Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
P&T Meeting Notes
December 19, 2018

Man:	…Nancy Lee who is one of our clinical pharmacists.
Petra Eichelsdoerfer:	Petra Eichelsdoerfer, United Healthcare.
Dave Johnson:	David Johnson, Molina Healthcare.
Diane Schwilke:	Diane Schwilke, committee member.
Nancy Lee:	Nancy Lee, committee member.
Alex Park:	Alex Park, committee member.
Virginia Buccola:	Virginia Buccola, committee member.
Dale Sanderson:	Dale Sanderson, committee member.
Lisa Chew:	Lisa Chew, committee member.
Jordan Storhaug:	Jordan Storhaug, committee member.
Catherine Brown:	Catherine Brown, committee member.
Susan Flatebo:	Susan Flatebo, committee member.
Amber Figueroa:	Amber Figueroa, committee member.
Leta Evaskus:	Leta Evaskus, Health Care Authority.
Donna Sullivan:	Donna Sullivan, Health Care Authority.
Umang Patel:	Umang Patel, Magellan Medicaid.
Ryan Pistoresi:	Ryan Pistoresi, Health Care Authority.

Emily Transue: Emily Transue, Health Care Authority.

Emily Peltier: Emily Peltier, Health Care Authority.

Jose Zarate: Jose Zarate, Health Care Authority.

Amy Irwin: Amy Irwin, Health Care Authority.

Leta Evaskus: Is anyone from L&I on the phone?

Jaymie Mai: Yeah, Jaymie Mai from L&I.

Lisa Chew: I think we have one person from the end of the table who…

Sarah Pearson: Sarah Pearson, Health Care Authority.

Lisa Chew: Thank you. Leta or Donna, do you have any announcements before moving on to electing a new Vice Chair?

Leta Evaskus: No, we can go on. I just want to say that Amber did volunteer to be co-chair if no one else wants to volunteer. Any nominations?

Amber Figueroa: It's a coveted position for sure.

Susan Flatebo: I nominate Amber Figueroa for committee co-chair.

Lisa Chew: I second. All those in favor?

Group: Aye.

Lisa Chew: Congratulations, Amber.

[applause]

Lisa Chew: And thank you Dale, this is your last meeting. Thank you for your service to the committee.

Leta Evaskus: Thank you, Dale. Sorry, I did not announce. This is your last meeting and we really appreciate the last six years that you've been on the committee.

Lisa Chew: All right. Let's move on to our first agenda item, calcitonin gene-related peptide inhibitors report. I think Leila is on the phone.

Leila Kahwati: Yeah, that's right. Can you hear me okay?

Lisa Chew: Yes. We're in the process of pulling up your slides now.

Leila Kahwati: Okay. Well, I can start talking and just let me know when you've got them loaded. Hi everybody. So thank you. My name is Leila Kahwati. I'm an associated director of the RTI University of North Carolina Evidence-Based Practice Center. We are one of the research partners on the Drug Effectiveness Review Project and I'll be presenting the systematic review on calcitonin gene-related peptide inhibitors for migraine headache prophylaxis. First I'll just set up the topic with some background and then briefly describe our method, but I'll spend the majority of time walking you through the finding. The slides that I'm using today were from an hour-long presentation that I gave in October to the Drug Effectiveness Review Project Stakeholders. In order to keep to the agenda time I may skip through a few slides quickly. So just let me know when you've got them up.

Lisa Chew: Your slides are up.

Leila Kahwati: Okay. So starting on slide 2 a little background. The International Classification of Headache Disorders defines the diagnostic criteria for migraines, which are considered attacks with headache that last between 4 and 72 hours with specific characteristics like unilateral pulsating quality aggravated by activity. And these headaches can be with or without aura symptoms which are sensory disturbances like light flashes, blind spots or tingling with other symptoms such as nausea, vomiting, or sensitivity to light.

Leta Evaskus: Leila? This is Leta. I'm really sorry to interrupt you. It's really hard to hear you. There seems to be either some feedback… it sounds really choppy.

Leila Kahwati: Hmm. I'm on a headset. Let me pick up my handset. Let me adjust. I'm moving the microphone literally right under…

Leta Evaskus: Yeah, that's a lot better. Thank you.

Leila Kahwati: Okay. Um, so chronic migraine is defined as 15 or more headaches per month for at least 3 months and episodic migraine is diagnosed for fewer than 15 headaches per month. So available migraine preventative treatments include antidepressants, anticonvulsants, beta blockers and botulinum toxin. Calcitonin gene-related peptide or CGRP is a neuropeptide comprised of 37 amino acids that plays a role in vasodilation of cerebral and dura blood vessels and thus is involved in the path of physiology of migraines. So CGRP inhibitors are human monoclonal antibodies that target either the CGRP receptor or the CGRP ligand. Unlike other available preventative medications, CGRP inhibitors were developed specifically for migraine prevention. Slide 3.

This table describes the current CGRP inhibitors. Three have been approved by the FDA, erenumab, fremanezumab and galcanezumab, all of which are administered subcutaneously every month or three months, depending on the drug and dose. And then there's eptinezumab which is administered by IV infusion every three months and is still in the process of being studied and will undergo FDA review at some point probably early next year.

Moving on to slide 4. This slide describes the methods we used for this review. These are the criteria that we used to define the scope. We included randomized controlled trials, prospective cohort studies or systematic reviews in adults with either episodic or chronic migraine that evaluated any of the four CGRP inhibitors I described on the previous slide and that compared one CGRP inhibitor with another inhibitor or with another preventative drug or with placebo. The efficacy outcomes that we were interested in here were migraine events, pain, function, quality of life, use of rescue therapy and several others. And then the

safety outcomes included tolerability, adverse events, and discontinuations because of adverse events. Slide 5.

We were guided by four key questions. The first one was about the efficacy of CGRP inhibitors for migraine prophylaxis. The second was on the frequency of adverse events. The third one was about subgroups for which the efficacy or safety might vary and then the fourth one was to describe the characteristics of ongoing studies of these inhibitors. Moving on to slide 6.

To conduct the review we used methods established by the Drug Effectiveness Review Project, which includes a systematic search of several data sources, and then study selection by two independent reviewers using the study selection criteria. We abstracted data, checked it for accuracy and then calculated findings not supplied by study authors when the data was available in the study or a supplement to do so. And we know when we've calculated findings by using italics on those numbers here in the presentation and also in the accompanying report. We conducted two independent assessments of study methodological quality using DERP quality assessment instruments which are based on international standards. These assessments result in a rating of good, fair or poor methodological quality. And then finally we assessed the quality of the body of evidence using the GRADE approach for up to six outcomes for each drug and indication. So for chronic migraine separately from episodic migraine. And as a reminder within GRADE the body of evidence can be rated as high, moderate, low or very low. Bodies of evidence comprised solely of randomized controlled trials start at a high quality level and then get down-graded from high as needed for study limitations due to risk of biased, inconsistency in precision, or other considerations such as publication bias. Now I will move into the findings. Slide 8.

Our literature search yielded 13 placebo-controlled randomized trials published in the peer review literature. All were multi-center RCTs and were sponsored by manufacturers. We rated all of them as fair methodologic quality primarily because of the extensive manufacturer involvement in the study design, data collection, analysis and manuscript preparation. One study, this was a study of eptinezumab, was also rated

fair because of selective outcome reporting. So three studies evaluated chronic migraine. One evaluated erenumab and two evaluated fremanezumab. Ten studies evaluated patients with episodic migraine, one was eptinezumab, three were of erenumab, two were fremanezumab and four were in galcanezumab. And then just a little bit about the patients in these studies. Some studies excluded participants that were taking other migraine preventive agents. Other studies allowed participants taking other preventive treatments to enroll in the study as long as the dose was stable and several months prior to treatment. And then participants with clinically significant medical or psychiatric conditions were generally excluded from study enrollment. In addition to the primary research studies, we also identified two systematic reviews. One was done by the Institute for Clinical and Economic Review or ICER. It included a network meta-analysis and we rated this review as good methodological quality. The other was done by the Canadian Agency for Drugs and Technologies in Health and we rated this review as poor methodological quality. Slide 9.

So first I'm going to describe the findings from the three studies in participants with chronic migraine. As a reminder, participants with chronic migraine have migraine headaches at 15 days or more per month. Moving on to slide 10.

So all the study findings in this presentation are laid out like this. So let me just orient you a bit to this table. So each study is presented in a single row. The author, the year, and the duration of follow-up is in the first column. The drug and the intervention and sample sizes of each group is in the second column. The third column contains results from the studies primary study endpoint. Typically, this is a change from baseline in a migraine event measure compared to placebo. The fourth column summarizes the frequency and percentage of participants with at least one serious adverse event for each study group and then the last column summarizes the frequencies and percentages of participants with adverse events leading to discontinuation. On some of the tables, including this one and some that follow, we've included some additional notes and these are located at the bottom of the table. So for chronic migraine one study evaluated erenumab. It's listed in the first row of this table. It involved a total of 667 participants and evaluated both a 70 mg

and a 140 mg dose over 12 weeks. The primary outcome was change from baseline in migraine days per month at week 12 and both doses resulted in a statistically significant decrease of 2.5 days for active treatment compared to placebo. And as you can also see in the third and fourth columns the incidence of serious adverse events and discontinuations were infrequent and similar across groups. Two studies evaluated fremanezumab. Those are located in the second and third rows of the table on slide 10. Both evaluated two treatment doses over 12 weeks. Both studies used an initial dose of 675 mg followed by 225 mg monthly doses. And then one study also looked at a 675 mg quarterly dose and the other study looked at a 900 mg monthly dose. So these two studies used different primary outcomes. One used change from baseline and headache hours per month and the other used the change from baseline in headache days per month. But despite the difference both showed a statistically significant decrease in headache hours or days compared to placebo and similar to the erenumab study a similar frequency of serious adverse events and discontinuations because of adverse events was observed across groups. Moving on to slide 11.

On this slide I've summarized some of the findings related to these three studies among the populations with chronic migraine. So the range of reduction from baseline in migraine days per month compared to placebo across these three studies was 1.7 to 2.5 days. In addition to these primary outcomes, the favorable treatment effect was observed on most all secondary migraine outcomes reported. So this includes outcomes such as days of acute medication use, headache days, and the percentage of participants with at least a 50% reduction in migraine days per month. Quality of life was only evaluated in one study of fremanezumab and in this particular study authors observed a significant improvement on the headache impact test compared to placebo. It was 2.4 points difference for the 225 mg dose and 1 point difference for the 675 mg dose. And just for some reference a clinically meaningful difference on this particular instrument is about 1.5 points. And that was established in a population of primary care patients with migraine headache. In terms of safety – treatment-related liver injury was rare and ranged from 0% to 1.7% across active and placebo groups. And then finally in terms of subgroups only one study reported on differences in outcomes by subgroups and it was one study of fremanezumab. They

reported efficacy outcomes among the subgroup of participants that were not taking preventative therapy at baseline and the treatment effect was similar to that that was observed in the full study population. Slide 12.

This is our summary of findings table where we've used GRADE to assess the quality of evidence for erenumab in chronic migraine. So all of our summary findings tables are structured like this. So let me just orient you to it first. So we include the comparison being evaluated just below the column header so in the yellow shaded row, so this is erenumab versus placebo. The first column contains the specific outcome that we graded along with the number of studies available for the outcome. The second column lists our grade assessment. And as a reminder the four options within grade are high, moderate, low or very low. And bodies of RCT evidence start at high rating. The third column describes the findings or the relationship between the drug and its placebo comparator and then the last column provides the rationale for our quality rating, specifically the reason or reasons why we downgraded from a high rating. So as you can see we assess the evidence as moderate quality for a significant improvement in migraine days per month, days with acute migraine medication use, and percentage with at least 50% reduction in the number of migraine days for erenumab compared to placebo. And we assessed the evidence for serious adverse events and discontinuations from adverse events as very low quality for no difference between erenumab and placebo. We down-graded the quality of evidence for all of these outcomes for study limitations related to the expensive manufacture involvement in studies that I mentioned earlier and then we further downgraded the safety outcomes because of very serious concerns about imprecision, event frequencies were quite low, and the study samples were not really large enough to generate precise estimates. Slide 13.

This is our summary of findings table for fremanezumab and chronic migraine and then similar to erenumab we assessed the evidence as moderate quality for significant improvements in the efficacy outcomes, so migraine days per month, days with acute medication use, and percentage with at least 50% reduction in the number of migraine days. In addition for fremanezumab we assessed the mean change in headache

impact test as moderate quality. So we down-graded all the quality of evidence for all of the efficacy outcomes for the same study limitations related to manufacturer involvement and similar to erenumab we assessed the evidence for serious adverse events and discontinuation as very low quality for no difference for the same study limitations I've already mentioned and because of very serious concerns about imprecision. Slide 14.

As I mentioned we identified two systematic reviews for consideration in this review. So the one by ICER searched data sources through early May of 2018 and included the same three studies that we also had identified. This review reported that active treatment with erenumab or fremanezumab was more effective than placebo on a variety of migraine event outcomes. This review also concluded no significant differences between active treatment and placebo for various adverse event outcomes. The second review from Canada searched data sources through mid-December 2017. This review included an additional study that was still in progress and an additional study only published in a conference abstract. This review also reported that active treatment with erenumab or fremanezumab was more effective than placebo and also reported infrequent adverse events. They cited a 1 to 2 percent of adverse events incidents. Slide 15.

So the ICER review also conducted a network meta-analysis which is a type of analysis that allows for indirect comparison of therapies from across studies including placebo-controlled trials. In this analysis indirect comparisons between various doses of erenumab and fremanezumab, onabotulinum toxin and topiramate 100 mg daily were evaluated. This analysis looked at three efficacy outcomes and three safety outcomes that are listed there on the slide. Study authors observed no significant differences in any of the pairwise comparisons for any of these outcomes between… either between the two CGRP inhibitors compared to each other or between either CGRP inhibitor and either botulinum toxin or topiramate.

Okay. We're going to next move into the findings for episodic migraine, but before I do let me just pause and see if there are any questions on chronic migraine? Okay. Hearing none I will continue.

So next we'll be looking up findings from the 10 studies and participants with episodic migraine. As a reminder episodic migraine are headaches that meet migraine headache criteria, but that occur fewer than 15 times per month. Slide 17.

So one Phase 1B study evaluated eptinezumab. It involved 174 participants evaluated a single 1,000 mg IV dose with follow-up over 12 weeks. I want to note that the ongoing Phase 3 trials of this drug are actually evaluating much lower doses, 300 mg and 100 mg. The primary study endpoint here was a safety outcome and the incidence of serious adverse events was infrequent and similar between groups. The author stated that the primary efficacy outcome for the study was change from baseline in migraine days per month at week 8, which they reported as statistically significant with a one-tailed test that favored active treatment. But we could not actually replicate their reported confidence interval which did not exclude the null effect. And we also calculated a P value of .06 using a two-tailed test. Further, the authors reported no significant change in this outcome at week 12. So it was significant at week 8, but not at week 12. Although the direction of effect for the other efficacy outcomes reported including quality of life, as measured by the headache impact test, favored active treatment, estimates were generally imprecise and some were not statistically significant. We do note that the study was the smallest of all included studies and likely does not have a large enough sample size to generate precise estimates for any of the efficacy outcomes. Moving on to slide 18.

This is a summary of findings table for GRADE for eptinezumab. As you can see we assessed the evidence as low quality for significant improvement in migraine days at… per month at 8 weeks, but not significant at 12 weeks. And low quality for no significant differences in the percentage with at least a 50% reduction in the number of migraine days or quality of life as measured by the headache impact test. The quality if evidence was downgraded for study limitations related to manufacturer involvement and selective outcome reporting and for imprecision because of the small sample size. We assessed the evidence for serious adverse events and discontinuations from adverse events as very low quality for no difference. And the evidence was downgraded for

the same study limitations I've mentioned before—manufacturer involvement and very serious concerns about imprecision. Moving on to slide 19.

So three studies evaluated erenumab at either 70 mg or 140 mg doses or both. Two evaluated this drug over a period of 12 weeks and one evaluated it up to six months. They all found similar statistically significant improvements in the change in migraine days per month that ranged between 1 and 1.9 days and the incidence of at least one serious adverse event or adverse events leading to discontinuation were similar between both doses of erenumab and placebo.

So on slide 20 is our summary of findings table for erenumab and episodic migraine. We assessed the evidence as moderate quality for significant improvements in migraine days per month, days of acute migraine medication use, and the percentage with at least a 50% reduction in the number of migraine days, quality of life as measured by MIDAS was also… we also assessed as moderate quality and then we downgraded the quality of evidence here for study limitations related to manufacturer involvement. We assessed the evidence for serious adverse events and discontinuations as very low quality for no difference between erenumab and placebo and downgraded for the same limitations I've already mentioned before—manufacturer involvement and imprecision. Slide 21.

These are two studies that… the two studies that evaluated fremanezumab. Both evaluated monthly doses of 225 mg. One also evaluated a monthly dose of 675 mg while the other evaluated a quarterly dose of 675 mg. Both evaluated outcomes up to 12 weeks and authors of both studies observed statistically significant improvements from baseline in monthly migraine days ranging from 1.3 to 2.8 days across the different doses and similar to the other drugs in this class the incidence of adverse events and discontinuations due to adverse events was infrequent and similar across groups.

On slide 22 is our summary findings table where we've used GRADE to rate the evidence for fremanezumab in episodic migraine. It's identical essentially to the summary for erenumab. We rated moderate quality for

the four efficacy outcomes and evaluated the two safety outcomes as very low quality. Moving on to slide 23.

Finally, four studies evaluated galcanezumab using various doses and frequency of dosing. So two of these studies evaluated outcomes up to 12 weeks. Those are the two studies shown on this slide. And then two of those studies evaluated outcomes up to six months and those studies are shown on the next slide. All studies observed statistically significant decreases from baseline in migraine days per month and, like the other drugs in this class, the incidents of adverse events and discontinuations from adverse events were infrequent and similar across active treatment doses than placebo.

On slide 24 these are the other two studies called EVOLVE-1 and EVOLVE-2 that evaluated galcanezumab over six months of follow-up and again findings are consistent from these studies compared to the studies with the shorter amount of follow-up. They showed a decrease of between 1.8 in two days compared to placebo in terms of migraine days per month and again similar incidents of adverse events. Slide 25.

This table is our summary of findings for galcanezumab for episodic migraines. Again, it's essentially similar to the ones for erenumab and fremanezumab in that we rated the quality of evidence is moderate for the four efficacy outcomes and very low for the two safety outcomes. Moving on to slide 26.

On this slide I've summarized some of the other findings from these 10 studies in populations of episodic migraine. So the range of reduction in migraine days per month compared to placebo across this body of evidence was between 0.9 and 2.8 days. A favorable treatment effect was observed on most all secondary migraine outcomes and quality of life measures reported for erenumab, fremanezumab and galcanezumab. And so these outcomes include things like days of acute medication use, headache days and percentage of participants with at least a 50% reduction in migraine days per month. Treatment-related liver injury was rare. So seven studies reported this finding really was just a sentence in… either at the end of the results or even in the discussion that said no effects on liver enzymes. Only one study actually reported frequencies

and the frequencies range from .3% to .7% across the groups. And then finally two studies of fremanezumab reported some efficacy outcomes among subgroups of participants who were not taking concomitant therapy… migraine preventative therapy at baseline and the treatment effect was the same as that that was observed in the full study population. Moving on to slide 27.

The same two reviews that I previously discussed also reported on findings for episodic migraine. So the one by ICER included six studies. This review reported that active treatment with erenumab, fremanezumab or galcanezumab was more effective than placebo in a variety of migraine event outcomes and also concluded no significant differences between active treatment and placebo for various adverse event outcomes. So this review did not include any studies on eptinezumab. The second review from Canada included 10 studies. It included one published only in a conference abstract and this review also concluded that active treatment was more effective than placebo and was associated with infrequent adverse events and they cited the incidence of between 1 and 2%. Moving on to slide 28.

ICER review also conducted a network meta-analysis for episodic migraine. This analysis evaluated indirect comparisons between various doses of erenumab, fremanezumab, galcanezumab, amitriptyline, propranolol and three doses of topiramate. Study authors observed no significant differences in any of the pairwise comparisons between CGRP inhibitors or between CGRP inhibitors and the other preventative medications for two of the three efficacy outcomes listed here on the slide. So days of acute medication use and percentage of participants with 50% reduction in migraine days. The authors also observed no differences in discontinuations because of adverse events or in serious adverse events. So for those four outcomes there were no pairwise differences.

In contrast, on slide 29 the authors did observe that compared to topiramate 50 mg daily that both doses of erenumab, so the 70 mg and the 140 mg dose and the 225 mg dose of fremanezumab and 120 mg dose of galcanezumab all… in pairwise comparisons resulted in a significant decrease in monthly migraine days. So again, for all of these…

for those four drugs and doses they showed a significant improvement in monthly migraine days relative to the topiramate 50 mg dose. Again, these are indirect comparisons. And then lastly in comparison to topiramate 200 mg both doses of erenumab had fewer all cause discontinuation. That was the only significant finding in the indirect comparisons. Moving on to slide 30.

Those are the findings. Let me just mention a few limitations of this evidence base. So as I already mentioned there was extensive manufacturer involvement in the study design, data collection and analysis, and manuscript preparation and this is reflected in our assignment of only fair [inaudible] quality and also resulted in downgrading of the quality of evidence under grade. We did not identify any head-to-head trials. So we don't have any trials that directly compared CGRP inhibitors to either another CGRP inhibitor or an alternative preventative medication. Most studies, as you saw, only went through six months of follow-up. So we don't have any studies that provide any evidence for longer term efficacy or safety results. None of the studies reported health care utilization or employment-related outcomes and then a few things to note on the generalizability of findings. So all of these studies used the run-in phase. Generally anywhere from 30 to 45 days where patients had to be compliant with a headache diary in order to continue with enrollment. So that may limit the generalized bill of findings to a more general population. Participants with clinically significant psychiatric or medical conditions or who were pregnant were excluded. As you all know that is fairly typical in trials. And then the study populations generally were mostly female and race and ethnicity were generally not reported. Moving on to slide 31.

The last set of slides here describe the ongoing phase 2 and 3 trials of CGRP inhibitors. There are 15 in total. Most, but not all of them are blinded. Most include efficacy and [inaudible] between 12 and 24 weeks. Typically they are looking at the reduction in monthly migraine days. So some use other migraine event end points. But none of them include efficacy follow-up longer than six months or safety follow-up longer than about a year. For the sake of time today I'm not to present the next few slides in detail that describe the ongoing studies, but you obviously have the slides for reference and I'm happy to address any specific questions.

If you'll jump ahead to slide 35 for some conclusions. So for chronic migraine we concluded erenumab and fremanezumab are more effective than placebo and have a similar frequency of adverse events compared to placebo. For episodic migraine, erenumab, fremanezumab and galcanezumab are more effective than placebo and have a similar frequency of adverse events compared to placebo. We concluded the evidence is limited for eptinezumab and couldn't really draw any definitive conclusions and one thing we want to… I want to point out that providers and patients or both may view the clinical significance of the actual treatment effect. So we're talking about, you know, anywhere from a day to 2.5 days fewer migraine days per month. That treatment effect might be viewed differently by different people depending on the severity and disability of their headache condition and the patient's ability to tolerate other preventative medications and of course other factors. Moving on to the last slide.

Additional conclusions – so there's no head-to-head studies currently available or that appear to be on the horizon. However, the treatment effect and safety of CGRP inhibitors appears to be similar to other migraine preventative drugs based on the indirect comparisons from the network meta-analysis. And additional placebo-controlled trials are in progress, but none will report efficacy outcomes longer than six months or safety outcomes longer than a year. So I'm happy to take any questions at this point.

Lisa Chew: Thank you, Leila. Any questions from the committee members? There are no questions, Leila. We have two stakeholders, Dr. Maria Agapova and Dr. Sylvia Churchill. Could you please come up to the podium? Please introduce yourself and who you represent and you will have three minutes for comments.

Maria Agapova: Hello. My name is Maria Agapova. I'm a medical outcomes liaison for Teva Pharmaceuticals. I want to thank the committee for giving me time to address you today and I will be talking on behalf of Ajovy or fremanezumab. This is one of the most thorough reviews of CGRP class, but I want to remind the audience that fremanezumab is targeting a slightly different… it's targeting the liken versus the receptor of the

[inaudible] gene related peptide and there are some distinguishing features. It's engineered selectively to target underlying migraine pathophysiology of specific changes to the monoclonal antibody. It has [inaudible] onset of effect which is different from your standard of care. We've seen separation from placebo as early as week one and it has shown efficacy and safety in combination with other migraine prevention therapies. This was mentioned earlier, 20% of the pivotal trial population were on one preventative concomitant therapy like [inaudible], for instance and there were no differences in that subgroup than in the total trial population.

Also an exploratory analysis we found that one in four patients taking fremanezumab had a 75% reduction in monthly migraine days versus 1 to 15 with the placebo. That's in the episodic migraine and chronic migraine one in five patients taking Ajovy experienced a 75% reduction in headaches compared to one in 10 in the placebo. So we are seeing some very dramatic increase… or decrease in monthly migraine days and headache days among some of the population.

And then we also have, just two days ago, shared top line results from the 3B study, which you'll find on slide 33 of the review, second to last trial, NCT03308968, and this was in the population of patients who had two to four previous failures in standard of care classes such as your tricyclic and antipsychotic… sorry, antidepressants and your beta blockers and we found highly significant differences in the monthly and quarterly dosing compared to the placebo. Somewhere in the treatment effective 3.5 for the monthly dose and 3.1 monthly migraine days in the quarterly dose. So much greater numbers than you would see in the pivotal trials of somewhere ranging one to two days.

We want to highlight that the Ajovy trials, the HALO took into consideration that migraine patients are busy, working professionals. The Global Burden Disease Study looked at, in 2015, looked at those patients under 50 and down that migraine was the third most disabling disease. So the [inaudible] developed both a quarterly and a monthly dose to address the need and adherence and persistence in this particular disease state. One of the other unmet needs is use of acute medications in this disease state and overuse of acute medication we

found, at least in the pivotal trials, significant reductions in the use of acute medications and medication over-use headache. I'll take any questions at this point. Thank you for your time.

Lisa Chew: Any questions? Thank you very much.

Sylvia Churchill: Hi. I'm Sylvia Churchill. I'm a health outcomes and pharmacoeconomic specialist from Amgen and I've been a pharmacist here in Washington State for 20 years. That was a very nice presentation that summarized a lot of data about the CGRP class. I just wanted to add a little information regarding the ongoing studies for erenumab or Aimovig because not all of them were listed in this report. So we are in our fourth year of a five-year long-term extension of our Phase 2 study in episodic migraine, 64-week results. So 12 weeks in the original trial plus 52 weeks in the extension. Those interim results have been recently published in the Neurology Journal and showed that there was a sustained efficacy of erenumab over the time with a low incidence of adverse effects and no safety signals were identified. Three-year data is available. It's been presented at conferences via oral presentation and posters, but they have not yet been published. Keep an eye open for those. Other studies that we're looking at… we have completed a one-year long-term extension of our chronic migraine study as well, 612 patients. We are studying pharmacokinetics of erenumab in patients under the age of 18. We are looking at drug interactions when combined with oral contraceptives. We look at blood pressure when it's given in conjunction with subcutaneous sumatriptan and we are also looking at the impact of giving erenumab concurrently with other oral preventive therapy. That's it. Are there any questions? All right. Thanks very much. You guys have a happy holiday.

Lisa Chew: Thank you very much. Okay. For the committee members I'm going to draw your attention to the last page of this section that shows the motion. I think this is a new class review and I think it is to review the motion to see if these medications should be included on the PDL.

Ryan Pistoresi: Yes, that is correct. This is the first time we've reviewed this class. So this will be a new class added to the PDL.

Nancy Lee: I'd like the committee members to consider… I don't know… well, I guess it's a question for Health Care Authority as well. In terms of distinguishing between chronic versus episodic migraine, because the conclusions are different in terms of medications that would follow under both… different I guess subgroups. And then also consider striking eptinezumab based off the very low quality evidence that RTI presented.

Ryan Pistoresi: So yes, what we have up here is just kind of the basic structure that we have for most motions and it's up to you to really decide what you want since this is the first time that we've had this motion. If you want to move in that direction you're more than welcome to. To address your point between chronic and acute we have the language in there that they are efficacious for their approved indications. So rather than splitting them out we generally have that as our language because as new indications get approved this then allows them to automatically move into that rather than having set ones for chronic and set ones for episodic. And then if you want to exclude the drug what you would do is if you do make a motion you would just name the drugs and then you could say one is not eligible to be a preferred drug on the preferred drug list. That would be adequate or if you did think that it is not safe or efficacious then you don't need to list it in that first kind of open bracket.

Diane Schwilke: Just for the sake of us being able to kind of look at it as a possible motion would you put… I kind of agree with Nancy about maybe not including the eptinezumab for now, but putting those three in there just for us to kind of consider as a starting place. So then it was in this review. Is it something that we need to mention? I guess it just stays in the drugs reviewed and we only put the three in the motion? Okay.

Ryan Pistoresi: Yes. So you can have those three if you feel that you had enough quality evidence to determine that they were safe and efficacious. However, since it is listed in the drugs review I would recommend having a separate line saying, you know, something about it so that way it's not being dropped off or forgotten at future reviews. That way you can say, you know, at this time in your motion that there is not enough quality evidence to make a determination that should be eligible to be preferred and so that way when we do our cost analysis we will then have it be

categorized differently so that way we really look at the drugs that you feel are safe and efficacious to be eligible to be preferred.

Leta Evaskus: To make a distinction you can also say that a drug is excluded from the PDL. So you can either say it's not eligible to be preferred so it will always be non-preferred or you can say it has to be excluded.

Donna Sullivan: The drug that you're talking about has not been approved yet. You could basically just leave it out of the motion and then it would not be included in the preferred status, the cost analysis that Ryan was talking about or you could point out that if it were to become FDA approved that you would want it to be not preferred if you don't think the evidence supports it being on the PDL.

Amber Figueroa: So just some discussion and so that I'm clear why you guys are saying this. I'm presuming that it is based on the slide showing… let's see, slide 18, showing quality of evidence low for the first three categories and very low for the second two. So low is one point below moderate and all of them were downgraded for study limitations. This one was downgraded for imprecision and I'm assuming it's because the N number was so low in the study with 88 people on placebo and 86 people on 1,000 mg. Is that correct? Is that what everybody is looking at?

Leila Kahwati: Amber, this is Leila. If I could just clarify. They were downgraded for low, but there is also no significant difference with placebo for two of those outcomes that are on that slide 18. That is really the difference between that and the other agents.

Amber Figueroa: Great, thank you.

Nancy Lee: Leila, I had a question about talking about the summary findings table grade for the medications that you reviewed. In terms of "safety" the grade or strength of evidence that you presented was very low and yet in your conclusion table… I mean it's kind of hard because the duration of the studies were short. I guess I'm trying to reconcile what's in the summary of findings or the gray table versus your conclusion slide.

Leila Kahwati: Yeah, so the summary of findings table the grade ratings those are really like on a continuum of certainty. So the very low, low, moderate and high really represent our certainty in those findings. So for the safety outcomes the findings are really… we think no difference between the inhibitors and placebo, but our certainty is very low because of the issues relating largely to the imprecision because these are rather infrequent events on top of studies that are not huge and so that creates a problem with the precision of the estimate. So it's the… the grade rating is really the certainty of the effect. It's not meaning there is no… that we can't conclude a relationship. Does that help?

Nancy Lee: Yes, thank you.

Alex Park: I just have a question. So as a new class review eligible for inclusion on the PDL if we approve the motion does that mean that it is equally preferred versus other migraine prophylaxis drugs that are already preferred such as beta blockers and so forth. There would be no kind of step wise therapy among those if we simply approve it [inaudible].

Ryan Pistoresi: Right. So if you approve it what happens next is it goes through a cost analysis. And so we look at some of the different scenarios of how these drugs could be preferred for UMP and… Jaymie, I don't know, is this class an L&I class or not?

Jaymie Mai: Because migraine isn't typically industrial related we're not participating in this drug class.

Ryan Pistoresi: Thank you, Jaymie. So this would be for UMP. So we would be looking specifically at UMP and we can look at one preferred drug, we could look at two preferred drugs, we could look at three preferred drugs, and just depending on what has the lowest net cost for the state is the option that we typically prefer. It could be one drug with step therapy or PA. It could be no step therapy or PA if they are all preferred. It just depends on what is the lowest net cost.

Man: Are you referring to within the CGRP class or within migraine prophylaxis drugs as a class?

Donna Sullivan: If you want to… there's two options. You can say that they should be second line therapy at which point we would use, you know, require use of the more traditional prevention drugs and then if they met the criteria for a CGRP then they would get the preferred one as opposed to them going straight to the CGRP's for initial prophylaxis. Or you can decide not to put this class on the PDL at all and we'll just handle it the way that we would handle all other drug classes that are not on the PDL.

Man: I'm not sure how we would phrase that into the motion, but I would be very much in favor of going for the first option that you characterized.

Donna Sullivan: I think in the motion we would put… you could put the CGRP inhibitors should be second line agents on the PDL and can or cannot be subject to therapeutic interchange and you guys decide can or can't.

Amber Figueroa: I think they all seem fairly similar. I think it would be okay if they were interchangeable.

Man: To complete the discussion with the committee on Nancy's point about the episodic versus chronic distinction I think they are all, by FDA indication, it says migraine prophylaxis so it's kind of a broader category. So I would be okay with not [inaudible] that out in the motion.

Donna Sullivan: Can you clarify what you said about whether or not they should be subject to therapeutic interchange?

Amber Figueroa: I'm just voicing my opinion that I think they should… they can be interchangeable.

Nancy Lee: I would… based on the information that we have today in terms of the evidence and that there is no head-to-head studies I would concur with Amber that they can, unless there is head-to-head studies that are going to be published that show otherwise.

Lisa Chew: Just to clarify since we're striking that first drug we don't need to make an additional statement. We can just leave that out of the motion.

Ryan Pistoresi: So, yes, you don't have to have anything about the drug that you are striking in the motion, but if you want to you could also add that in saying that, you know, it may be considered not reviewed until further evidence proves it is safe and efficacious. Or you can say it is not eligible to be preferred. It's really up to you to decide how you want it to be treated in the motion.

Donna Sullivan: The only reason I would recommend you do something like that so that five years from now when we come back and say, "Why isn't this drug in the motion?" We remember without having to go back through all of the transcripts and find out what we decided today.

Lisa Chew: Can we add that? I won't be here in five years, but…

Leta Evaskus: So how would you like it written?

Lisa Chew: Ryan, you just mentioned something about waiting until further evidence

Ryan Pistoresi: Yeah. So if you want some recommendation language you could say eptinezumab should be considered not reviewed and not eligible to be preferred on the preferred drug list at this time. And so then that way when we come back to this and you, you know, are going to say, you know, the scan was adequate and you want to reiterate the prior motion you may be able to change that at that time. So having that information in here makes it easier the next time you review this as a P&T Committee.

Donna Sullivan: And you might… instead of saying "not considered" you might put "should be considered not reviewed and not eligible to be on the preferred until higher quality evidence is established".

Lisa Chew: Do committee members want to review the motion? If someone feels comfortable making an initial motion…

Alex Park: Just a clarification in the motion. What special populations did we consider evidence for?

Amber Figueroa: I think the only thing they said was people who are already using prevention medications versus people who weren't using them.

Alex Park: Okay.

Ryan Pistoresi: That's one of the standard ones that we have in other motions is special populations and that's because in the key questions there is a question about, you know, are there subgroups for which safety or efficacy differ, which is then why we have that. So we have a safety question, we have an efficacy question, and then we have this special populations questions, which is why it's kind of in the general foundation of the motions. But if you want to, you know, remove it because you don't feel that there is enough quality evidence you're more than able to do so.

Man: I would suggest that the committee consider that because… I guess what I think is special populations with this particular [inaudible] I'm thinking of children, pregnant individuals, cardiovascular disease individuals, and so forth, and I don't think we've heard much evidence about that. So I would be in favor of removing that.

Amber Figueroa: Okay. After considering the evidence of safety and efficacy for the treatment of migraine prophylaxis, I move that erenumab, fremanezumab, galcanezumab are safe and efficacious for the treatment of their approved indications. The CGRP inhibitors should be second line agents on the Washington PDL. Erenumab, fremanezumab, galcanezumab can be subject to therapeutic interchange in the Washington Preferred Drug List. Eptinezumab should be considered not reviewed and not eligible to be preferred on the Washington PDL until higher quality evidence has been established.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any apposed? And the motion carries. Now we're going to move on to asthma and the COPD scan. Curtis?

Curtis Harrod: Thank you so much. Can you hear me?

Lisa Chew: Yes.

Curtis Harrod: Great. So hi. My name is Curtis Harrod. I'm the DERP Drug Effectiveness Review Project research director at the Center for Evidence-Based Policy. Today I'll be presenting on the second scan since the first update of drugs to treat asthma or COPD. This scan was completed by our research vendor, the Pacific Northwest EPC. As you heard on the call today RTI is one of our new research vendors.

Let's proceed to slide number 1 onto our overview slide. I'll present this the first time and my colleague, as well as myself, at the end of the presentation session… I will just go ahead and skip over some of these slides.

Starting to topic history then we'll move to PICO and key questions, then go on to methods, findings, and then wrap up with the summary.

So on slide 2 for our topic history. The first update was done in June 2016. The first scan for this product was done in June of 2017 and today I'll be presenting that second scan. Slide 3.

I have our population listed in our PICO here. For chronic asthma we're doing… or persistent or chronic asthma we're dealing with adults, as well as pediatric patients at least one year of age or older. And then for COPD we're just dealing with adults. Slide 4.

We have a number of interventions in this scan and so I'll just give a high level overview of them here and then we'll dive into some specifics in subsequent slides. So the orientation for these are the drug names in your far left column, brand names in the middle column and then far right is the FDA approval date. For long-acting beta-2 agonists we have five interventions within this scan and then for long-acting muscarinic antagonists or LAMAs there are six. So proceeding on to our next slide.

Looking at inhaled corticosteroids we have 11 drugs that we're reviewing in this scan. One that I'll point out is the QVAR Redihaler that I'll discuss later on. Proceeding to slide 6.

We have a continuation of the interventions. This time we're looking at the combination therapies. So a dual therapy of the inhaled corticosteroids and a long-acting beta-2 agonist. There are six of those in this scan and then a combination therapy of the long-acting beta agonists and the long-acting muscarinic antagonists. There are four of those. Slide 7.

We have the triple therapy—Trelegy Ellipta and that is the only triple therapy of the inhaled corticosteroid, the LAMA and LABA combination. And then we have four leukotriene modifiers and one phosphodiesterase-4 inhibitor. So those are our interventions. Now I'll proceed to slide 8.

For our comparisons we're looking at head-to-head studies and for our outcomes there are several starting with asthma and COPD, control, quality of life, functionality, emergent medical need such as emergency department visits and urgent care visits, hospitalization, mortality and then adverse events consisting of overall adverse events, withdrawals due to adverse events and specific adverse events. Slide 9.

Here we have our key questions. There are three of them for this scan and connected to the report. Again, we're looking at comparative efficacy and harms with questions 1 and 2 both in the long-acting inhaled and long-acting oral medications for asthma or COPD and then our third question recovering subgroups. Again, do these differ by efficacy or harms? Slide 10.

This is another slide I'll present this first time and then we'll skip in subsequent presentations. So for our methods we searched from May 2017 to May 2018. We searched MEDLINE both electronic databases, the U.S. FDA website, and then for this scan we looked at additional systematic review databases of CADTH and AHRQ. And then for new drugs we searched the CenterWatch website to identify those. Proceeding to our transition slide of 11.

That's our findings. We'll start to dive into what we found in this scan. I'll just emphasize here that for scans it is just an overview of what we identify. It's not a summary or synthesis of the evidence. So slide 12.

We found no new drugs identified in this scan. However, we did identify three new formulations and/or indications. So starting with glycopyrrolate or Lonhala Magnair that was approved on December 5, 2017 for COPD. Then our triple therapy the Trelegy Ellipta with fluticasone, umeclidinium and vilanterol and this was approved for COPD on September 18, 2017. And then for our third one here, it's an inhaled corticosteroid dealing with beclomethasone, the QVAR Redihaler. And so that was approved on August 3, 2017 for individuals with asthma at least four years of age or older. Slide 13.

With our new serious harms we did not identify any new black boxed warnings for drugs reviewed in this scan. However, we did find that a black boxed warning has been removed during this period of time. That occurred on December 20, 2017. So this is a dual therapy of the inhaled corticosteroid and long-acting beta-2 agonists such as Advair and Symbicort. And so there was a previous black boxed warning indicating increased asthma-related hospitalizations, intubation, and asthma-related deaths and that has subsequently been removed. Slide 14.

We identified one new systematic review. This is an AHRQ review published in 2018. The title is Intermittent Inhaled Corticosteroids and Long-Acting Muscarinic Antagonists for Asthma. We'll proceed to what we found with individual studies.

So on slide 15 we have new randomized control trials. These are broken up first by devices, head-to-head comparison of devices, and then drug-to-drugs in subsequent slides. So there are seven overall. I have four that would only fit in this table and three will be on the subsequent table. You can see the orientation for these are the far left column we have our author and year of the study, as well as the trial number. The second column displays their sample size and duration. Our population is listed in the third column and then the comparisons are displayed in the fourth column. I'd just like to point your attention to the Bremner study. That is the second row. They have the Trilogy Ellipta medication, the triple therapy being compared in this population. So proceeding to slide 16.

This is a continuation of the delivery devices that are head-to-head. These are the three remaining. Again, seven were found in this scan and I would point you to the last study on this third row here and they are comparing the QVAR Redihaler has an intervention in this study. That's the new formulation. Slide 17.

We have 10 RCTs overall comparing drugs. As you can see the range of studies here, again, varying from around 250 participants in one to over 1,500 in another. The second row, the Ferguson et al. 2017 study that's the Lonhala Magnair medication, glycopyrrolate comparison. And so that's maybe of interest to you all. Moving on to slide 18.

I caught a type-o and you have noticed this too. Looking at the final row, the SUMMIT trial there is an extra number in there. The sample is large, but just not that large. There are 16,485 individuals in the study. There is an extra 4. So apologies for that and that is also present in your scan report. So the error was in both cases there by the Pacific Northwest EPC. And so for the population we're looking at COPD with increased risk of cardiovascular disease in that study. So again a very large study. They followed participants for 1.8 years approximately.

We'll proceed now to the summary. The update was done in 2016. This is a second scan. So I'll summarize everything that we found since that time. No new drugs have been identified since that update was completed in June 2016. There are six new formulations of or indications for existing drugs. Three were new in this scan. No new black boxed warnings have been identified. One has been removed that I mentioned to you all with the dual therapy. There is one new AHRQ comparative effectiveness review. There are 11 new trials comparing devices head-to-head. Seven were identified in this scan. Thirteen new head-to-head trials have been identified in this scan. Thirteen new head-to-head trials have included drugs, 10 were new in this scan, and then secondary analysis, which are only available for time purposes within the document scan as opposed to the slide set. That is my presentation. I'm happy to take any questions from you all today.

Lisa Chew: Thank you, Curtis. Any questions from the committee members?

Amber Figueroa: Thank you for that. Going back to slide 15 can you clarify what the acronyms of MDPI versus DPI mean?

Curtis Harrod: Yeah, that is the mechanism of the inhaler. I apologize I did not include the acronym on there. I can look that up in the scan report in the meantime if we want to move on to other questions?

Nancy Lee: DPI I believe stands for dry powder inhalation and then MDI standards for metered dose inhalation.

Amber Figueroa: Powder inhalation? I haven't seen a P in there.

Dave Johnson: Yeah, and one is the metered dry powder inhalation versus just the breath-activated dry powder inhalation.

Amber Figueroa: Okay.

Curtis Harrod: Yeah, that's in the report, which I believe you all have access to, as well. On page 8 MDPI is multi-dose powder inhaler. MPI is the metered dose inhaler and then the DPI is the dry powder inhaler.

Lisa Chew: Any other questions? We have two stakeholders, Nicolas Nguyen and Long Nguyen. If you could please come up to the podium. Please introduce yourself and state who you represent and you'll have three minutes for comments.

Nicolas Nguyen: Based on Dr. Figueroa's question I also brought the device just for visual. I'm going to leave it right there for you guys to see. [Inaudible – stepped away from the microphone.]

So hello. My name is Nic Nguyen. I am the director of health economics and outcomes research with Sunovion. Thanks for the opportunity to present the clinical and pharmacoeconomic profile of Lonhala Magnair that you see there. Patient's get that entire unit, as well as the nifty fanny pack there when they get prescribed the drug. Lonhala is the first and only nebulized LAMA. It's indicated for the long-term treatment of COPD and Lonhala solution is available in a 1 mL single-use vial kind of like this containing 25 mcg of glycopyrrolate for use with vial nebulization

with the Magnair device. Lonhala Magnair is not a rescue medication. The device is a closed system designed for use with Lonhala pre-filled vials only. They get about 60 of these a month. Using a vibrating membrane technology the Magnair is virtually silent as you guys can see or hear, portable and designed to [inaudible] Lonhala in two to three minutes with normal title breathing. Lonhala may be an acceptable option for patients with low peak [inaudible] flow rate. They can't really inspire with a DPI or an MDI those hand-held inhalers. There's a lot of coordinated activities if they have dexterity issues or cognitive issues. This is an alternative that they can use. In two Phase-3 confirmatory trials Lonhala 25 mcg was shown to be superior to placebo in improving [inaudible], [inaudible], which was the primary endpoint. In addition, significant improvements were observed in 12 [inaudible] as well as in health-related quality of life as measured by the SGRQ. The most common adverse reactions in the two 12-week placebo-controlled studies were dyspnea and urinary tract infection. In the 48-week long-term safety study as mentioned by Curtis it… it a… active comparator trial Lonhala versus hand-held Tiotropium and over 48 weeks there was sustained improvement in FEV1 as well as similar exacerbation rates between Lonhala and Tiotropium. The adverse events reported in that 48-week study were similar to the two 12-week placebo-controlled trials. In a Sunovion-developed that's [inaudible] base predicting outcomes in patients with COPD who may have difficulty using a hand-held inhaler device, the number needed to treat for NNT to avoid one exacerbation was estimated to be 9.8 patients for Lonhala and 15.5 patients for Tiotropium.

The results suggest that Lonhala, and that beep right there suggests, it is completed. The results suggest that Lonhala may represent an alternative option for patients who are unable to use hand-held treatments in COPD. While the 2018 [inaudible] report does not endorse any specific treatment, it does recommend the use of long-acting bronchodilator alone or in combination for maintenance therapy. Additionally, there is clear emphasis on correction halation device technique and the choice of inhalation device should be tailed for the individual.

In closing, the clinical and outcomes data shown for Lonhala Magnair provides a treatment option with high potential value in terms of efficacy and budget impact. On behalf of Sunovion I respectfully request that Lonhala Magnair be added to the preferred drug list for COPD patients and Medicare beneficiaries in Washington. I'm happy to address any questions.

Amber Figueroa: Can you show us how they hold that?

Nicolas Nguyen: It comes two vials per packet. So there are 30 packets total every month that they get. [Inaudible – stepped away from the microphone.] Are there any other questions? If anyone would like the gold recommendations there's an update recently, I just want to let you guys know that, and it provides more detail and includes information on eosinophils, as well as information on severity and what to treat for patients. Thank you so much.

Lisa Chew: Thank you very much.

Long Nguyen: Good morning. My name is Long Nguyen. I am the health outcome liaison representing GlaxoSmithKline. Nick and I are not related and I don't have a nifty apparatus like he does to show you. However, my comments today are really related to the recent scan that Curtis mentioned and presented previously in the class review scan for COPD and asthma.

First of all, as Curtis mentioned, the scan ran from May of 2017 to May 2018, which according to the findings the scan missed the most significant, largest, randomized clinical trial ever done in patients with COPD. The trial was published in the New England Journal of Medicine in April 2018 involving 10,300 plus patients studied evaluating the reduction of exacerbations comparing Trilogy, which is the only first triple combination inhaler in a single inhaler to a dual agent LAMA/LABA and an ICS LABA in the same inhaler. That significant trial resulted in showing that Trilogy shows a significant 34% reduction in severe exacerbation leading to hospitalizations compared to a LAMA/LABA and additionally is the first largest trial that was able to demonstrate a reduction in COPD mortality to 42%. Because the significant data available from this

landmark IMPACT trial that prompted the COPD Committee last month, November 9th, to revise their recommendation treatment for COPD to include triple combination therapy as part of an escalating regimen for patients who are currently on a LAMA/LABA or an ICS LABA and continue to have exacerbations and symptoms. And so with that I… in addition to what was presented in the scan, the publication of the IMPACT trial prompted the FDA to make a significant label change from Trilogy to expand its indication to the long-term once-daily treatment for patients with air flow obstruction in patients with COPD and also a reduction in exacerbation in patients with a history of exacerbations. That was significant enough that it resulted in a major revision both in the gold 2019 guidelines, as well as the COPD Foundations.

In conclusion with that, the scan also missed a new drug approved by the FDA in May 2018 which is an ICS monotherapy or [inaudible] Ellipta for pediatric patients 5 to 11 years old with chronic asthma 50 mcg. So on behalf of GSK I ask the committee to request a full class review with the COPD asthma class to include these… the IMPACT trial and additional number of subgroup analysis that was presented both at ERS, as well as [inaudible] in the last three months to stay consistent with the gold recommendations in identifying the right patients that is appropriate for triple combination therapy such as Trilogy. Thank you very much for your time and if there are any questions I would be happy to answer them.

Curtis Harrod: Although we did not do this scan, the evidence-based practice center at Pacific Northwest did. The [inaudible], et al. study of over 10,000 that Long just mentioned was published in the New England Journal of Medicine on May 3, 2018. That does take a little bit of time to be captured in… of its Medline so that likely was not captured in the original search strategy and then the approved drug was also outside of this scan date, which ended on May 1, 2018. I just wanted to clarify that.

Lisa Chew: Thank you. Okay. So the committee members turn to the motion. It looks like there's six different drug classes here and I think we have to either make a motion that the scan is adequate or we want a more… or we want to request an updated class review. Should we go class by class? Okay. So let's start with the inhaled corticosteroids.

Leta Evaskus: You could do one approval for the entire scan since it was one presentation.

Dale Sanderson: I have a question for Curtis. In terms of history we've always encouraged the beta agonist to be given first and then allow that to take effect before providing the steroid. With these combination products is that an issue at all?

Curtis Harrod: Thanks for your question. Again, just to clarify we did not dive into the effectiveness or harms of these so I could not inform you on what the data [inaudible] with regard to that. I would defer to the pharmacist in the room for any clarifications on use.

Amber Figueroa: In clinical practice basically when you're looking at asthma you're determining how frequent their exacerbations are and their nighttime symptoms and giving it a label first and then based on the recommendations sometimes it says to not sure step, you know, if it is severe then you would hit it dually, but if it does stay step wise then you do beta first and then if that's not going controlling them they you would stop the beta and do the dual therapy in one inhaler if that is what you felt would be best.

Dale Sanderson: Okay. Thank you.

Amber Figueroa: One copay. Just to clarify, are we assessing the adequacy of the scan?

Ryan Pistoresi: Yes. The first thing that you'll do is you can accept the scan as adequate and that can… to Leta's point that can be applied to every single drug class in these motions so you don't have to keep asking the same question each time. And then from there you'll then go through each motion and then you can either reiterate or you can change it based off of any other discussion or information.

Lisa Chew: Just a question, what is the frequency of the scans? Are they annually or…

Ryan Pistoresi: That's a great question. Right now we are going under a transition with the Center for Evidence-Based Policy and we are actually going to be

transitioning into a new type of document called a Surveillance Document, which may or may not be annual. For classes like these in which there are ongoing changes states are interested in continuing to review it and I can imagine that they would be on an annual type basis, but other drug classes that are older on the PDL including one that we will be reviewing next we are recommending to archive it because there hasn't been a lot of interest in states and that these ongoing scans are producing a lot of information about new evidence and so we may be seeing some of these older drugs be reviewed less frequently or be archived here at P&T whereas some of these other drug classes we may be getting more robust information in terms of these new products. So with these scans, all that we're looking at is, "Has there been any new evidence on the horizon?" These new surveillance documents may be able to go a bit further than that. Curtis, I know you're on the phone. If you want to provide maybe a little bit of information about what we may expect in the future. I think that would be appreciated.

Curtis Harrod: Thanks, Ryan. You did a nice job of explaining it. I think the transition and the evolution of the product and we'll be piloting that moving forward to see how we can best meet the needs of our drug effectiveness review project participants. And so that will be clarified. We will hopefully present them in the upcoming months and we hope to have a prioritized list of surveillance topics and I would assume that the Drug Effectiveness Review Project would likely be interested in this for instance as it is an active area. Where Ryan pointed out the next scan, I think it is scan 8 or 9 potentially in this series for hormone therapy, that that will be archived. So we will dive into more of the meaningfulness of the study as opposed to just a body count is one step that we will be evolving on looking at sample size, looking at the importance of outcomes relative to previous studies and does it add to the body of literature?

Lisa Chew: I think given the timeframe of this scan I move that the scan be accepted as adequate.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. So now we can go through class by class and look at the prior motion and see whether or not we want to reiterate the prior motion or make amendments to that. The A stands for those meds approved for asthma, the C by the drug represents approved for COPD and I think there are some further along that are some grayed out medications that cannot be… they are not reviewed so they cannot be included in the motion. So let's start with inhaled corticosteroids.

Catherine Brown: I move to reiterate the prior motion.

Lisa Chew: I second. All those in favor say aye.

Group: Aye.

Lisa Chew: All those opposed same sign. And the motion carries. Let's move on to the long-acting beta agonists.

Amber Figueroa: Going back. Do we… for the steroids do we need to address different mechanisms of device or it's all…? The MDPI, the DPI, the… it just looks like we did in the past for powder and aerosol. I guess that maybe has the… the fluticasone.

Ryan Pistoresi: That's a good point. We do… we typically have not in other drug classes, but for this one, because there are different delivery methods and different dosage forms between the aerosols and the powders, it looks like we have. But because this was a scan we really didn't break it out by the different device types. All that we did is, in a later motion, is we kind of had to combine new drug classes into the LAMA/LABA combinations because we didn't have motions for the ICS LAMAs or the ICS LAMA/LABAs. Those were the only changes that we had with this scan since the last update. If you would like, the next time we review it, we can call them out specifically, but because we haven't done that for a lot of the other drug classes we don't typically have, you know, like extended release broken out or different brand names by different manufacturers.

We usually just try to keep it by the drug name. That's the approach we took with these motions.

Amber Figueroa: So then can we… just to keep it generic then can we adjust that motion to reiterate… except to remove the… I mean can we just say mometasone?

Ryan Pistoresi: Yes, we can have it just be the drug name and that way it would be consistent with the other drug names and that way it would also include, you know, new devices or new salt forms.

Donna Sullivan: I think one of the reasons why we did it in the past is that there are times where one of the formulations has an indication for COPD, but not asthma and so you would need to distinguish which product actually had which indication. And that might be… it's not the case for the mometasone but I know it is the case in some of the other inhalers where they have one indication, but not the other. And so we have broken them out because of that.

Amber Figueroa: But doesn't that get captured with that generic "for the treatment of their approved indications"?

Ryan Pistoresi: That is correct. I think the reason that we did that in the past was for the ICS LABA with the fluticasone, salmeterol, DPI and the fluticasone, salmeterol MDI. They do have different approved indications and I think because we wanted to apply this AC nomenclature throughout all the different motions we likely did the same for the mometasone. Hard to say because they did this like three years ago so I don't necessarily remember the rationale, but I do remember going through and kind of readjusting the drugs in this. But to your point we don't necessarily need to. I just did that to help me go through the different drugs for the cost analysis afterwards and be able to kind of organize the drugs between the asthma drugs and the COPD drugs.

Amber Figueroa: So do you just want to leave it the same? I mean I'm just looking at fluticasone has the different deliveries now as well. So if we're going to consistently do that we need to be consistent throughout all of the categories or we can just nix it and put the name.

Man: I agree with you, Amber. One thing I am troubled by is that when we get some of these data reviews they are comparing fluticasone MDPI versus… we're comparing the devices, as well, with the same drug. I'm not sure if that affects how we address this in the motion because we're looking at the comparative efficacy of the devices.

Donna Sullivan: For purposes of this since it says scan and we're not considering any new evidence, for clerical purposes we can go back and add in all of the different delivery systems and you can still make your motion with the caveat that we will include all of the different devices and delivery systems with their indication for the official motion and we… so then the next time you review that class, and if it gets updated, we will all of those different devices and products that will then be eligible to be included on the PDL.

Amber Figueroa: That sounds good to me, too. So can we redo that prior motion with that little caveat?

Lisa Chew: Yes.

Jordan Storhaug: I don't even know if we need to. Do we need another motion or can we just say that is a clerical piece?

Donna Sullivan: I think you could either make another motion or we could just agree that we will do that for the next… that we assume that that means all of the different products are included in the name and for clerical purposes we will break them out in the future. Or you could say you reiterate the motion and include all the devices so that we're making sure that we intended to include all of the different devices for the other products that we didn't split out. It's really up to you guys.

Amber Figueroa: I move that we reiterate the prior motion with the caveat that the device delivery mode be clerically added, as well as the diagnostic indication.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. So I would assume this would happen for all of the classes? We want to do this for all of the classes?

Donna Sullivan: Yes, I would agree.

Lisa Chew: So let's move on to the long-acting beta agonists.

Nancy Lee: I reiterate the previous motion for long-acting beta agonists.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Let's move on to the leukotriene modifiers.

Catherine Brown: I move to reiterate the prior motion.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Let's move on to the ICS/LABA combinations.

Diane Schwilke: I move that we reiterate the prior motion.

Nancy Lee: I second that motion.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Now to the LAMA/LABA combinations.

Amber Figueroa: I move that we reiterate the prior motion.

Lisa Chew: I second. All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Now the phosphodiesterase inhibitors.

Jordan Storhaug: I move that we reiterate the prior motion.

Diane Schwilke: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Now we're on to the long-acting muscarinic antagonists.

Diane Schwilke: I move that we reiterate the prior motion.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. We're going to be moving onto the hormone therapy scan with Beth.

Beth Shaw: So I'll take you through the scan and [inaudible] for hormone therapy. The overview of the presentation will be as you've seen. We can move to slide 2.

You can see topic history for this scan. So the update report was published in October 2007 with a full synthesis of the evidence and their searches were conducted through March 2007. Since then there have been a series of scans with the last one being compared in September 2016.

On slide 3 you can see the background of this report, but basically women report experiencing a range of menopausal symptoms that can start before the menopause and continue after the menopause. These are closely associated with hormonal changes and hence hormone therapy can be used to treat these symptoms.

On slide 4 you can see the PICO that we used. So the population is women in that menopausal transition and women after menopause. In terms of interventions we're looking for hormone therapy so that the estrogen-based therapies either alone or in combination with progestin or progesterone and Table 1 in the full report details all the hormone therapies that we looked at. We were looking at comparators that included another FDA-approved therapy, but we also were looking for comparators such as no treatment or placebo. And we were looking for a range of outcomes. Primarily for symptom relief and osteoporosis-related outcomes. We were also looking for safety and other outcomes such as weight change or cardiovascular events.

On slide 5 you can see the key questions that we were addressing in this scan. We were looking at trials that looked at the effectiveness of these therapies. That was both for reducing menopausal symptoms, but also preventing low bone density and fractures. We were looking for safety and that's both in the short-term use and long-term. So that's five or more years. We were looking for subgroups of patients in whom effectiveness and harms may vary.

Slide 6 just reports the methods and I just want to highlight that the search here was conducted from August 2016 to July 2018. We can move now into the findings.

So first of all we were looking for new drugs or formulations and on slide 8 you can see that since the last update report in 2007 we have identified seven new hormone therapy drugs or formulations. And of these seven two were identified in this scan. So there's one first generic approval for Estradiol cream and one new formulation of Imvexxy.

In terms of findings on new indications and safety warnings… so if we move to slide 10 now. Since the last scan in 2016 we didn't identify any new indications, but we did see that new safety information has been added to the prescribing label. This was related to the risk of ovarian cancer associated with estrogen therapy.

In terms of what we found on systematic reviews. So if we move to slide 12 you can see that since the last update report in 2007 we've identified eight systematic reviews and of these eight since the last found in 2016 we identified two new systematic reviews. You can see the details of these on the next slide. So the two studies you can see here we've got the author, year, the aim, the population, intervention, study designs that these systematic reviews included, and the outcome. The first systematic review was looking at updated evidence for the U.S. Preventive Services Task Force and this is about the use of hormone therapy and reducing risks for chronic conditions. Similarly, the second systematic review here was looking at the effects of long-term hormone therapy, which they defined as at least one years' duration and they were looking at those outcomes such as mortality, coronary events, stroke, cancer, etc.

So if we move now in the findings of the randomized controlled trials, so that is now on slide 15, we can see that since the last update report in 2007 there have been 58 relevant trials identified or reported in 74 publications. Of these 10 are head-to-head trials and 48 are placebo or no treatment-controlled trials. And in this scan since September 2016 of those 48 studies five new placebo-controlled trials have been identified. One trials evaluated estrogen alone and four trials evaluated combination of estrogen and progestin or progesterone.

And on slide 16 you can see the details of these trials. Again, the details of the author, year and study name, along with the population, intervention, comparison and outcomes. These are all placebo-

controlled trials, but we are looking for a range of outcomes including [inaudible] marketers, cognitive function, quality of life, etc.

So really, in summary, since the last update report we've identified seven newly approved hormone therapy drugs and formulations, one new first generic approval and one new formulation in this scan. There have been eight new systematic reviews, again two of which were identified in this scan, and 58 trials, five new placebo-controlled trials identified in this can, and we've also identified that new prescribing information on the increased risk of ovarian cancer associated with hormone therapy. Happy to take any questions.

Lisa Chew: Thank you, Beth. Any questions from the committee? And there are no stakeholders. Let's move to the motion. Here we're going to make a motion as to whether we accept the scan as adequate or we are requesting an updated class review.

Nancy Lee: I propose… motion to accept the scan number 8 for hormone therapy for post-menopausal women or women in menopausal transition state as adequate… the scan is adequate.

Lisa Chew: I second. All those in favor say aye.

Group: Aye.

Lisa Chew: Any oppose? The motion carries. So now we move to the actual motion whether we want to reiterate the prior motion or make modifications to the previous motion.

Amber Figueroa: It looks like the proposal is to archive it. So for some of our newer members can you guys review what archiving is?

Leta Evaskus: First we're going to do the motion the way we always would and then we will do the motion to archive and that just means that we are not going to make any updates to the drug class unless the committee suggests we bring it back out.

Donna Sullivan: Basically what happens is the class, you know, is getting old. There's not a lot of new evidence coming out so if there was new evidence that were to be published the committee or the state would bring it back to be re-evaluated. When we archive a drug class we might make changes to the drugs that are preferred based on cost, but we would continue to follow the most current motion or the last motion that you made on how you want us to treat this particular class. So they would still be on the PDL we just wouldn't kind of bring them back to you unless there is really new evidence that changes how we would address these drugs.

Lisa Chew: Thanks, Donna. So committee, let's look at the first motion about the actual drug class whether we want to reiterate the prior motion.

Susan Flatebo: I move to reiterate the prior motion.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any oppose? The motion carries. Now on the opposite… the next page this is the motion regarding archiving.

Amber Figueroa: After considering the scan presented today I move to archive the following drug class from further regular review by the P&T Committee, estrogens.

Susan Flatebo: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any oppose? The motion carries. Everybody doing okay? Should we continue with second generation? We'll take a 15-minute break and reconvene like 5 after 11.

Ryan Pistoresi: There are snacks in the front corner, as well.

Lisa Chew: Why don't we go ahead and get started. We'll be talking about second generation antipsychotics. Brittany, are you on the phone?

Brittany Lazur: Hi, I'm here.

Lisa Chew: All right. Your slides are up.

Brittany Lazur: Great, thank you. So my name is Brittany Lazur. I'm from the Center for Evidence-Based Policy and I will be presenting the most recent scan on second generation antipsychotics, which is scan 2. Let's go to the next slide, please.

This is just an overview of the presentation today which has been previously described in other presentations. So I'll go ahead and skip to slide 2.

To provide a little bit of history on this topic, the last full report was update 5, which was completed in October 2016 with searches through July of 2016 and the last scan on this topic was completed in April 2017. Next slide, please.

So in terms of the populations that were included in this scan we focused on five clinical populations that you see here so schizophrenia, bipolar disorder, major depressive disorder, autism spectrum, and disruptive, impulse control, or conduct disorders. We were interested in different age populations so adults, adolescents or children for these specific clinical populations and you'll see which age groups we were focusing on for each clinical population here. Slide 4.

This slide illustrates the interventions that were included in this scan. So it's quite a comprehensive list of the second generation antipsychotics. I would like to refer you to the full scan document, Table 1, so you can see all the formulations of each of these included drugs. Next slide, please.

So on slide 5 in terms of comparisons we were looking for evidence comparing second generation antipsychotics to other second generation

antipsychotics that were previously listed and we were looking for this for all populations. We also looked for placebo-controlled evidence for children and adolescents of bipolar disorder, autism spectrum disorder or disruptive, impulse control or conduct disorders. We also looked for placebo-controlled evidence in adults with major depressive disorder as an add-on or background to therapy. In terms of outcomes we were interested in quality of life, symptom response, functional capacity, hospitalization, persistence and mortality and we also looked for adverse events. I would like to refer you to the full scan document again for a complete list of outcomes.

On slide 6 the key question for this scan were really centered around the clinical… or comparative effectiveness and harms of these five clinical populations that we've previously described. So you'll see schizophrenia, major depressive disorder, bipolar, autism spectrum and the conduct disorders. We also had a key question dedicated to subgroups. So benefits and harms in new subgroups such as those with substance abuse and obesity. Slide 7.

In terms of our methods, methods have been previously described in some of these other presentations today, but I wanted to note that our searches span from March 2017 through September of 2018. Next slide, please.

In terms of our findings slide 8 we did not identify any newly approved drugs in this scan. However, we did identify three new formulations. You'll see here in this table on this slide. So to orient you to this table we first have the generic name and brand name in the first two columns, next followed by the date of approval, the formulation and the frequency of administration in the next three columns and then finally the indication for each new formulation. One of the new formulations that we identified was a new formulation of aripiprazole, by Abilify MyCite Kit. This is a drug device combination with an adjustable censor. This is an oral tablet dosed once daily in adults with schizophrenia, bipolar disorder or major depressive disorder. The second formulation is of aripiprazole lauroxil. This is the Aristada Initio Kit. This is an injection for the initiation of aripiprazole and this helps to achieve a quicker dose to aripiprazole and this is indicated for adults with schizophrenia. The final

formulation that we identified in this scan is risperidone. It's called the Perseris Kit and this is monthly administration in adults with schizophrenia. So all of these formulations are really aimed to address issues of compliance and continuity of care. Next slide, please.

So on slide 9 we identified two new indications for drugs included in this scan. The first was for the Abilify Maintena Kit so the extended release injection of aripiprazole. This indication was expanded to include maintenance monotherapy in adults with bipolar disorder. The second indication was for Latuda. This is the lurasidone oral tablet and this indication was expanded to include the monotherapy in pediatric patients 10 to 17 years with bipolar disorder. We did not identify any new serious harms or boxed warnings in prior scans or this current scan. Next slide, please.

So we're on slide 10 and this illustrates the new systematic review that we've identified since the last report. So cumulatively since the last report we've identified four new reviews. In this scan we identified three which are presented in this table. So in the first column we have the author, year and organization that produced the preview. The second column is the population that was focused on. Third column is interventions that were addressed and then the fourth column are the outcomes that were addressed in these reviews. So we identified two reviews from the agency for healthcare research and quality and one review from Cochrane. The first review that you see listed here, Butler, et al. is specifically in adults with bipolar disorder. You can see that they included a number of the second generation antipsychotics that were interested in this scan and these focus on functional capacity and quality of life, response and adverse events. The second review that we identified, the Cochrane Review in the second row, specifically with [inaudible] in children with disruptive behavior disorders. They focused on a smaller group of drugs so risperidone, quetiapine and ziprasidone and they again were focused on response and adverse events, as well as functional capacity. The final review that we identified in this scan, the third row here, focused specifically on adults with schizophrenia. These compared a larger group of second generation antipsychotics to other second generation antipsychotics focusing on functional capacity, symptom response, quality of life and adverse events. Next slide, please.

So we're on slide 11 here. In terms of the new randomized controlled trials we identified we found a total of five new head-to-head trials since the last report, four which were found in this scan, a total of four new secondary analyses of head-to-head trials since the last report, two that were found in the [inaudible] for this scan, and finally five new placebo-controlled trials since the last report on this topic, four of which were identified in this scan. Next slide, please.

So we're on slide 12. I'd like to refer you to the full scan report, Tables 4 through 6, for additional details on each of the included studies that we have identified in this scan. But for an overview in terms of the four head-to-head trials that we found all trials were in adults or adolescents with schizophrenia and three of these trials compared olanzapine to paliperidone, risperidone or ziprasidone. And the fourth trial compared risperidone to cariprazine. In terms of the new secondary analysis that we identified in this scan, so we found two of those, these secondary analyses presented additional outcomes from the QUALIFY trial that was specifically in adults with schizophrenia and additional outcomes included things such as quality of life. In terms of the placebo-controlled trials we identified there were four of those. We found two trials of aripiprazole in children or adolescents. One of these was with bipolar disorder and one was children or adolescents with autism spectrum disorder. We found one trial of lurasidone in children or adolescents with bipolar depression. And finally one trial of risperidone with methylphenidate in children with oppositional defiant disorder and ADHD. Next slide, please.

So we're on slide 13 and to wrap up with a little bit of summary. Since the last update report we've identified no newly approved drugs. However, we did identify those three newly approved formulations, Abilify MyCite Kit, Aristada Initio and Perseris. We identified two new expanded indications for a second generation antipsychotic. So those were for Abilify Maintena and Latuda. We did not identify any new boxed warnings. We did identify four new systematic reviews, three of which were found in the searches for this scan. And finally we found five new head-to-head trials, four in this scan; four new secondary analyses, two found in this scan; and five new placebo-controlled trials, four of

which were found in this scan. That concludes my presentation and I'd be happy to take any questions.

Dale Sanderson: Has there been any breakdown in terms of treating bipolar disorder the various aspects of that? So bipolar depression, bipolar mania and maintenance like prophylaxis for both?

Brittany Lazur: That's a good question. The purposes of this scan document we didn't delve into the findings of the report and it wasn't really borne out in our review of the abstracts and the full text that they delineated the evidence by these comparisons, but that is a good question.

Lisa Chew: Any other questions from the committee? So there are four stakeholders. Dr. Paul Thompson, Dr. Mae Kwong, Nick Seifter and Dr. Valerie Ng. If you could come up to the podium, please. Introduce yourself and who you represent. You will have three minutes each for comments.

Paul Thompson: Hi. Good morning. My name is Paul Thompson. I'm a psychiatric pharmacist and medical science director for Alkermes. I'm delighted to be able to speak with you this morning and introduce you more to what Aristada Initio is. Aristada Initio in combination with oral aripiprazole is indicated for the initiation of Aristada used for treatment of schizophrenia in adults. Aristada Initio is not interchangeable with Aristada due to differing pharmacokinetic profiles. Aristada Initio comes in one dosage form 675 mg and it's given with one 30 mg dose of oral therapy to provide a one-day initiation regimen which can be continued at any of the dosing intervals that are currently approved for Aristada whether it is four-week, six-week or two-month. Aristada Initio is indicated for single use in initiating and not for repeated use. It is an intermuscular injectable so it needs to be administered by a healthcare professional. For patients that are naïve to aripiprazole tolerability with oral should be handled first prior to utilizing it. Since there is only one dose of Aristada Initio patients that are either 2D6 poor metabolizers or on strong 2D63A4 inducers of inhibitors should be using the 21 days of oral therapy rather than the single dose because it does not… it cannot be modified.

The main formulation differences between Aristada and Aristada Initio they are both the same molecule. Aripiprazole lauroxil the big difference is the particle size. One of the… Aristada is in the micrometer range, Aristada Initio is in the nanometer range, which affects the pharmacokinetics absorption and distribution.

The adverse events in our clinical trials looking at the one-day initiation regimen between the 21-day initiation regimens with oral the adverse events were similar between the two groups, as well as in the pharmacokinetic studies. The safety of the one-day initiation regimen was similar and consistent to what we saw with the original Aristada trials. So Aristada Initio is part of this one-day initiation regimen for Aristada long-acting which can provide up to the… every two-month dosing interval with the current dosing that are available on the market and approved. I would just like to thank you the committee for their time and open it up for questions and thank you for considering Aristada Initio for review for PDL as the current Aristada is currently on your PDL. Any questions?

Lisa Chew: Thank you very much.

Mae Kwong: Good morning. My name is Mae Kwong. I'm a pharmacist with Janssen Scientific Affairs. I'm here today to speak with you regarding the long-acting injectables Invega Sustenna and Invega Trinza. Both Invega Sustenna and Invega Trinza contain paliperidone [inaudible] as an active ingredient in our eight antipsychotics indicated for the treatment of schizophrenia. Additionally, Sustenna is indicated for the treatment of schizoaffective disorder. Sustenna is a once-monthly injection whereas Trinza is the only long-acting injectable delivered every three months. In a 12-month follow-up using Medicaid claims once monthly injectables were compared to twice monthly risperidone injectable. Once monthly injectables experienced a significantly better mean adherence, longer median persistence, lower hazard of discontinuing and lower rates of outpatient/inpatient and long-term care visits. In Medicaid patients initiating long-acting therapies versus oral antipsychotics Invega Sustenna was associated with significantly fewer outpatient visits, inpatient days, long-term care visits and home care services and had statistically significant better adherence overall, as well as persistence. These

decreased medical costs were offset by about half of the prescription cost. The PRIDE Study, which is now in the label for Invega Sustenna is the only long-acting injectable antipsychotic shown to delay relapse versus oral antipsychotics in a randomized comparative study conducted in real world patients with schizophrenia and a history of incarceration. These patients are normally not enrolled into clinical trials. The study shows superiority for Sustenna in delaying relapse by six months. Multiple studies have demonstrated improvements in adherence and persistence, as well as decreased healthcare resource utilization resulting in lower medical costs which may offset the pharmacy costs associated with this drugs. Given that not every medical will work for every patient with this debilitating disease, we understand that it is critically important to have an armamentarium of drugs available to these patients. For that reason I ask the committee to continue keeping Invega Sustenna and Trinza on the PDL for Medicaid patients in Washington. Thank you.

Lisa Chew: Any questions? Thank you.

Nick Seifter: Greetings. My name is Nick Seifter. I'm a pharmacist in Washington and I'm a field director of HAOR for Sunovion Pharmaceuticals. I appreciate the time here to speak on behalf of Latuda or lurasidone. I especially appreciate Dale Sanderson's question because the answer to your question is, "Yes, systematically and thoroughly." That's the purpose of my discussion here today is to help provide some information to support the DERP literature scan and also support you when it comes time to evaluate that literature for PDL considerations.

So I'm going to address questions 1, 3, provide a nuance for really important clarification in the indication for lurasidone and I'll also identify three systematic literature reviews that were not in the scan, but were published within that timeframe.

I'll start with the indications. So lurasidone is indicated for the treatment of schizophrenia in adults and adolescents 13 to 17 years of age. That's not the nuance. Here comes the nuance. So lurasidone is the only agent in the class with an indication for adults as both monotherapy and adjunctive therapy with lithium or valproate to treat… here it is, "major depressive episodes associated with bipolar 1 disorder". That's a really

important clarification and I hope you consider that when it comes time to review. It's not bipolar disorders. This is major depressive episodes. So it's either bipolar 1 or you can refer to it as bipolar depression.

Additionally, in March 2018 lurasidone received an indication for the treatment of pediatric patients 10 and 17 years of age with bipolar depression as monotherapy. I'll refer you full prescribing information for warnings, precautions and adverse events.

For question 3 regarding the bipolar population I would ask you to consider the internationally-recognized global guidelines for the treatment of mood and anxiety disorders and this included a literature review and an expert panel known throughout the world for their review. This is the CANMAT and ISBD, which is the Canadian Network for Mood and Anxiety Treatments and International Society for Bipolar Disorders. And they recommend lurasidone among first line therapies as monotherapy or adjunctive therapy with lithium or divalproex for acute bipolar depression in adults and lurasidone is also the only recommended first line therapy for children and adolescents with bipolar depressions, the only one.

Addressing question 1 with schizophrenia population – in January, Florida Medicaid… or the Florida Medicaid psychotherapeutic medication guidelines were produced and this is done by a group of nationally-recognized experts and they have one recognized psychiatrist within that disorder to do a full literature review, present it to the committee, and then they produce it… they publish… they publicize it as an open source document that is intended to be the U.S. guidelines for treatment. In these guidelines they recommend lurasidone among first line therapies for bipolar depression and schizophrenia and state that lurasidone has a better metabolic profile than quetiapine for bipolar depression.

And lastly there is a systemic… an independently done systematic review that was published by Crouse in June of 2018 in the Journal of European Neuropsychopharmacology. In this meta-analysis that includes 28 randomized-controlled antipsychotic drug trials with multiple efficacy and tolerability outcomes specifically in children and adolescents with schizophrenia. For the primary outcome of mean change and overall

symptoms lurasidone was significantly better than placebo and fluphenazine and similar to all other antipsychotics except for clozapine. With regard to weight gain lurasidone was similar to placebo and significantly better than risperidone, paliperidone, clozapine, quetiapine and olanzapine. And regarding prolactin increase lurasidone was similar to placebo and superior to paliperidone, olanzapine, paliperidone and risperidone.

So in closing I appreciate your time and consideration and hope that lurasidone addresses the need for well-tolerated and cost-effective agents to patients with schizophrenia and bipolar depression and I respectively ask that you consider this in the DERP literature scan and for future considerations for the PDL. Do you have any questions?

Dale Sanderson: Is there any attempts to reformulate this in a way that would not require the food issue in terms of needing to be taken so close to food intake?

Nick Seifter: So the high protein meal? At this time there is not any ongoing development as far as formulation or administration that I'm aware of. There aren't any trials that are filed with clinicaltrials.gov at this time or any development around that. I can elaborate further there's other nuances around why that is, and if you'd like to hear that I'd be happy to have a [inaudible] conversation. Any other questions? Okay. Thank you.

Lisa Chew: Thank you.

Valerie Ng: Esteemed members of the P&T Committee, good morning. My name is Valerie Ng and I'm a pharmacist and I'm with Indivior managed care medical science team. I'd like to thank you for your time and for the opportunity to share with you information on Perseris, which is an extended release injectable suspension of risperidone for subcutaneous use. Perseris is indicated for the treatment of schizophrenia in adults. It is to be administered by a healthcare professional subcutaneously in the abdominal area. Perseris is initiated with either 90 mg or 120 mg once a month and no more than one dose per month. Based on average plasma concentrations of risperidone and its total active [inaudible] 90 mg Perseris corresponds to 3 mg per day of oral risperidone while the 120 mg corresponds to 4 mg of oral risperidone per day. Neither a loading

dose nor a supplemental oral risperidone is recommended and that's one of the main differentiating factors. The most common adverse events during the clinical trials observed were somnolence, sedation, musculoskeletal pain, and weight gain, which are consistent with that of the systematic safety profile of that of oral risperidone. For complete safety information and boxed warning of Perseris please refer to the prescribing information that's available online.

So the FDA approval of Perseris was based on a phase 3 study assessing the safety and efficacy of the Perseris in patients 18 to 55 years of age with a diagnosis of schizophrenia who exhibited an acute episode within eight weeks of the screening for the study. The phase 3 study was a randomized double-blind placebo-controlled eight-weight in-patient study of 337 patients receiving 90 mg or 120 mg of Perseris or placebo. The efficacy of Perseris was demonstrated by statistically significant improvements of the primary and secondary clinical endpoints which were a PAN score at a positive and negative syndrome scale total score and the CGIS which is the Clinical Global Impression Severity of illness scores respectively.

In closing I would respectfully request the committee to consider the addition or the coverage of Perseris as an additional treatment option for patients who are diagnosed with schizophrenia. At this time I'll be happy to take any questions you may have.

Lisa Chew: Questions? Thank you. All right. So to the committee, let's look at the motion. This is a scan so we have to make a motion as to whether we think the scan is adequate or whether we want a more in-depth review and then either we want to reiterate the prior motion or make modifications.

Donna Sullivan: I just wanted to point out that the new formulations that were identified in this scan are not eligible to be on the PDL until we have a full update of the class. I just wanted to remind you of that. And they are on slide 8. Thank you.

Leta Evaskus: I'm just going to add these in grade out under the drugs reviewed.

Susan Flatebo: I'd like to make a move to accept the scan as adequate.

Amber Figueroa: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries.

Virginia Buccola: I would like to propose that the previous motion be upheld.

Dale Sanderson: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Let's move on to the newer diabetes scan with Curtis.

Curtis Harrod: Thank you so much. So I'll be presenting on newer diabetes medications and combinations and this is our final scan of today's meeting. This is going to be the first scan since the third update on this report.

So let's go ahead and go to slide 2 so we can walk through quickly the topic history. The original report by DERP was done in February 2011. A streamlined or narrower report was done in June 2014. The second update of that report was done in July 2016 and then the third update was completed in September 2017. So again this is the first scan connected to that third update.

So proceeding to the next slide, slide #3 for our PICO. Starting with our population we were focused fully on adults with type 2 diabetes. We have a number of interventions within this scan, as well. I'll walk through a high level as I did previously with the SGLT2 inhibitors. There are three in this review and then for the DPP4 inhibitors there are four drugs in this review. So we'll move on to slide 4.

Starting with the combination of the SGLT2 inhibitors with the DPP4 inhibitor there are two medications. For SGLT2 inhibitors with metformin there are five. For the DPP4 inhibitor with TZD we have one medication, Oseni. And then DPP4 inhibitors with metformin there are six medications included in this scan.

So continuing on to slide number 5, and this is the last set of the interventions with subcutaneous injection drugs in this table. The GLP1 agonists there are six of those medications and then the GLP1 agonists with long-acting insulin there are two. So moving on to slide 6.

Looking at our comparators in general we are interested in just head-to-head effectiveness studies. However, for key question 1, and I'll walk you through that question in an upcoming slide, we are interested in placebo comparisons for that question only.

Moving on to slide 7 for out outcomes. Broken down here by efficacy and effectiveness, as well as harms we're looking at mortality, cardiovascular outcomes, HbA1c so the blood glucose levels of [inaudible] time, body weight and then harms looking at adverse events, serious adverse events and then withdrawals due to adverse events.

Moving on to our key questions on slide 8 there are four key questions. The first one as a reminder is looking at placebo trials and so we're looking at efficacy and effectiveness of newer diabetes medications and our outcome here is for cardiovascular events. For questions two and three we have comparative efficacy effectiveness as well as harms for newer diabetes medications, and then our fourth question is by subgroups for these efficacy and effectiveness as well as harms outcomes. Slide 9.

I'll just highlight our search period which was May 12, 2017 to August 5, 2018 for this scan.

So getting into our findings if we can move onto slide 11 we're looking at new drugs or formulations. Starting with the first one ertugliflozin or the SGLT2 inhibitor. It's an oral medication and was approved by the FDA as

an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. The second row of highlights ertugliflozin plus metformin so this is, again, an SGLT2 inhibitor plus metformin. This is also an adjunct to diet and exercise to improve glycemic control and you can see how the nuance there is about adequate control of regimen containing ertugliflozin and isolation or metformin and isolation or in patients who are already treated with both medications. Our final new drug or formulation is semaglutide and is a GLP1 agonist. It's a subcutaneous injection and similar to ertugliflozin and isolation it's an adjunct to diet and exercise to improve glycemic control in type 2 diabetics. Moving on to slide 12.

Liraglutide or Victoza was approved for a new indication in August 2018 to reduce the risk of major events of CV in adults with type 2 diabetes with established cardiovascular disease. Slide 13.

Canagliflozin or Invokana was indicated with a new black boxed warning in May 2017. So at the very beginning of this scan cycle or this report. And they have an increased risk of leg and foot amputations and so that is coming out of the CANVAS and CANVAS R trials. The FDA, again, did that on May 16, 2017.

Moving on to our systematic reviews we identified four new systematic reviews since this scan has been done and so focusing on the Bethal et al. 2018 RCTs were included in this, four of them, and you can see the first row I highlight this as the primary outcomes for cardiovascular-related. Continuing on to the next slide, slide 15.

This is our randomized controlled trials and we have five overall. I point you to the Holman et al. 2017. That's the second row the EXSCEL trial. And not only are there a large sample size, close to 15,000 participants, but also again cardiovascular outcomes were of interest in that study. Slide 16.

We did identify a secondary analyses from the EMPA-REG OUTCOME trial, Zinman et al. did the publication on this and so this is a placebo-controlled trial for empagliflozin, which was included previously. They

are comparing men versus women within the study on CV outcomes. Slide 17.

This is a wrap up of our scan, as well as the contacts since the last report, which is just this scan. The report was done September 2017 and since that time we've identified three new drugs or formulations, ertugliflozin, ertugliflozin plus metformin, and semaglutide also. A new indication has been provided for liraglutide and then a new FDA black boxed warning has been applied to canagliflozin Invokana. Four new systematic reviews were identified. One of importance because of CV outcomes being studied within that and then five new RCTs, one with CV outcomes and a large sample. The one secondary analysis from the EMPA-REG OUTCOME trial we also identified.

Thanks so much and I'm happy to take any questions.

Lisa Chew: Thank you, Curtis. Any questions from the committee? There are no questions but there are two stakeholders, Dr. Anthony Hoovler and Dr. Mae Kwong. If you could please come up to the podium, introduce yourself and who you represent and you'll have three minutes each.

Anthony Hoovler: Good morning everyone. My name is Anthony Hoovler. I'm a board certified endocrinologist here in Washington and a senior medical liaison with Novo Nordisk and I'm going to share some highlights with you today regarding Ozempic. It was approved in December of last year. It's the newest once weekly GLP1 indicated, as you heard, as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. Similar to other longer-acting GLP1s there's a boxed warning with Ozempic regarding potential risks of thyroid C-cell tumors and as such anyone with a personal or family history of MTC in patients with MEN2 should not use Ozempic. And is with all GLP1 receptor agonists the Ozempic label includes warnings and precautions regarding pancreatitis. GI side effects are the most commonly reported adverse events with Ozempic and I would refer you to the PI for additional safety information. In regards to safety and efficacy, Ozempic has been studied in the sustained clinical development program, which is a comprehensive program enrolling more than 8,000 adults with type 2 diabetes, six phase 3A studies are actually in the label. There's actually one phase 3B study,

SUSTAIN 7, which is consistent with the label. In regards to efficacy in head-to-head trials 30 to 56 weeks in duration, Ozempic 0.5 mg dose demonstrated A1C reductions from 1.2 to 1.5% and 1 mg dose demonstrated A1C reductions ranging from 1.4 to 1.8%. While not indicated for weight loss, weight effect was a secondary endpoint in the clinical program. Mean weight loss of 7 to 10 pounds for the lower dose of Ozempic and mean weight loss of 10 to 14 pounds was noted with the higher dose. Two head-to-head trials comparing Ozempic to other once-weekly GLP1s have been published, SUSTAIN 3 compared Ozempic to Bydureon and SUSTAIN 7 compared Ozempic to Trulicity. Both trials demonstrated that therapy with Ozempic resulted in greater A1C reductions. The greater percentage of patients achieving A1C targets and greater weight loss versus comparators. As you know, cardiovascular safety data is increasingly employed in the management decisions for patients with type 2 diabetes as reflected by the recent ADA consensus update of October this year and cardiovascular safety information is actually included in the Ozempic label even a launch from SUSTAIN 6 trial and when compared to placebo plus standard of care Ozempic met the primary endpoint of non-inferiority.

Ozempic is available in one pen carton for initial titration in the lower dose and a two pen carton for maintenance on the larger 1 mg dose and Nova fine plus needles are included in the packaging hence there is no requirement for a second prescription. With the data presented including cardiovascular safety data in the label at launch and data from two head-to-head studies comparing Ozempic to other agents within the once weekly GLP1 receptor class I would respectfully request that you consider adding Ozempic to the PDL. Thank you and any questions I'd be happy to entertain.

Lisa Chew: Thank you very much.

Mae Kwong: Good morning again. My name is Mae Kwong. I'm a pharmacist with the Real World Value and Evidence Team of Janssen. I'm here to speak today about Invokana canagliflozin, which is currently available as a preferred agent on the Washington PDL. In October of this year Invokana received a new indication making it the only oral type 2 diabetes medication to reduce the risk of major adverse cardiovascular events including

cardiovascular death, MI or stroke in adult patients with type 2 diabetes in established cardiovascular disease. The CREDENCE study is a randomized phase 3 study assessing whether canagliflozin 100 mg reduces the risk of kidney failure in cardiovascular events compared to placebo in type 2 diabetes patients and stage 2 or 3 chronic kidney disease and macroalbuminuria who are already on standard of care including ACEs and ARBs. The study enrolled over 4,000 patients and was stopped early for efficacy in the canagliflozin arm. Results will be shared with the FDA and presented at an upcoming medical meeting.

Based on a recent publication called Observe 4D this includes a large retrospective observational comparative analysis using four U.S. claims database, including both commercial, as well as Medicaid patients. This study was undertaken to evaluate the risk of below-knee lower extremity amputation and hospitalization for heart failure. Comparisons were made between new users of canagliflozin versus other SGLT2 inhibitors, as well as canagliflozin versus non-SGLT2 inhibitors. According to real… and this was based on real world practice. The study enrolled over… or looked at over 700,000 patients and based on this evaluation the results showed that no evidence of increased risk of below-knee amputation was seen for canagliflozin versus other SGLT2 inhibitors, as well as other non-SGLT2 inhibitors. For hospitalization for heart failure no difference in risk was observed for canagliflozin versus the other SGLT2 inhibitors, but a difference was seen compared to canagliflozin versus non-SGLT2 inhibitors benefiting canagliflozin. For these reasons I thank the committee for continuing to make Invokana available to your Washington Medicaid patients and thank you for hearing me a second time today.

Lisa Chew: Thank you. Any questions? Thank you very much. Okay. So we're going to be looking at the motion for this group. This is similar to the asthma and COPD. It looks like there are three drug classes. So we'll first make a motion on whether the scan is accepted as adequate or not for all three classes.

Susan Flatebo: I move to make this… I move to accept the scan as adequate.

Dale Sanderson: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any oppose? The motion carries. Okay. Let's look specifically at the DPP4 inhibitors and whether we want to reiterate the prior motion or make any modifications.

Amber Figueroa: I move that we reiterate the prior motion.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any oppose? The motion carries. Let's move on to the next class of the GLP1 agonists.

Susan Flatebo: I move to reiterate the prior motion.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any oppose? The motion carries. Now we're onto the SGLT2 inhibitors.

Jordan Storhaug: I move that we reiterate the prior motion.

Alex Park: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any oppose? The motion carries.

Leta Evaskus: I suggest having lunch and starting the DUR after lunch.

Lisa Chew: Okay. So we will adjourn the P&T Committee and resume at 12:45. Okay. Great. Thank you.

All right. We are going to convene the Drug Utilization Review Board and we will start with hepatitis C with a presentation from Umang Patel.

Umang Patel: Thank you. On the next slide just like we've done previously we'll do a brief overview of the disease state, the indications, dosage and formulations, and guideline updates. Let's go to slide 4.

Just a quick overview. So hepatitis C, which I'll be abbreviating as HCV infection is the most common, chronic, blood-born infection in the U.S. In appropriately 15 to 25% of patients who become infected with hep C the virus is eliminated during the acute phase of the infection by T cell-mediated antiviral mechanisms; however, in the other 75% to 85% of patients, HCV persists for decades. It is estimated that about 23 to 46,000 children in the U.S. have hep C. Approximately 2.7 million people in the U.S. are chronically infected, although it is estimated that nearly 75% of these people may be unaware of their infection due to the insidious progression of the disease. It accounts for about 40% of chronic liver disease in the U.S. and in patients with the chronic hep C infection followed for 20 years disease progression to cirrhosis occurs in about 20 to 25%. Of those who develop cirrhosis approximately 30% will develop end-stage liver disease over the next 10 years and 1 to 2% will develop hepatocellular carcinoma. Hep C infection is the most common reason for liver transplant and results in an estimated 8 to 10,000 deaths per year in the U.S. The most important risk for hep C infection is injection drug use, which accounts for at least 60% of the cases. Other modes of transmission include mother-to-infant, receive a blood or organ donation prior to 1992, occupational exposures, chronic hemodialysis and contaminated devices shared for non-injection drug use intranasal illicit drug use. Sexual transmission also occurs but generally seems to be inefficient except among those who have HIV, specifically men who have unprotected sex with men. Other risk factors include incarceration and receiving a tattoo in an unregulated setting and it is estimated that about

29% of incarcerated persons in North America are an anti-HCV positive. Next slide.

So as you can imagine this disease state presentation is robust. I will not go through it all for the sake of time, but there will be information presented in front of you and I will be going through things such as the mechanism of action and I did receive a request to go over specific side effects or blacked box warnings or things like that. With this therapeutic state medications have numerous side effects so I'll go over the biggest ones, the most prevalent ones and the black boxed warnings as well. So here we have the medications. We'll discuss the indications are stratified by subgroup. The first here you have interferons, which consistent of Pegasys and PEG-Intron. As you can see the indications are in front of you. Now for these two, just to give you a little bit of clinical background, the mechanism of action, most interferon compounds are naturally occurring small proteins and glycoproteins produced and secreted by cells in response to the viral infection. And what they do is they bind the specific membrane receptors on the cell surface. Once it is bound it initiates a complex intercellular event including the induction of certain enzymes and suppresses cell proliferation. The second subclass will have ribavirins which continues over the next few slides. This specific ribavirin is available in a generic form. To give you clinical background on that, ribavirin is a nucleoside analog with antiviral activity which disrupts the cellular [inaudible] metabolism. It can also act as an RNA virus mitogen and increase the mutation rate of the RNA virus in the hep C virus. It is notable that ribavirin monotherapy is not effective for the treatment of hep C and ribavirin should not be used alone for this indication. On the next slide we'll continue with the ribavirin subclass.

Here we have Rebetol and Ribasphere, both again available in generic form. Now for… previously for the interferons in terms of contraindications I did want to point out for PEGinterferon alpha it is contraindicated in patients with autoimmune hepatitis, hepatic decompensation or hypersensitivity to any of its product compounds. For Pegasys it's contraindicated in the presence of hepatic decompensation specified by Child Pugh B and C and cerotic patients. Lastly, for that class PEG-Intron is contraindicated, again, in the presence of hepatic decompensation B and C and patients who have

hypersensitivity reactions. On this slide here for medications like ribavirin it's contraindicated in patients with hemoglobinopothies such as [inaudible], sickle cell anemia, and patients who have hypersensitivity as well.

On the next slide here you will see the ribavirin continued where we have Moderiba along with two different medication subclasses here. We have oral NS5A inhibitors which consistent of Daklinza and oral NS5B polymerase inhibitors which consist of Sovaldi. None of these medications are available in a generic form. Just to note, the FDA did report that Bristol-Myers Squibb has planned to cease distribution of Daklinza 90 mg in December 2018, so now. Again, a little bit of clinical background for NS5 inhibitors. So sofosbuvir is a single agent and it's… as a part of Epclusa, Harvoni and Vosevi. How this one works is it is basically a disruptor for the NS5B RNA dependent RNA polymerase, which is required for viral replication and for 5A it is very similar, which essentially it inhibits the NS5A viral replication as well in the hep C virus.

On the next slide here we'll oral combination products. Here we have Mavyret, Zepatier, Harvoni, Viekira and Viekira XR and Technivie as well. And these all… some of these do have protease inhibitor combined in there, which consists of [inaudible], bear with me on the pronunciation. We have glecaprevier, which is part of Mavyret. We have grazoprevir, which is part of Zepatier. We have paritaprevier, which part of Viekira and we have voxilaprevier, which is part of Vosevi. And these protease inhibitors inhibit the NS3 and the 4A protease, which is essential for the viral replication. And lastly we also have ritonavir, which is part of Viekira and Viekira and Technivie. It is not active against the hep C virus. It is a CYP3A inhibitor, which increases the plasma concentration of paritaprevir, which is the hep C acting agent. For protease inhibitors for the contraindications still on this slide here we have [inaudible], which is contraindicated in patients with moderate to severe hepatic impairments or Child Pugh Class B or C. We have Mavyret, which is contraindicated in patients with severe hepatic impairment, which is Class C. Harvoni does not have any contraindications worth noting and Technivie is contraindicated in patients with moderate and severe hepatic impairment Class B and C. And lastly Viekira Pak and Viekira XR is contraindicated in patients with moderate and severe hepatic

impairment, again B and C, as well. And on the last slide here we have the last two combination products. We have Epclusa and we have Vosevi. Again, neither of these are available in generic form as well and their respective indications are listed depending on the specific genotype that the patient has. The only contraindication for Vosevi is it contraindicated in patients taking ribavirin due to decrease plasma concentration of the medication, which can result in loss of efficacy.

We'll move forward to the dosing and availability here. As you can see this will include dosing, duration of therapy and availability as well. For dosing, the dosing is… depending on the medication it is stratified by genotype, age and/or weight-based. As we move forward you'll see. For Pegasys and PEG-Intron you'll see that the dosage is broken down by genotype, HIV coinfection and [inaudible] along with their respective duration of therapy on the right hand side. I'll give you a minute to see this and then we'll go to the next.

On the next slide here we're just continuing. We have Daklinza and we have Sovaldi. Again, these are… the dosage is stratified specifically by the genotype with the duration, with the respective genotype and the availability. All of these medications are available as tablets.

The next slide here we'll have the oral combination where we have ribavirin and Mavyret. Just to give a little bit of special or… special population information, as well. Ribavirin is category X, pregnancy category X. Its exposure can cause birth defects and/or death of the exposed fetus. It's contraindicated in pregnant women or by men whose female partners are pregnant and the IDSA guidelines for the treatment of hep C state that females who have used ribavirin and sexual partners of ribavirin-treated males should not become pregnant for at least six months after discontinuation of ribavirin. For PEG-Intron alpha it is pregnancy category C. Harvoni, Sovaldi, Viekira Pak, Technivie are all pregnancy category B. Daklinza, Zepatier, Epclusa, Vosevi, Mavyret and Viekira XR were not assigned a pregnancy category and not adequate human data was available to establish whether or not they pose a risk. When it comes to dual or triple therapy the pregnancy category of the most restrictive individual drug should be used in the combination when you're considering it for your patients.

So on slide 13 here you'll see we also have Harvoni and Viekira Pak. Here you can see Harvoni's dosing is very intricate where it is stratified between genotypes 1 through 6 along with the patient's Child Pugh score, as well. A unique specialty population to keep an eye out for is also… there has been… in this class there has been notations for ethnicity. Several trials have demonstrated African Americans and Latinos are less likely than non-Hispanic whites to respond to dual therapy with interferons and ribavirins. The reasons for these differences are not known, but they just saw that there was a difference. Higher concentrations of [inaudible] and [inaudible] plasma concentrations were observed in Asians compared to Caucasians. The hypothesis is Asians experienced a higher rate of ALT elevation in the clinical trials, but no dose adjustment of these two medications is recommended based on race and ethnicity, just something to note.

On the next slide here we have Viekira XR, Technivie and Sovaldi. Again, the dosing is stratified by genotype and/or HIV coinfection.

On the next slide here we have Epclusa and Vosevi. Now as you kind of take a look at this, in terms of patients who have renal impairment there are some dose adjustments that are recommended. For PEG-Intron dosage should be reduced by 25% for patients who have moderate renal impairment, which is classified as a creatinine clearance of 30 to 50. Pegasys dose should be reduced in patients with a creatinine clearance of less than 30 and those who have end stage renal disease and hemodialysis. Excuse me, ribavirin has a dose adjustment recommended of creatinine clearance less than 30 or if the patient is on hemodialysis. And then are no dose adjustments recommended by Technivie, Daklinza, Zepatier, Mavyret, Viekira Pak, Viekira XR for patients with mild, moderate or severe renal impairment.

On the next slide here we'll go into… we have ribavirin generic for Copegus, ribavirin Rebetol, ribavirin RibaPak. We have Ribasphere and we have Moderiba. And for the dosage when it says "as listed below" for the combination therapy slides it's referring to the combinations that we referred to. I know there is a lot of dosing information there and on the next slide we'll essentially go over the guidelines.

How exactly on slide 18 the hepatitis C guidelines by the AASLD and IDSA have it stratified in their guidelines from 2017… have it stratified by the specific genotype that patients have. Now again, I'm not going to go into the specifics of each single one, but this is how it is stratified. So for genotype 1a recommended treatments. Then it is stratified by other treatment-naïve or treatment-experienced and treatment-experienced is defined as previous failure of PEG-Interferon or ribavirin. And then it's further stratified by whether or not the patient has cirrhosis or does not have cirrhosis. Based on those three parameters you'll find the duration of the treatment and the duration in terms of weeks and you'll finally find the rating on the side, Class 1, Level A is the strongest.

On the next slide here you'll see 1a alternative treatments and again it's stratified by treatment-naïve or treatment experience. And then further broken down by cirrhosis or no cirrhosis. It goes on further for… same fashion for genotype 1b.

On then slide you'll see, again, treatment-naïve, treatment-experienced and then 1b alternative treatments, as well. I'll just give you guys a minute to look at this and then we'll just keep going.

On slide 20 here we have genotype 1 regardless of subtype unless noted. So if you are… if you know it is genotype 1, but unsure of the subtype then you can obviously… this section would be for your patient. We have alternative treatments, as well.

On the next slide here we have genotype 1, excuse me, genotype 2 recommended treatments as well. This is broken down by treatment-naïve, treatment-experienced, so previous failure of PEG-Interferon or ribavirin and treatment-experienced previous failure of sofosbuvir and ribavirin as well.

On the next slide you'll see genotype 2 alternatives and genotype 3 recommended treatments, as well. For genotype 3 recommended treatments it is broken down by treatment-naïve, treatment-experienced previous failure of PEG-Interferon and ribavirin and treatment-experienced previous failure of NS5A inhibitors.

The next three slides… so the next slide will be genotype 3 alternative and genotype 4 recommended.

And then genotype 4 recommended treatments continued and genotype 4 alternative treatments. And again treatment experiences defined as PEG-Interferon and ribavirin in these two genotypes.

The last slide will break down genotype 5 and 6. I know this was very chart heavy and numerically heavy, but I open the floor for any questions for this.

Lisa Chew: Any questions for Umang? Donna and Leta, should we do the motion and stakeholders and then motion before moving onto your portion?

Donna Sullivan: Yes, please.

Lisa Chew: We have two stakeholders for this section. We have Dr. Margaret Olmon and Stuart O'Brochta. If you could come up to the podium, please, introduce yourself and state who you represent and you will have three minutes.

Margaret Olmon: Good afternoon. I'm Dr. Margaret Olmon with medical affairs at Abbvie. I'd like to thank the committee for having Mavyret available as a pangenotypic treatment option for HCV patients without cirrhosis or with compensated cirrhosis and respectfully ask that Mavyret can continue to be available for the Medicaid patients in Washington. Mavyret is the only once-daily pangenotypic ribavirin-free regimen FDA approved to treat patients with chronic hepatitis C virus across all genotypes 1 through 6. This includes those who do and do not have cirrhosis, have treatment experience, have HIV or have chronic kidney disease. Mavyret can also be administered to patients after a kidney or liver transplant regardless of baseline renal disease. Up to 95% of patients with HCV can be treated with Mavyret and the vast majority of patients awaiting treatment in Washington are eligible for an eight-week treatment course of therapy.

Relative to safety, Mavyret carries a boxed warning regarding the risk of hepatitis C reactivation in patients coinfected with HCV and HBV as do all

direct acting antivirals. Mavyret has two contraindications, one for patients with severe hepatic impairment, Child Pugh C, and the other for patients taking concomitant Entecavir or Rifampin. The most common adverse reaction in clinical trials in greater than 10% of patients were headache and fatigue and the AEs were comparable among patients who had compensated cirrhosis and without cirrhosis. Mavyret is well tolerated. It requires no liver monitoring or baseline resistance testing and no dosing or duration adjustments are needed for patients with HIV coinfection or for any level of renal impairment, including dialysis. This has only been a short summary. For complete safety and prescribing information, please refer online to www.rxabbvie.com. As you decide the next steps for treatment of patients with HCV in Washington I respectfully request that you keep Mavyret available as a preferred medication. Thank you so much and I'm happy to answer any questions you might have. Thank you.

Lisa Chew: Thank you.

Stuart O'Brochta: Hello and thank you, again, for allowing me to speak. My name is Stuart O'Brochta with Gilead Scientists and I'm a medical scientist there. I too want to thank you, the Washington P&T, for continuing to allow providers to choose the correct direct-acting agent for treatment hepatitis C and making Epclusa available to providers to make that best decision. I'd like to highlight a few key points about Epclusa today. I provided Donna with a handout of all the key clinical information, safety, and clinical data. So I won't refer directly to all the numbers there. But I would like to highlight the key attributes of Epclusa that differentiates it in the hepatitis C treatment [inaudible] from others currently available, which allows it to be used in the highest percentage of HIV-infected patients. Epclusa is the only one pill once-a-day protease-free, which is a very important distinction as pointed out by Umang. Pangenotypic and [inaudible] meaning all genotypes of course, simplified 12-week regimen for all HIV patients with the one exception of severe renal disease, which I would like to note is less than 2% of the population. So it's a very small number of patients. We intend to file data that has been presented recently and previously in the past though to get that label updated, because there is significant data to show safety of sofosbuvir, but currently, just to be clear, is not part of our label.

Epclusa has the highest rate of SVR in the real world evidence. Clinical data [inaudible] in clinical trials to get drugs approved, but how do they perform in the real world? This is when you compare it to any of the other available regimens. This is the most pronounced in genotype 3, which is becoming more a problem in patients who inject drugs, which we know is a significant driver of HCV infection, advanced fibrosis and decompensated cirrhosis where you cannot use a PI regimen. Many experienced treaters would prefer to use Epclusa in an advanced patient even though other agents are approved in that area. The data demonstrates that while the current treatment population of advanced patients has been treated, there are many undiagnosed as Umang pointed out, and those patients are being diagnosed as late stage advanced fibrosis. So having an agent to treat those patients is very important. Also the real world data demonstrates that what I just said that providers would prefer to use an Epclusa-based regimen because the higher percentage of real-world data leans towards advanced patients with Epclusa and those patients still have the highest rates of SVR when compared to other agents.

Lastly, as far as difficult populations, I've mentioned the people that inject drugs or [inaudible], those patients tend to have lower adherence and it's been shown that Epclusa still remains high SVR rates in those patients that have had significant drops in their adherence. Another important distinction in a population that may be challenged with life issues. Epclusa is also unique as pointed having the NS5B inhibitor sofosbuvir which is the only currently pangenotypic regimen with that aspect. This also causes it to have the significant high barrier to resistance as far not needing pre-treatment on testing for resistance and extremely low resistance rates shown when failure. But having Vosevi available on your formulary… sofosbuvir… Vosevi is shown to salvage sofosbuvir [inaudible], which are very limited with very large numbers of data to support that if retreatment is necessary in those small numbers of patients.

So finally I'd like to mention something about the… there's no difference in SVR rates with patients that use PPIs. I know that's been an issue for the Washington Health Authority. Even though our label with Epclusa

does not indicate you cannot use it with a PPI there's been some concern based on some of the kinetic data. The most recent data presented at ASLD around that issue has shown no difference as patients using standard doses of PPIs with Epclusa. So that would not limit your population either.

Lisa Chew: Please wrap up your comments.

Stuart O'Brochta: I will do that right now. Thank you. So I would respectfully ask the Washington Medicaid to continue to allow providers choice for the best agent in their HIV treatment, but if you choose to limit to less than the currently available agents, Epclusa should be part of this option based on the depth of scientific data available and provider preference. Thank you and I would answer any questions.

Lisa Chew: Any questions? Thank you.

Stuart O'Brochta: Thank you very much.

Lisa Chew: Donna, do you want to walk us through the motion?

Donna Sullivan: Sure. So I'm actually going to kind of back us up a few steps. I don't have the ability to show our policy, but there is a little bit more to our policy than what ended up in your slides. So I just wanted to…

Woman: [inaudible]

Donna Sullivan: Yeah, I guess I could do that. Okay. So what I have here is the policy that we have posted on our Apple Health website. So we do require prior authorization for the hepatitis C drugs. Really what we're looking for is for the patient to show that they actually have chronic hepatitis C. As Umang said, you know, there is a small amount of patients that spontaneously clear the disease. So we defined chronic as being anybody who has F1 liver fibrosis score or Metavir score we assume that they are already chronic. So for patients that are less than F1 we just require six months between like a diagnostic screening and a viral load or six months between two viral loads showing that they still have detectible viral load and then we assume that that patient is chronic. We do limit the

prescriber to a specialist. However, certain primary care providers, if they do some CE, there's University of Washington has CE, we will approve those primary care providers to prescribe the medications. So we are loosening that requirement. We're also participating… if a provider is participating in Project ECHO then we don't require them to be a specialist. And so C is really that… speaking to if the provider has gone through some CE training and provides that to HCA we will put them on our list of approved prescribers.

So we do require documentation of lab tests. That really just shows what the genotype. We ask for their liver fibrosis scoring and we also look at their renal… what their renal function is. Mostly what we're doing is making sure that the prescribers are prescribing the right drug for the proper duration and one of the preferred drugs. So we're really not… this is really just the criteria that we're looking at. There's really nothing else that would exclude a patient from getting treatment. So we no longer require them to be abstinent from alcohol or IV drug use. We haven't required that in several years. I just wanted to point that out. Patients that really are too sick to be treated we do exclude. So if they are, you know, obviously if they are taking a medication that it is contraindicated they have to stop that medication in order to be treated. If they are planning to become pregnant or are pregnant these drugs are not shown to be… there's no evidence of use I think in pregnancy that we've reviewed if they have… sometimes there are organ diseases too… is too severe. They need the transplant before they should be treated. So that's up to the doctor. And we look at, you know, their MELD scores and that all has to do with their readiness for transplant. So I'm not going to go into that in great detail. We do have Mavyret, Epclusa and Vosevi as our preferred products. So they are equally preferred on our PDL, except for Vosevi we do actually limit it to what we call salvage therapy. So people that have tried and failed, you know, Harvoni or Sovaldi or even Epclusa and we have had those patients. We've had numerous treatment failures. For whatever reason we're not sure, but we do see quite a bit of retreatment requests. And so Vosevi is really saved for that salvage therapy. That's pretty much the… our policy.

Going back to the motion then, so we consider, you know, that the antivirals are safe for their FDA labeled indications and I just want to

clarify the second bullet where it says, you know, all non-preferred products require a trial of two preferred products with the same indication. It's not so much that we require them to try to fail those drugs. It's that we usually won't approve them unless they have a clinical reason why they can't take one of the preferred drugs. So you can call it a trial, but a… a trial and failure, but it's really that we're pushing patients to the less costly alternatives that are just as equally efficacious. If there is a non-preferred drug for any clinically appropriate reason, if there's a contraindication to a drug that's preferred, that the non-preferred drugs don't have that contraindication, then they would be approved for that reason. So our recommendation is to continue the current limits as we just reviewed them.

Lisa Chew: Any questions for Donna?

Amber Figueroa: I move that the Apple Health Medicaid Program implement the limitations for the hepatitis C antiviral drug class listed on slide 26 as recommended.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Then the motion carries. Donna, did you need to talk to the…

Donna Sullivan: So I wanted to talk to you a little about what we're doing around hepatitis C coming up in the next year. So the reason why we brought the class back to review so soon is that the governor released a directive to Department of Health and the Health Care Authority for the two agencies to work together to create an elimination strategy around hepatitis C. So I wanted to just present what… some of the work that we've been doing and what the plan is going forward.

So Umang gave us a brief overview of the clinical course of the disease so I'm not going to get into that, but we estimate about 65,000

Washingtonians actually have hepatitis C right now and not all of them know that they have the disease, which is leading to some of the spread of the disease. We've had a steady increase in the reported cases of hepatitis C with 40,000 new cases being reported between 2012 and 2017. In addition, we have spent, in the state of Washington, more than $114,000,000 just for hospitalization charges related to treating patients that have the disease. It's the most common blood-born infection in the United States. It kills more people every year than any of the other reportable infectious diseases and then hospital costs, again, are reported there. You can see in the graph on the right that the number of chronic cases per year really started increasing in 2012 and have more than doubled since then. What we've seen with the hepatitis C epidemic is that there is kind of two cohorts. The first cohort is the baby boomers. So it is people that were born between 1945 and 1965. Most of those people were, you know, some of their infection was due to injecting drugs, but some of it was due to transplants or blood infusions if they received those prior to the 1970s and early 80s when those products were being screened for hepatitis C. The second wave that we're seeing is where the increase in the prevalence is coming from and it's the younger population. Most of them are age 37 or younger and we believe that, and I think it is contributing from IV drug use, the increase in the opioid epidemic and the increase in using injectable drugs.

So the State of Washington it is pretty much spread across the entire state. We see a denser prevalence in the more rural counties. There are probably more people along the I-5 corridor that have hepatitis C, but when you look at the density of the population it is really out there in the rural county. So it is a state-wide problem and we also know that incarcerated patients are more likely to have the hepatitis C than non-incarcerated patients.

Specially in Washington among the state agencies that cover… or pay for hepatitis C treatment for patients, we're taking Department of Corrections, Department of Social and Health Services, so our state hospitals, Labor and Industries, and the Health Care Authority, the Medicaid Program, as well as Public Employees and soon to be School Employees Program we estimate about 35,000 individuals within our agencies have hepatitis C with the prisons being about 2,000. Medicaid…

these number hasn't been updated. It's actually closer to 30,000 and then our public employees around 3,000 and Labor and Industries and DSHS together about another 100 patients. So over the years we have spent quite a bit of money on hepatitis C. This is specifically the Medicaid annual expenditure and I just want to explain how to read this slide. The dark blue band at the bottom of each column is the amount of state dollars that is spent on hepatitis C. The light green is the federal matching funds that we get from CMS and then the dark green is the amount of rebate or discount that comes back from the manufacturers in federal rebate. So the height of the column is like the total cost, but the blue is what the state actually spends. And you might think of, well, the state… that seems like a very small amount, the reason being a lot of our patients are in the expansion population so Washington was lucky to be one of those expansion population states with Medicaid. So we are getting 100% federal match on the medications from the federal government through, I believe it was 2017, and now we're getting 95% and it will go down to 90%. So we do pay… it is a heavy burden to the state, but we're paying a smaller portion than you might expect.

The agencies in total is this next slide. So looking at over the fiscal years the different agencies. Medicaid obviously has paid the most as far as the total cost of the care followed by Uniform Medical Plan and the Department of Corrections with L&I and DSHS making up the smallest portion. You'll notice that the cost is coming down. Mostly this is two-pronged—one, we see fewer patients coming into care. We think we might have treated most of the people that we have identified already with hepatitis C and in addition to that in 2017 we really started to see the introduction of the pangenotypic drugs and then really much more competition in price in the marketplace. So expenditures have come down. This is just a graph of those patients that have been treated per year. Total we treat almost 4,000 patients per year in 2017 and it is, like I said, it is falling in 2018. And then you can see this is like the average cost of care for the different agencies. Over the years there is a trend down to where the commercial usually pays more than the Medicaid population, which is the dark blue line on the bottom, but you can see the non-Medicaid programs are now paying roughly the same amount for treatment, which is still significantly more than what the Medicaid program is paying. So Governor Inslee's directive was a plan to eliminate

hepatitis C in the State of Washington. It's really a two-step approach. So it's the elimination of hepatitis C from the Department of Health who will be focusing on identifying and screening patients for hepatitis C and giving them links to care, and then for the Health Care Authority to really do more innovative purchasing and seeing if we can get even better prices for the medications so that we can afford to treat everyone across the state. We will be the first state in the nation to actually have a two-pronged approach. Both the coordinated public health strategy in addition to a purchasing strategy. So our goal for the State of Washington we want to develop and implement an elimination plan focusing on the public health outreach and purchasing. Again, we had 30,000 patients with the… the goal is to really significantly reduce the number of Washington residents that are infected with hepatitis C over the course of the next four years.

So I want to talk a little bit about what does elimination mean. Elimination does not mean eradication. There's a lot of talk with the CVC and eradication would mean that the hepatitis C virus no longer is found in the State of Washington and that's not what we're talking about. What we're talking about is removing the public health threat of hepatitis C so patients… no infections are rare and that when they do occur they are quickly identified and those patients are quickly brought into care and that the incidence and the spread of the disease is really nominal. So the WHO, World Health Organization, has set a goal for hepatitis C elimination worldwide by 2030 and that's looking at 90% of those that have hepatitis C are diagnosed, 80% of those that have it get treated by 2030, that we have a 90% reduction in incidence, and a 65% reduction in mortality.

So our plan… we realized that this requires, again, that really strong intensive public health strategy. The department of health has put together a coordinating committee that is meeting monthly. Those meetings are… they're not "open public meetings" required by law, but they are meetings that are open to the public. So anybody is able to call into those meetings or come to the meetings when they are held in person. The Department of Health has the link on their website. I apologize, I don't have it with me, but if you want to find out about meeting information you can go to the Department of Health's website

and find that. So it is a multi-year public health outreach approach. We understand we have to find those patients that have not been diagnosed with hepatitis C, get them screened, and if they come up having a positive antibody test, getting the confirmatory RNA test and then linking them up with a prescriber that can actually help them get their medications.

For the Health Care Authority the innovative drug procurement we're going to be leveraging more market competition. We'll be releasing a request for proposals and bona fides in January of 2019 and then eventually… initially we'll be focusing on state agencies that I mentioned, but really the plan is once we get that program set up is to roll out this program statewide. So it would be purchasing on behalf of all payers in the State of Washington. We're thinking something like how the Vaccine for Kids Program works. That's still to be… we still need to figure out how that's going to work and whether or not we currently have the proper authority in place, but that will come in years later.

Specially, the Health Care Authority will issue a request for proposals. We're looking for an alternative payment model. For Medicaid we're focusing on what is being, you know, touted as a subscription model and you might ask, what does that mean? And what that really means is that we will take the money that we have been paying for hepatitis C and we'll continue to pay the same… roughly the same amount or proportionately the same amount, but we'll be able to treat as many people as we can. So instead of having to pay, you know, $50,000, I'm making this number up, per course of treatment and then that just… there's no limit to that. We might agree to paying a certain amount of money. Let's say, you know, make it a ridiculous number, $300,000,000 or something like that, and then after we spend that amount of money we could treat as many people as we can and we wouldn't pay anymore for that. We're also… for the non-Medicaid population they are also included in the procurement and we'll be asking… they won't be subject to the subscription model, but we will be asking for more significant discounts. We're also including things that are called bona fides to support the public health outreach and a bona fide is a service that CMS allows manufacturers to pay for on behalf of an entity and it is services that they might have otherwise paid for. So it's… we're looking at medical case

managers to put in places such as the opioid treatment centers using the HUB and Spoke model, getting nurses out there to screen patients as they are coming in for their opioid treatment, going to rural clinics, community clinics and really just trying to increase that screening and then also providing case management to help those patients that do have hepatitis C connect with a provider that can work with them. We're also looking for pharmacists, pharmacists under collaborative practice agreements with other prescribers. We are currently working across the state in rural clinics, the Yakima Valley Farm Worker's Clinic is one of them, where the pharmacists are really doing all of the screening and the treatment of the patients that are coming in with hepatitis C. So we're looking on expanding that model specifically in the rural areas where there might be a shortage of providers. And then nurses also were thinking of, again, working on the HUB and Spoke model for opioid use disorder, of getting nurses there that could also dispense maybe hepatitis C medications every day as they come in for their buprenorphine or their methadone or whichever medication they might be coming in for.

So again we're focusing on… initially on the state purchased health care programs—so the agencies that are listed there. And then the goal is to try to expand that expand statewide.

The process will be in early January we'll be issuing a request for proposals. After the request for proposals we'll be collecting questions from potential bidders. We'll be holding a bidders conference and then we post the answers to those questions online so that everybody has access to the same information. We expect the proposals to be due sometime late February maybe early March. There will be an evaluation period that might include oral interviews with the bidders. We'll do some negotiating for best and final so that we can make sure that we get the best deal and then we'll announce the apparent successful bidder we're thinking probably May or June, which gives time to get the contracts signed and completed and then hopefully they will beginning work in early July of next year.

These are just some of our state partners working with the Department of Health. Our Public Employees and Schools Employees Program, Apple Health, Labor and Industries, Corrections, the Department of Social and

Health Services. Our non-state partners so Magellan Rx is helping us with some of the contract they provided a lot of input to the value-based purchasing agreement that we will be using for Medicaid. We're getting technical assistance from the Center for Evidence-Based Policy, Oregon's Health and Sciences University. We're a participant in their SMART D Project and that's the State Medicaid Alternative Reimbursement and Purchasing Test for high cross drugs and then Moda Health, our administrator for the Uniform Medical Plans, Pharmacy Benefit is also assisting in the preparation of the request for proposals. Questions from the committee? We are in the process of starting an active procurement. So if there are any questions for anybody in the audience or stakeholders we're asking that you submit that to our contracts department with the email address here and in the subject line put the HCV Elimination in the subject line. It will get forwarded to the appropriate contracts manager, not the Health Care Authority, and we will answer as many questions as we can, but because we're in this… beginning this procurement phase there's not a lot of information that we're able to share and once we release the RFP then we can get those… we can start collecting those questions and making sure that we do provide the proper answers. Thank you.

Lisa Chew: Thank you, Donna. Any questions for Donna? So let's move on to the multiple sclerosis agents.

Umang Patel: Perfect. Thank you. So the next slide here we'll see multiple sclerosis is a complex human autoimmune type inflammatory disease of the central nervous system. More than 2.3 million people worldwide have MS. Multiple sclerosis occurs most commonly in whites, with rare cases in African-American and Asian-Americans. Although the etiology is predominantly unknown, it is characterized pathologically by demyelination and subsequent axonal degeneration. The nerve degeneration associated with MS can result in a wide variety of symptoms including sensory disturbances so numbness, paresthesias, burning and pain in the libs, optic nerve dysfunction, ataxia, fatigue, and bladder, bowel and sexual dysfunction. Severe cases may result in partial or complete paralysis. And while cognitive impairment occurs in approximately 50% of people with MS, only 10% experience serious intellectual deterioration. MS can be categorized as either relapsing-

remitting observed in 85% to 90% of patients or primary progressive observed in 10%. Relapses or attacks typically present sub acutely, with symptoms developing over hours to several days, persisting for several days or weeks, and then gradually dissipating.

On the next slide here you'll see an overview of the disease state. So the clinical course of MS falls into one of the following categories with the potential to progress from less severe to more serious types: So the first you'll see is relapsing-remitting or RRMS. Clearly defined, self-limited attacks of neurological dysfunction, followed by periods of remission without disease progression. Most patients experience a recovery of function that is often, but not always, complete. Then you have primary progressive MS or PPMS which is nearly continuous worsening of disease not interrupted by distinct relapses and some of these individuals have occasional plateaus and temporary minor improvements. You have secondary progressive MS which is SPMS. Relapsing-remitting disease course at onset, followed by progression with or without occasional relapses, minor remissions, and plateaus; and most patients eventually convert to progressive MS from this stage. The fourth being progressive-relapsing MS PRMS, which is progressive disease from onset, with clear, acute relapses that may or may not resolve with fully recovery; and unlike RRMS, the periods between the relapses are characterized by continuing disease progression. And lastly you have clinically isolated syndromes and these are the first episode of neurologic symptoms due to inflammation or demyelination lasting at least 24 hours. Patients with MRI-detected brain lesions consistent with MS are at high risk of developing MS.

On the next slide here you'll see the medications and their respective indications. You have Lemtrada, Ampyra, Tecfidera, Gilenya, Copaxone, Avonex, Rebif, Plegridy, Betaseron, Extavia, Tysabri, Ocrevus and Aubagio. Now as you can see all are brand, aside from Ampyra and Copaxone which are available in generic forms. In addition, all are indicated for relapsing forms of MS. Now tacking onto the Ampyra is also indicated for improving walking in patients with MS demonstrated by walking speed. And just for completeness sake Tysabri also has an additional indication for Crone's Disease that we're not discussing in this. Now to take a step back clinically in terms of mechanism of action these

are all immunomodulators and their mechanism of action impacts the immunological pathophysiology of MS. Interferon beta binds to the self-surface specific receptors initiating a whole pathway that ends with the secretion of antiviral, antiproliferative immunomodulator gene products. While interferon beta has no direct effect in the CNS it rapidly, about in two weeks, blocks blood brain barrier leakage and resolves gadolinium enhanced MRI activity.

On the next slide here you'll see the dosing and availability. This is broken down over the next few slides. Here you have the medication, the dosage, specific comments such as instructions or things to note for those medications, and availabilities. So please note that the availability is variable. You'll see Lemtrada is available as a single-use vile. You'll see that Ampyra is available as tablets. Gilenya and Tecfidera are capsules and Copaxone is available as a single-dose pre-filled syringe.

In terms of special populations for pediatrics Gilenya is approved in patients greater than or equal to 10 years of age. No other drug in this class review is indicated for pediatric use. And in terms of pregnancy Copaxone is pregnancy category B. Lemtrada, Ampyra, Avonex, Plegridy, Rebif, Extavia are pregnancy category C and there are limited observationals of data with betaseron in pregnant women who have not generally indicated a drug-associated risk.

On the next slide we'll continue the dosing and availability. We have Avonex, Avonex prefilled syringe, Avonex pen, Rebif, Rebif Rebidose and Plegridy. All of these are available as pre-filled syringes and Avonex is available as a powder that comes with a diluent. Again, in terms of special populations for hepatic and renal impairment, for hepatic impairment blood levels of Gilenya, but not it's active metabolite are doubled in patients with severe hepatic impairment, but no dosing adjustment is advised at this point. And there's no significant pharmacokinetic difference found in patients with mild hepatic impairment versus normal for patients taking Ocrevus. For renal Lemtrada… patients with severe renal impairment should be monitored for adverse reactions due to increased drug exposure less filtration. Ampyra is in patients with severe to… moderate to severe renal impairment. So creatinine clearance less than 50. Ampyra is

contraindicated. And Ocrevus there's no significant PK difference found in patients with mild renal impairment.

For the next and last slide for the dosing and availability we have the continued… we have Betaseron, Extavia, Tysabri, Ocrevus and Aubagio. Ocrevus and Tysabri are available as single-use vials. Extavia and Betaseron are available as powder for injection and lastly Aubagio is available as tablets. Now in terms of contraindications and warnings this class similarly, but not as extensively as hep C does have a good amount of contraindications so I will go over some of the main ones here. In terms of Lemtrada it is contraindicated in patients who are infected with HIV because it can cause prolonged reduction in CD4 plus lymphocytes. It may increase the risk of malignancies including thyroid cancer, melanoma and lymphoproliferative disorders like lymphoma. Ampyra may cause anaphylaxis and severe allergic reactions including respiratory compromise, urticaria and angioedema. It is recommended if that does occur then seek medical attention and discontinue the medication. For Tecfidera it may cause flushing; things such as redness, itching and burning sensation and this is usually a mild severity. For Gilenya it is contraindicated in patients who have a history or a presence of Mobitz type 2 second degree or third degree AV block or [inaudible] syndrome. For Copaxone warnings are associated including post injection site reactions… a reaction which can be immediate consists of various symptoms including flushing, chest pain, palpitations, and it may occur within seconds to minutes following the injection. Most of the symptoms are observed within the hour. After the hour it's less likely. Tysabri is contraindicated in patients with PML and in patients with a prior hypersensitivity reaction. And Ocrevus is contraindicated in patients with a history of life-threatening infusion reactions. The last one, thank you for bearing with me, Aubagio is contraindicated in patients with severe hepatic impairment and it is also contraindicated in patients with current leflunomide therapy. Now there is a REMS Program with this class. Agents within this class that do have a REMS Program are Lemtrada and Tysabri due to the autoimmunity infusion reactions and malignancy that I mentioned. It has the REMS Program for prescribers, patients, pharmacies and healthcare facility programs. Due to the risk of the serious adverse effects, including the increased risk of PML, the REMS for

the Tysabri is for all four and patient enrollment following a full evaluation of the risk and benefits and required.

Now we'll jump over to the guidelines. According to the American Academy of Neurology in 2018, these new updated guidelines discussed patient counseling including patient readiness, medication adherence and treatment related adverse effects, therapy initiation and treatment selection, switching, and discontinuation. Notably, they clarify that prescribers should counsel patients with MS that treatments are intended to reduce relapses and new MRI lesion activity; they are not intended for symptom improvement. For treatment options clinicians should offer DMT to people with a relapsing form of MS with recent clinical relapses or MRI activity. After discussing the risks and benefits, clinicians should prescribe DMT to patients with a single clinical demyelinating event and two or more brain lesions characteristics of MS in those who decide they want this therapy. Clinicians should prescribe alemtuzumab, fingolimod, or natalizumab for people with highly active MS. Clinicians may recommend azathioprine or cladribine for people with relapsing form of MS who do not have access to approved DMTs, but they should not prescribe mitoxantrone to people with MS unless the potential therapeutic benefit greatly outweighs the risk. Similarly, natalizumab treatment should only be initiated in patients with MS with positive anti-JCV antibody indexes and for PPMS clinicians should offer ocrelizumab to those who are likely to benefit unless the risks outweigh the benefit.

Continuing the AAN guidelines regarding treatment switching, clinicians should evaluate disease activity, adherence, adverse effects and pharmacology when switching DMTs in patients with breakthrough disease. A change to non-injectable or less frequently injected treatments or a change due to adverse effects impacting adherence may be considered based on patient feedback. So a switch or a dosage adjustment may be warranted due to lab abnormalities, pregnancy, PML risk, malignancy, serious infections, and in those with select antibodies. Clinicians should then advocate that stable MS patients, defined as no relapses, no disability progression, stable imaging, continue their current treatment unless a trial off therapy is warranted by both the prescriber and the patient; however, discontinuation may be advised in patients

with SPMS who do not have ongoing relapses and have not been ambulatory for greater than or equal to two years.

And on the last slide here the International Pediatric MS Study Group and the American Academy of Neurology in 2016 with a combo guideline recommend that clinicians treat children with MS in order to prevent relapses, prevent new lesions, and delay disability, which is of particular concern in pediatricians since they have a higher relapse rate, more significant inflammation on MRI. DMT use in pediatric MS remains off label in the majority of countries. They state that interferon, beta and glatiramer should be considered standard of care in this population and that treatment should be started early. Although the clinician should counsel families regarding the expectations, a treatment switch may be warranted if there is inadequate or suboptimal response. Clinical trials may be available and useful for those who require escalating or emerging treatments and note that these were published prior to the FDA approval of fingolimod for relapsing forms of MS in pediatric patients that I mentioned earlier of patients greater than or equal to 10 years of age. Any questions?

Lisa Chew: Any questions for Umang? So we have two stakeholders, Dr. Shirley Quach and Dr. Rosalynde Finch. Could you please come up to the podium, introduce yourself and who you represent? You will have three minutes.

Shirley Quach: Good afternoon members of the P&T Committee. My name is Shirley Quach and I'm the managed care liaison at Genentech. Although Ocrevus was briefly mentioned, my understanding is that a more detailed review of Ocrevus will be presented at a future P&T meeting and I just wanted to share some information with you.

Ocrevus is FDA approved for patients with relapsing forms of MS based on our clinical trials OFFER 1 and 2 where Ocrevus demonstrated superiority over interferon beta 1A, which is currently a preferred agent. Ocrevus is also the first and only FDA approved agents for patients with primary progressive forms of MS. Within the MS review that was just shared with you it summarizes the AAN guidelines and I just wanted to provide some context to you. Although the AAN guidelines were updated

in 2018, the data cutoff for data review was actually November 2016 so in the guidelines Ocrevus was not recommended for patients with highly… or was not listed as an agent for patients with highly active disease. However, our subgroup analyses was published after that cutoff date and does demonstrate efficacy in patients with highly active disease. I also want to caveat that the AAN guidelines do not provide a definition for highly active disease and that this definition is variable among clinicians, payers and also even within the pivotal trials for the other MS agents. And the third thing that I want to call out is ICER. ICER did a 2017 review of the MS disease modifying therapies and ICER is an Institute for Clinical and Efficacy Review and is a non-biased, independent research organization that seeks to improve health care by providing comprehensive clinical and cost-effectiveness analyses of treatments, tests and procedures. Within their review ICER ranked Ocrevus among one of the most effective in reducing relapses and also delaying disability. Not only that, the Ocrevus also had the lowest adverse event rate among all the disease modifying therapies that were evaluated.

Again, I just wanted to thank the members of the committee for your time and your thoughtful review of the MS class and if you have any questions, please feel free to reach out. Thank you.

Lisa Chew: Question? Thank you.

Rosalynde Finch: Hi. My name is Lynda Finch. I'm a medical value liaison for Biogen, the manufacturer of Avonex, Plegridy, Tecfidera and Tysabri, but I'm going to focus my comments on Tysabri today. So the AAN guidelines that were presented and briefed today highlight the importance of access to highly effective therapies for patients with highly active disease. What Washington Medicaid currently has in place for Tysabri is a requirement for the failure of two other disease-modifying therapies before a patient can receive Tysabri. The CMS guidelines, which were updated last year also state that because of the severity of disease can vary at onset with some individuals experiencing very early aggressive disease, that patients and their treating physician should have access to all available options. And then further, the CMS guidelines site evidence to support Tysabri as an option for initial therapy for people with early aggressive disease and that is disease that is characterized by frequent relapses with incomplete

recovery and accumulation of MRI lesions. In our clinical trials with Tysabri the highly active disease subgroup had a significantly reduced annualized relapse rate of 81% and significantly reduced risk of sustained disability progression of 53% compared with placebo. So it may be more effective than in the overall population. Our long-term real world studies have supported that when patients initiate Tysabri earlier in the disease course when they have less disability that they are going to have long-term outcomes. So that supports the therapy earlier in the disease course.

The other thing that I wanted to touch on today was a mention that Tysabri should be initiated only in people with MS who have anti JCV antibody index above .9 when there is reasonable chance of benefit compared with the risk of PML. The anti JCV index values have been developed actually by Biogen and they've been shown to be a useful risk stratification tool to provide further differentiation of PML risk, but this is in conjunction with the use of duration of therapy and this is only in patients who have no prior use of immunosuppressants. So when you evaluate together with duration of therapy it gives you a better overall picture of the PML risk. When you look at patients who have a JCV index of .9 to 1.5, even after six years of therapy, their risk is no different than the overall group, which is 3 in 1,000. I would suggest that the patient and the physician together have a better understanding of the risk benefit and that decision should be left up to them if they have the full consideration of the history of that patient's disease and the severity of their disease.

So to conclude I would like to ask that Tysabri be allowed for initial use… so first line use in patients with highly active disease. That there be a pathway for those patients and that the risk benefit assessment be left as a decision made by the physician and patient. Thank you very much and I'll take any questions.

Lisa Chew: Thank you very much. Donna, would you walk us through the motion?

Donna Sullivan: Sure. So our recommendation is that all the multiple sclerosis agents are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products

require a trial of two preferred products with the same indication and different active ingredients before a non-preferred drug will be authorized unless the preferred drugs are contraindicated, not clinically appropriate or there is only one preferred product.

Amber Figueroa: When did we last discuss this? I remember we had a physician speak and I thought that we had made the decision that, a physician that had MS, or am I totally dreaming that up?

Donna Sullivan: I don't recall. I don't think it's been that long since we reviewed these classes yet. We're trying to get on a cycle with Magellan's… when Magellan updates their clinical reviews to get on a cycle. So you'll see… things might come back in the next couple of meetings that we've reviewed recently, but it's because we are trying to get onto a cycle. In the future I'm hoping to have like every December we'll review X, Y, Z drug classes and then in February we'll do these ones and it will be the same each month that… we have a meeting it will be the same drug classes, but I do not recall. I don't…

Amber Figueroa: Can you clarify the current policy because I really feel like at that meeting that was one of the big points that we discussed was that we wanted physicians to have access to what they felt would be best for the patient and not…

Donna Sullivan: And I believe, Ryan, you can correct me if I'm wrong, I think we took all of these off of prior authorization. So there is no policy other than the preferred status. Ocrevus will have a policy, but I don't… we're going to be publishing that at probably the next meeting or bringing it to you. But at this point in time I don't think any of the MS drugs have a prior authorization on them. We just ask that they try one of the preferred drugs, or two of the preferred drugs first. Amy, does that ring a bell to you that we removed PA from MS drugs?

Amy Irwin: It doesn't, but I can…

Donna Sullivan: Okay. Thanks.

Dave Johnson: Donna, yes, we did.

Donna Sullivan: That's what I thought. Speak up guys. That's why we are here.

Dave Johnson: You asked Amy.

Amber Figueroa: Can you clarify where we would find what's preferred?

Leta Evaskus: What's in the binder is the Washington PDL, not the Apple Health PDL.

Amy Irwin: We actually do apply PA to Ampyra.

Donna Sullivan: I don't consider that an MS drug because it doesn't treat the actual disease. It treats a symptom. Hang on a second. I will let you know what those preferred drugs are.

Amy Irwin: I have it pulled up. I can tell you the preferred drugs. Avonex, Betaseron, Copaxone, Gilenya, Rebif and Tecfidera.

Donna Sullivan: I know you can't see this, but let me see if I can make it better. So, yeah, Avonex and all of its forms, Betaseron, Copaxone, the Gilenya, not the Gilenya .25 because I believe it has a generic, and then Rebif in all of its dosage forms, Tecfidera and it looks like that is it.

Amber Figueroa: Thank you. I think that is just helpful because sometimes when we make these blanket statements we don't have any idea if there is only preferreds or what the choices are for physicians to choose from. So thank you for that.

Donna Sullivan: You're welcome.

Susan Flatebo: I move that the Apple Health Medicaid Program implement the limitations for the multiple sclerosis agents listed on slide 38 as recommended.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. We move on to the Apple Health Preferred Drug List.

Donna Sullivan: So the Apple Health Preferred Drug, these slides that are in your packet or that were handed out to you, I just want to clarify it's not the entire preferred drug list. It's just the drug classes that are going to go live starting January 2019. So the entire PDL is posted on our website. There's 87 slides, I think and we're going to go through them pretty quickly.

We're starting with the anorectal agents. We have two preferred drugs in this particular class and this is the ones that are containing the steroids. So hydrocortisone Pramoxine and then the Lidocaine hydrocortisone.

The next one is just the anorectal agents, the rectal steroids. So there's several that are preferred with a few that are non-preferred.

And then we have Rectiv which is also preferred. It's one of the vasodilating agents.

Antidepressants, the alpha-2 receptor antagonists. We have Mirtazapine preferred and then Maprotiline and the brand Remeron is not preferred.

We have the MAOIs that are going live in January as well so we have Emsam, Phenelzine, and Tranylcypromine or the sulfate is preferred. The generic and then the others listed are not preferred.

The norepinephrine-dopamine reuptake inhibitors the Bupropion XL extended release will be preferred and then the others listed are not.

We have the antidepressant SSRI class will be implemented in January with predominantly the generic products being preferred and the branded products being non-preferred.

The SNRI antidepressants, again, predominantly the generic options are preferred with the branded options non-preferred. Venlafaxine ER generic is also non-preferred.

Serotonin modulators – Trazodone is preferred with the others being not preferred.

The tricyclic agents, again, generics mostly preferred. Some of the older generics are non-preferred like the clomipramine and then all branded products are non-preferred.

Injectable antifungals. We don't expect a lot of outpatient use in this, but sometimes they are used in compounding. We're going through every single class that will be on the PDL eventually, but this is just the antifungal injectables.

The antiparasitics, specifically the amebicides. The Solosec will be preferred. I think it's the only agent in that class.

Antimalarials we'll be preferring Atovaquone/Proguanil comb, Chloroquine Phosphate, Coartem, Hydroychloroquine, Mefloquine, Primaquine and Quinine. And then Daraprim, Malarone, Plaquenil and Qualaquin are non-preferred.

The antipsychotic/antimanic agents Lithium, Lithium ER with the brand Lithobid not preferred. I think we did grandfather that class. David? I can't remember if we did or not. Considering that it is a brand I'm not sure if we did or not.

With antipsychotic first generation we did grandfather these drugs. The generics are preferred for the most part with the brand names being not preferred.

The antipsychotic/antimanic agents, the Equetro, Nuplazid and Vraylar these are more of the anticonvulsants that are also having antipsychotic/antimanic agents or indications.

Antipsychotic combinations – so we've made pretty much all of the combinations non-preferred. Specifically if they have generic ingredients they are much more expensive than the individual drugs. So we've made those not preferred.

The CMV antivirals, Cidofovir, Ganciclovir, Valganciclovir and Prevymis are preferred with Cytovene and Valcyte as non-preferred.

Hepatitis B, again, mostly generics are preferred. Brands are not preferred.

Herpes agents are the same. The Acyclovir ointment is not preferred. It's not really that effective so we did make it not preferred compared to the oral versions.

Influenza agents the Oseltamivir, Rapivab, and Rimantadine are preferred and then the Flumadine, Tamiflu and Xofluza are not preferred.

The RSV agents Ribavirin is also indicated for RSV in addition to the hepatitis C and the Virazole is not preferred.

The asthma agents so the leukotriene modifiers Montelukast and Zafirlukast remain preferred with the others not preferred.

The Xanthines… I'm sorry, I'm ready the wrong slide.

The phosphodiesterase inhibitors Daliresp is preferred and I think it's the only one in that class.

The Xanthines so the Aminophylline, Theochron, Thophylline preferred. The others are non-preferred.

Moving to contraceptives. So all contraceptives are preferred. There was a law passed in the last legislative session that mandates that all purchases in the State of Washington cover all FDA approved products. So everything is preferred regardless of whether it is a brand or generic. That includes the IUDs, the rings, the ointments, the oral contraceptives, the OTC contraceptives—everything. That was a lot of slides.

So moving onto the corticosteroids. We're on slide 45. The glucocorticosteroids… the combination so betamethasone, betamethasone acetate, and the Dermacinrx Cinlone are preferred. The Celestone-Soluspan is not.

The straight corticosteroids pretty much all of the generics are preferred. There's a few brands in there that are preferred as well.

The next slide shows what is not preferred. And these are the non-topical corticosteroids. Again, we don't expect many of the injectable ones to be covered under the outpatient side, but if they are used in compounding or sometimes they are used for patients with adrenal insufficiency as rescue agents to have on hand within like… almost like you would with an Epi-Pen.

Mineralcorticoids, fludrocortisone is preferred.

Moving into dermatologics. So Imiquimod for the immunomodulating agents is preferred.

Amber Figueroa: Can we back up for a second to the injectable steroids. I'm thinking of joint injections as far as most common. Does that apply here?

Donna Sullivan: Typically not. So if… drugs that are covered under the medical benefit we are not implementing the PDL on all drugs covered under the medical benefit. So things that are… drugs that would be used in conjunction with a procedure, and I'm not the medical coder and biller expert, but sometimes those are included in the procedure price. Sometimes they are billed separately so our intent is not to interfere with that process. There will be at times when there are drugs covered under the medical benefit, like if they are an infusion, where we might have preferred agents that are required to use first. We're not trying to interfere with things that are delivered in conjunction with a procedure.

Amber Figueroa: Sorry, I messed up your flow.

Donna Sullivan: That's all right. Moving to slide 50, wound care products. Regranex is preferred.

Digestive aids we're adding the Creon and Zenpep. There's a couple more products that have come out in this class. So just reiterating that Creon and Zenpep remained preferred and then the others are not preferred.

Endocrine and metabolic agents progesterones so Hydroyprogesterone Caproate is preferred, Makena. Note the autoinjector is non-preferred, but the Makena vials are preferred. Medroxyprogesterone Acetate, Norethindrone and Progesterone are preferred.

The vaginal progesterones Crinone is the only one that's there. We have it on prior authorization. It's non-preferred and I don't know what the criteria are, but I believe it is significantly priced.

The gastrointestinal agents' gallstone solubilizing agents, Ursodiol is preferred. All of the others are non-preferred.

Short bowel syndrome Gattex is preferred.

H. pylori drugs, the Pylera is preferred. The H. pylori products are really just combination packs of all the antibiotics and PPIs and sometimes the [inaudible] and they are really, really expensive compared to just taking the medications, you know, prescribing them individually. There's no cost sharing so we made the… this just turned off… we made the combined products non-preferred. Somebody is telling me something. So that's if… if you had any questions regarding that, that's why they are all non-preferred.

The miscellaneous ulcer drugs Carafate, Misoprostol, Methscopolamine, Propantheline, Sucralfate, those are all preferred and the others are not.

The GI or genitourinary agents, excuse me, the acidifiers so K-Phos will be preferred.

The cystinosis agents Cystagon preferred. Procysbi is not preferred.

The interstitial cystitis Elmiron is preferred and Rimso-50 is preferred. I think those are the only two in the class and they do require PA.

The prostatic hypertrophy gents pretty much the generics are preferred and the brand names are non-preferred. David's agreeing with me.

Genitourinary agents, urinary stone agents, the Lithostat and Thiola are preferred.

Moving to gout agents, page 63, Allopurinol, pretty much the generics are preferred. Aloprim, Colchicine, Probenecid and then the Colchicine tablets are not preferred. They are priced much, much higher than the capsule so we are non-preferring the tablets. And then the brand names of those are not preferred, as well.

The hereditary angioedema agents Cinryze, Firazyr, Haegarda, Kalbitor and Ruccoest are all preferred and then Berinert and Takhzyro are not preferred. These were, I'm pretty sure, grandfathered if they were already on those.

The hematologic agents – other. These are Activase, don't expect that outpatient too much unless it's being used maybe for home health for like the tube. And then the Ceprotin, Panhematin, Pentoxifylline, Protamine, Soliris and Tnkase, those are require PA. Mostly… other than the Pentoxifylline it would be, why are you dispensing this from an outpatient pharmacy? And mostly for in-home use, if appropriate.

The agents for Gaucher Disease, the Miglustat, Zavesca, are preferred. Cerdelga, Cerezyme, Elelyso and Vpriv are not preferred.

The agents for sickle cell anemia Droxia and Siklos are preferred and the Endari is not preferred.

The hematopoietic agents, the thrombopoiesis stimulating proteins so Doptelet, Mulpleta, Nplate, Promacta, Tavalisse are all… all of these in this class are preferred.

The hemostatic systemic, the Aminocaproic acid, Cyklokapron and Tranexamic acid are all preferred and require PA.

The hemostatics oral so Amicar, Tranexamic Acid oral products are preferred and Lysteda is not preferred.

The barbiturates, the hypnotics, sedatives, sleep disorder, specifically the barbiturates so Amytal, Pentabarbital, Phenobarbital are preferred and then the Butisol and Seconal are non-preferred.

The benzodiazepine hypnotics, the generics Midazolam, Temazepam, Triazolam preferred. Estazolam, Flurazepam, Halcion and Midazolam syrup is not preferred, as well as the brand Restoril.

Note to come on the benzodiazepines. There was a… we'll be probably going more into restricting these in combination with opioids in the short-term future with the new law that was passed as well as more opioid initiatives that are coming from the state. So right now they are not on prior authorization, but there will probably be more limitations on these medications as we go forward.

Now it's really telling me something. It's frozen.

So slide 73 the non-benzodiazepine we are preferring the Zolpidem, Zolpidem ER all of the other non-benzodiazepine products are not preferred.

The selective melatonin we're preferring Rozerem over Hetlioz.

Tricyclic agents are not preferred. So the Silenor, Belsomra. We're on page 75 if you're trying to catch up.

Skeletal muscle relaxants Baclofen, Cyclobenzaprine, Dantrium, Methocarbamol, Revonto, Ryanodex and Tizanidine are preferred. Non-preferred are all of these that are listed. I'm not going to run through them all. Carisoprodol does require prior authorization and we have very, very, very little utilization of that if you're interested.

The ALS agents so we prefer the Riluzole. Rilutek and Tiglutik are both non-preferred.

The antimyasthenic cholinergic products so Enlon, Neostigmine, Pyridostigmine, Regonol are preferred. Guanidine and Mestinon are non-preferred.

Slide 80 looking at the ophthalmic antibiotic-steroid combinations. So we're preferring the Neomycin/Polymyxin/Dexamethasone products, the Sulfacetamide, Prednisolone, Tobradex and the Tobramycin/ Dexamethasone. I think that's the solution. So the ointment is the brand preferred. The other one, I think, is the solution and then the others listed are not preferred.

Ophthalmic antifungals the one in class is preferred – Natacyn.

Ophthalmic antivirals so the Trifluridine is preferred. Viroptic and Zirgan are non-preferred.

Movement disorders so Tetrabenazine is preferred. Austedo, Ingrezza and Xenazine are non-preferred and we will be bringing a policy for you guys. They will require prior authorization. We just haven't completed that one yet. So we'll be bringing that to you soon.

The psychotherapeutic agents other – the Ergoloid Mesylates, Pimozide are preferred and then a lot of these are used for fibromyalgia. They are on the other side and non-preferred. If you're asking why they are lumped together like this there's Medi-Span, which is a drug reference table provider. I'm not really sure what they are classified as. They lump these together. So we're following kind of their classification. So if you might ask why these drugs are lumped together they really have nothing to do with each other, that's because that is how Medi-Span is classifying them. And so we are recognizing that so we're doing that tried-and-failed we recognize that it's not appropriate to try and fail some of these drugs within this particular class so we make sure that they have the right indications or we put them all on PA to make sure that they are being used appropriately. I wanted to point that out to you.

And then the smoking deterrents. Most of these, I think, are already on the PDL but we're just updating this class with the bupropion, the Chantix are both preferred, and then the Zyban, which is the brand bupropion is not preferred.

For the cystic fibrosis agents all of the brands are preferred or all of the products are preferred and they do require prior authorization to make sure that they are being used according to label.

And then substance use disorder there is the drug Lucemyra, which requires prior authorization. So we gave it a non-preferred status. And that is it.

Lisa Chew: Thank you, Donna. Any questions for Donna?

Donna Sullivan: Did we make it a motion to approve it? Can we just have you guys make a motion real quick to approve?

Amber Figueroa: Substance use disorder doesn't have any suboxone.

Donna Sullivan: This is the substance use disorder "other". So the partial agonists that have been on the PDL for some time now so I'm not sure which ones. So there are… Vivitrol, I think, is preferred. There are the sublingual, buprenorphine products preferred, as well. I'm not sure, but yeah… this is… this is a different category that is not one of the partial opiate agonists.

Nancy Lee: I move to approve or accept the Apple Health preferred drug list as presented.

Amber Figueroa: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries and I think we are adjourned and happy holidays and thank you for the donuts, David.

Donna Sullivan: See you next year and Dale thank you so much for all the service for the last six years. It's been a pleasure.

Dale Sanderson: It's been my pleasure.