0	10	$216.38
All Others				1,235	$238,312.71	$192.97	$0.00	25.5	65.9	0	179	$99,166.16
MX - Excessive Duration Alert				4,978	$389,113.68	$78.17	$0.00	25.8	61.9	0	404	$123,106.36

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

PA - Drug-Age Precaution

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	PROMETHAZINE HCL	AGE LESS THAN 4	Message Only	9	$86.79	$9.64	$0.00	5.7	133.3	0	0	$0.00
2	PROMETHAZINE/ DEXTROMETHOR	AGE LESS THAN 4	Message Only	7	$70.07	$10.01	$0.00	9.1	75.0	0	0	$0.00
3	PROMETHAZINE-DM	AGE LESS THAN 4	Message Only	6	$42.49	$7.08	$0.00	12.5	93.3	0	0	$0.00
4	PROMETHAZINE HCL PLAIN	AGE LESS THAN 4	Message Only	0	$0.00	$0.00	$0.00	0.00	0.00	0	2	$9.63
4	PROMETHEGAN	AGE LESS THAN 4	Message Only	2	$194.10	$97.05	$0.00	3.5	11.0	0	0	$0.00
PA - Drug-Age Precaution				24	$393.45	$16.39	$0.00	8.2	96.1	0	2	$9.63

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

TD - Therapeutic Duplication

Rank	Top Drug	Therapy / Reason	DUR Response	Total Paid Rxs	Total Plan Paid	Plan Paid Per Rx	Member Paid Per Rx	Days Supply Per Rx	Quantity Per Rx	Total Rejected Rxs	Total Reversed Rxs	Total Reversed Amount
1	MORPHINE SULFATE	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,026	$6,077.85	$5.92	$0.00	4.4	15.4	0	710	$2,007.12
2	QUETIAPINE FUMARATE	ORAL ANTIPSYCHOTICS	Message Only	1,272	$19,598.69	$15.41	$0.00	27.0	39.4	0	120	$1,145.82
3	HYDROMORPHONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	911	$4,915.59	$5.40	$0.00	4.1	14.8	0	478	$1,319.01
4	HYDROCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,178	$18,196.97	$15.45	$0.00	15.1	58.5	0	176	$898.60
5	OXYCODONE/ ACETAMINOPHEN	SHORT ACTING NARCOTIC ANALGESI	Message Only	1,011	$29,309.53	$28.99	$0.00	13.1	51.9	0	210	$1,375.90
6	OXYCODONE HCL	SHORT ACTING NARCOTIC ANALGESI	Message Only	950	$27,394.33	$28.84	$0.00	21.8	96.6	0	82	$958.37
7	RISPERIDONE	ORAL ANTIPSYCHOTICS	Message Only	913	$10,765.56	$11.79	$0.00	26.6	43.5	0	67	$656.98
8	KETOROLAC TROMETHAMINE	NON-STEROIDAL ANTI-INFLAMMATOR	Message Only	705	$2,543.45	$3.61	$0.00	1.1	2.3	0	139	$356.45
9	LISINOPRIL	ANGIOTENSIN BLOCKERS	Message Only	671	$4,108.02	$6.12	$0.00	30.5	34.1	0	161	$475.54
10	LORAZEPAM	BENZODIAZEPINES	Message Only	559	$2,580.78	$4.62	$0.00	9.6	22.1	0	200	$237.88
All Others				34,515	$5,678,446.90	$164.52	$0.00	24.8	79.0	8,259	6,459	$1,308,356.81
TD - Therapeutic Duplication				43,711	$5,803,937.67	$132.78	$0.00	22.9	70.8	8,259	8,802	$1,317,788.48

* Rankings are based on the following order: Total Rxs (Paid + Rejected + Reversed) descending, total Rejected Rxs descending and Top Drug/Client Rider ascending.

Selected Filters

Client(s): Nevada Medicaid - HPES

Carrier(s): NVM-NEVADA MEDICAID

Account(s): ALL

Group(s): ALL

Date Type:	Date Filled Submitted
Primary Start Date:	Apr 1, 2016
Primary End Date:	Jun 30, 2016
Relative Date Description:	N/A
Select Report Group By:	Product
Top Values Displayed:	10
Display Report Description:	No