Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
Transcription
August 19, 2020

Leta Evaskus: It's 9:00 and I know some people are still logging in, but Ginni why don't you kick us off.

Ginni Buccola: Great. Let's go ahead. So good morning. I'm Virginia or Ginni Buccola, the P&T Committee Chair. We're going to go ahead and convene the P&T Committee meeting and I'd like to go ahead and welcome everyone who is here and go through our introduction list. After I say your name if you could just say that you're here it would be great. So I'm going to start with the P&T Committee members starting with Alex Park?

Alex Park: Alex Park, committee member. Present.

Ginni Buccola: Diane Schwilke?

Diane Schwilke: Good morning. I'm here.

Ginni Buccola: Jordan Storhaug?

Jordan Storhaug: Here.

Ginni Buccola: Nancy Lee?

Nancy Lee: Here.

Ginni Buccola: Leah Marcotte?

Leah Marcotte: Here.

Ginni Buccola: Connie Huynh

Connie Huynh: Here.

Ginni Buccola: And now moving on to the Health Care Authority members starting with Leta Evaskus.

Leta Evaskus: Here.

Ginni Buccola: Donna Sullivan?

Donna Sullivan: I'm here.

Ginni Buccola: And Ryan Pistoresi? We'll move on to Luke Dearden?

Luke Dearden: Here.

Ginni Buccola: Amy Irwin? Moving to Jose Zarate? Moving to Ryan Taketomo? Moving to Marissa Tabile?

Marissa Tabile: Here.

Ginni Buccola: Chris Chen?

Chris Chen: Morning.

Ginni Buccola: L&I Members Jaymie Mai? Moving to our Magellan Medicaid Administration member Umang Patel?

Umang Patel: Here.

Ginni Buccola: And our DERP presenter today Curtis Harrod?

Curtis Harrod: Here.

Ginni Buccola: And our managed care organization reps Jennifer Wang with Molina?

Leta Evaskus: I'm going to have to unmute them. One second.

Jennifer Wang: How are you?

Ginni Buccola: And Petra Eichelsdoerfer with United?

Petra Eichelsdoerfer: I'm here.

Ginni Buccola: And Catherine Vu with Community Health Plan?

Catherine Vu: I'm here.

Ginni Buccola: Okay. Um, thanks for everybody being here. My apologies for my name. People should send me a personal email if I'm really butchering their last name so I don't continue to do this in our future meetings. But good morning and I'll hand it back to Leta to go over any meeting logistics.

Leta Evaskus: Great. Thank you, Ginni. So the committee and all presenters have been added to the meeting as organizers. You can mute and unmute yourselves. Please mute yourself when not speaking to limit the background noise. The go-to webinar limits the numbers of cameras that can be shared at one time. So the presenter will share their webcam while speaking and then the P&T Committee Chair, Ginni, will share hers and up to five other committee members can share their webcams during the discussions and motions. You can turn off your webcam when you're not presenting. For stakeholder participation, the chair will read the list of stakeholder names who pre-registered to speak. I will unmute you as she calls your name. Afterwards the chair will ask if there are any other stakeholders that would like to speak. Use the "raise hand" icon and I will call on you and unmute you. You'll have three minutes to speak. You can also use the "question" function and I will address your questions during the stakeholder time.

The meeting is being recorded so please state your name every time you speak. All right. Thank you.

Ginni Buccola: So we're going to get… we have one brief… we have a small P&T Committee agenda this morning. We're going to have a CGRP update report from Curtis Harrod with DERP and we'll have stakeholders after that. So I'll turn it over to you Harrod. Thanks.

Curtis Harrod: Thank you very much. I'm happy to be here with you this morning. So today I'll be giving an update, systematic review update on calcitonin gene-related peptide inhibitors or CGRP for migraine prevention and treatment and for cluster of headache prevention. We're going to be covering multiple indications today. Advance to the next slide.

This is just our standard overview. [recording cuts out]

Leta Evaskus: Curtis, we can't hear you. Curtis? We cannot hear you.

Donna Sullivan: He can't hear us either.

Ginni Buccola: We can't hear you.

Leta Evaskus: Curtis, do you want to try calling back in?

Curtis Harrold: Alrighty, how about now? Sorry about that. I heard one of the panel members talking about technical issues with a broadband. I'm at the Center for Evidence-Based Policy because of that issue. So sorry about

the audio issues. You saw the overview of the presentation. I won't walk through that again. These are just common abbreviations that we will be talking about through the presentation. We're mainly here to save texts later on. So you'll see CGRP inhibitors up there and then you'll see some epidemiological clinical research terms like absolute risk difference, odds ratio, risk ratio, confidence interval and things like that.

On slide number 4 here we're in the background section. We'll start out with migraine headache and then we'll go into a pattern that you'll see here in a minute. So regarding diagnostic criteria for a migraine headache—headache attacks can occur from 4 hours, one-fourth of a day all the way to three days or 72 hours and this can occur with or without aura. The definition of chronic and episodic migraine has some variations. So chronic is 15 or more headache days per month and that occurs for at least a three-month period of time. Episodic migraine is fewer than 15 headache days per month. So that's the discrepancy on the… or the nuance between chronic and episodic migraines. There are preventive treatments before CGRP inhibitors came to the market and those preventive treatments include antidepressants, anticonvulsants, beta blockers, and botulinum toxin or BOTOX. There are few treatments beyond just preventative treatments and those are triptans, dihydroergotamine, nonsteroidal anti-inflammatories or NSAIDS and anti-nausea drugs. So CGRP is actually a neuropeptide and it is involved in the pathophysiology of having a migraine headache. Everywhere else you think you can inhibit that and it may prevent it from occurring. Slide 5.

We're going to transition here from migraine to cluster headache. So cluster headaches sound awful. Personally I think they do not have them, but they are multiple headaches occurring within a period of days, weeks or months. These are called cluster periods. Symptoms of these are very severe. So severe pain, which is usually unilateral and located around the eye with tearing and running nose and sweating will result from that. There are also episodic and chronic cluster headaches. First with episodic. So with at least two clusters this can range from a week all the way to one year in time. These are separated by pain-free remission of three months or longer and that makes it episodic. Chronic is basically the lack of sustained remission between clusters. Similar to migraines we have acute treatments, simple oxygen or triptans, lidocaine and ergots. Preventive treatments include verapamil, steroids, ergots, topiramate, lithium and nerve blocks. So the etiology of a cluster headache is a bit not as well known around… relative to a migraine. So CGRP is believed to be a part of the [inaudible] physiology in hopes that if it is inhibited would prevent a cluster headache. Slide 6, please.

So the figure in front of you has three columns and I'll walk you through each one. So we'll start with the monoclonal antibody targeting the CGRP receptor. So that's targeting the receptor. That's erenumab subcutaneous injection. It's a shade of blue to indicate that the FDA has only approved this treatment for migraine prevention. The middle column is monoclonal antibodies targeting the CGRP ligand. So the previous erenumab targeted receptor. These are going to target the CGRP ligand. So that's eptinezumab, which is an intravenous infusion. And that was put on the market in February of 2020. So it's the most recent infusion basically of the [inaudible] you will get through orals here in a second. And then fremanezumab is a subcutaneous injection. Both of these are only approved for migraine prevention. Moving to galcanezumab which is a subcutaneous injection and this is approved for migraine and cluster headaches. So cluster headaches was added recently as an indication and is captured for the first time within this report. Then we have small molecule inhibitors. So these are antagonists of CGRP in which we have rimegepant, which is an oral agent. Rimegepant was approved, if I'm not mistaken, in December of 2019 where ubrogepant was approved in February of 2020. So again these are fairly recent and encompassed in this report for the first time and these two oral agents are only approved for acute migraine treatment. So there will be different outcomes based on these different indications and we'll talk about those in the findings section. Slide 7.

So this is just walking you through the difference between the 2018 systematic review. Also [inaudible] was presented to Washington and the 2018 systematic review just included those four CGRP inhibitors whether they are IV or subcutaneous and that's eptinezumab, erenumab, fremanezumab and galcanezumab and they charted one indication that is migraine prevention. So this update I'll be presenting to you today is an expanded scope and so we have two additional drugs that is rimegepant and ubrogepant, the oral agents, and then additional indications with acute migraine treatment and cluster headache prevention. Slide 8.

I'll walk you through the PICOS for the report and some of which was just covered, but for adults we'll be looking for individuals who suffer from episodic or chronic migraine, chronic cluster headache, as well as acute migraine headache. The intervention will be those CGRP inhibitors that we just walked about within the figure and our comparators include our placebo and sham controlled trials, as well as other CGRP inhibitors being compared to each other or pharmacological agents like triptans for instance. Slide 9.

So for outcomes we have a few here. So migraine events, pain relief. And then we get into more patient important outcomes such as quality of life, functionality and disability, use of rescue medications, number of ER visitors or primary care visits, and then our suite of adverse events with [inaudible] within our DERP reports. For study designs we included randomized trials, as well as perspective observational cohort studies, but those were only for harms. So only harms were included for observational studies. At least that's all that we looked for. Slide 10, please.

So we have three key questions – first, what is the effectiveness of CGRP inhibitors? Second, what are the harms? First we'll look around efficacy and harms for sub-q and then our third key question is subgroup differences. So are these performing differently by agenda for instance or by age? We explored that, but of course we're limited to what's available in the literature. Slide 11 and then 12.

So we are in the method section. Just briefly here we conducted a comprehensive literature search indicated by systematic reviews. So we used PubMed, Embase, Cochrane Library, and we searched those databases from date of inception of that database up to October 31, 2019. At that point we conducted active surveillance through March 31st. So what the takeaway should be here is that the report is up-to-date to basically April 1st of this year. So if a study has been published since April to this day it will not be encompassing today's presentation. Once we have identified the eligible studies we did individual level study methodological quality assessments and I'll walk through that in the next slide. But we also used OpenEpi, which is a software program to calculate absolute risk differences, risk ratios and confidence intervals. And then we used grade to assess the overall quality of the evidence for an individual outcome. And I'll walk the specifics on that real quick. Slide 13.

This slide highlights our three bucks for methodological quality. So we have good, fair and poor. Just briefly a good methodological quality study has transparent methods that are appropriate given the study design and context and have limited to no conflict of interest. A fair methodological quality study may have incomplete information regarding their method. So you may not be able to one thing or another. Some additional biases as well as meaningful templates of interest. A poor methodological quality study has clear flaws that will introduce significant bias indicated by a poor rating. That can be significant imbalances between baseline characteristics between groups, no allocation concealment, substantial conflicts of interest, etc. Slide 14.

So this is the overview of GRADE for quality of evidence ratings. We have three buckets for gradings with the quality assessment for a study. So that's at the individual study level where grade is at the outcome level. So we have four levels – high, moderate, low and very low. At the top of your screen you'll see our outcomes that we assess using the grade approach like migraine and headache days per month, pain relief, functional outcomes, quality of life, and then serious adverse events and discontinuations due to adverse events. So when we have let's say three or four randomized controlled trials we'll start at high. So those are randomized trials and that's where they start at a grade grading and then we can downgrade from there. So for instance if those four trials have a smattering of effect a couple said it was significantly different, a couple said they weren't significantly different or even in the opposite direction we would have a thing that we can inconsistency and downgrade one level from high to moderate. If there is substantial risks of bias within those studies we may go from moderate to low. So we downgrade based on those issues and a few others I won't walk through today. Where a cohort study start at low and you can go down or you can go up. So if there's a dose response such as the milligrams of medication increasing and the effects increasing we're more confident that that is the intervention or exposure and as a result we may go from low to moderate. If there is bias feed in those cohort studies, let's say they didn't adjust for a compounding factors we go from low to very low. And very low is our basement. We cannot go below that and high is our ceiling and we can't go above that. So I'll walk through those as well as get some interpretation when we talk about high, moderate, low and very low within our findings. Slide 15 and then 16.

So we're going to get into our published studies. A little bit of an overview here. This is our literature flow diagram, again, connected to a previous report. I'm going to draw your attention immediately to the green box and we'll spend our time talking about that today. So overall we conducted a narrative synthesis. So you will not see a meta-analysis. We just did a narrative synthesis, not a quantitative synthesis. There are 27 eligible randomized controlled trials included in our report, 32 publications were connected to that. There is a… one too many issues here as is time and literature based. So you can see the previous report is just medical review. Again, in 2018 there were 13 RCTs and 14 publications. The body of evidence has doubled within two years. Some of that is because we expanded the indications and there's new medications approved by good oral agents. Slide 17, please.

So we have 27 randomized controlled trials as I mentioned, 13 of which are from our previous review, 14 of which are new for this review. All 27 were placebo-controlled trials. So there are no head-to-head studies. I will say that although I don't cover it today, [inaudible] is an active comparator and one upcoming randomized controlled trial, but that's not expected to be public for a little while still. But there is a head-to-head study register in clinical trials and that will be the first body of evidence. So I'm just wanting to say there are 26 fair methodological quality studies largely rated that because of the substantial conflicts of interest within each study. The sponsorship was by the manufacturer that sometimes help with authorship or study designs. The authors were paid by the manufacturers to write these reports. So those are all conflicts of interest that we're observing here and a large part of why these are fair methodological quality. There's one poor methodological study of the 27. Now based on the indications we have one cluster headache prevention study, 13 episodic migraine prevention studies, 6 chronic migraine prevention, and then 7 acute migraine treatment. For key questions, so key questions 1 and 2, efficacy and harms just as a reminder we have 23 studies all capture those outcomes. So efficacy and harms. Key question 2 is harms and we have one study that only analyzed harms and then conveniently, for all three key questions, we have three studies. So the third key question, as a reminder is based on subgroups. So we had three studies addressing that. Then we go to slide 18.

This is just an overview of commonly reported outcomes within the literature and what we'll be talking about today. You'll hear these frequently so get ready. Chance in days per month with regard to migraine was a very common outcome. Another metric, just a little twist on that, is the proportion reduction of at least 50% or greater in number of monthly migraine days. So if they had the population that had at least 50% or higher of those that qualify as that outcome and one study went ahead and raised the bar a little bit and listed 75%, but the more common outcome is 50% or more in the number of monthly migraine days. And then we get into functionality, as well as quality of life measures. So HIT-6 headache impact tests, six items, indicated by HIT-6. Then we have MIDAS, which is the Migraine Disability Assessment. The MPFID, which is the Migraine Physical Function Impact Diary. An MSQL, which is the Migraine-specific Quality of Life Questionnaire. For acute treatments, again, these are ubrogepant and rimegepant. They have outcomes of freedom from pain two hours post dose. So a very quick follow-up period for outcomes in intensely acute migraine treatment. So then freedom from the most bothersome symptom, which may be pain in this case, but it is the most bothersome symptom according to the participant in the study, two hours post dose. So a couple of freedom-

related outcomes for those oral agents. And last we have our cluster headache prevention. So these are attacks per week. So you saw the monthly for migraines and then the cluster headache we have attacks per week. Slide 19.

This is going to start our key questions. So we're going to start with key question 1. We're going to start with chronic migraine prevention and then move into cluster and then acute. This is just going to be the pattern that we'll talk about today.

So on slide 20 here we have eptinezumab versus placebo. One randomized controlled trial we identified with 665 participants and this will be a theme. So findings were reported at 12 weeks and we have a GRADE rating of moderate. So that translates to we are fairly confident in this association. An additional study may change our mind slightly, but not substantially where low and very low will basically say we are very uncertain in these findings and high is saying basically that any additional studies done would not change our mind. So here we're at moderate. So we have moderate quality of evidence for clinical improvements and as I mentioned some studies have a 75% reduction instead of 50. So this is one 75% or more reduction number of migraine days per month. The placebo group had 24% of participants report that. So one in four of the placebo group reported a greater than 75% reduction in number of migraine days per month where the intervention groups 100 mg and 300 mg. So we have two doses for eptinezumab, 37% and 38% respectively and one was significantly different. That's the 300 mg as indicated by a P value of less than 05 where the other 100 mg was marginally significantly different, but not. And that's at .07 P value. Now we also observed significantly larger improvements for both 100 mg and 300 mg dose in changing these headache days per month and a 50% reduction in headache days per month. So we also did do the 50% measure, which you'll see consistently throughout. Overall we see significant improvements, specifically around that 300 mg dose. So functioning we see a change in the HIT-6 which is larger in the 300 mg dose, but not different for the 100 mg dose. So we see a trend here with 300 mg seems to be more efficacious than the 100 mg and again this is all relative to a placebo to put that in context again. Slide 21.

So moving on from eptinezumab we're going to get into erenumab. So we have one randomized trial, 667 individuals. Findings were reported at 12 weeks and the clinical improvement outcome was a moderate quality of evidence rating. So the change in mean monthly headache days for the 70 mg and 140 mg dose was actually the same. So a reduction of 2.5 days per month versus a placebo and this was significant. And then we

saw significantly larger improvements for acute migraine medication use for rescue therapies and then a 50% reduction in number of migraine days per month for both the 70 mg and 140 mg doses. For functionality we have a GRADE rating of moderate again. And for the 70 mg and 140 mg doses we saw significantly larger improvements as measured by HIT-6, MIDAS and MSQL. Slide 22.

So fremanezumab is next. We have three randomized controlled trials with a little over 2,200 participants. Findings are reported at 12 weeks. Sorry if I sound like a broken record, but that is the gist of it today. So clinical improvement was moderate quality of evidence and there's significantly larger improvements in migraine days per month. This ranged across the three trials from 1.7 to 3.5 days across dosage, again, and studies. There is significantly larger improvements on all secondary efficacy outcomes across the doses and studies within these groups. Now for functionality only two of the three trials measured functionality, which accounted for close to 2,000 participants. So you can see there is a smaller third study which had a little bit over 200 participants. So they did not measure functionality here, but we do have two randomized controlled trials and do have a GRADE rating of moderate again with significantly larger improvements as measured by the MIDAS with fremanezumab versus placebo. Slide 23.

Galcanezumab is our last one on the docket for chronic migraine prevention and that's one randomized controlled trial with over 1,100 participants. Findings were reported at 12 weeks with clinical GRADE rating of moderate. So these see significant reductions again in migraine days per month. So 2.1 mean, that's the reduction, 2.1 on the 120 mg dose and 1.9 on the 240 mg dose. So here we don't see necessarily like a dose response where the 120 is comparable to the 240. A significantly larger improvement for nearly all secondary efficacy outcomes was observed and this encompasses both a rescue medicine use [inaudible] that 50% reduction in migraine days. For functionality we have GRADE rating of moderate and that is a significant improvement observed on the MSQL for both the 120 and 240 mg at 12 weeks. So this is galcanezumab. Slide 24.

This is our wrap-up slide just covering what we talked about and you can see there is a lot of homogeneity within our findings. This is indicated basically because the studies were designed quite comparably, which is sometimes nice to have for a systematic review where you have the same outcomes and timelines and follow-up and it makes the synthesis much easier. So just to digest this very quickly, eptinezumab and galcanezumab are new to this update and overall across this [inaudible] we have

moderate quality of evidence and all of the CGRP inhibitor versus placebo, but again the placebo is the comparator in this case. Slide 25.

So episodic migraine prevention will be our next indication tackled and let's go to slide 26 to start with those.

So for episodic migraine eptinezumab versus placebo was studied in two randomized trials with close to 1,100 participants. The findings were reported at 12 weeks. So clinical improvement was have two randomized trials with a moderate quality of evidence rating. We saw significantly larger improvements in migraine days per month in the larger of the two studies. So there is one study with much larger and they observed a .7 days reduction for the 100 mg dose and 1.1 days for the 300 mg dose. So as I said, these are a little bit smaller and in some cases on the effect size and the reduction in days and again just focusing on the fact that we're looking at migraine prevention, which episodic migraine prevention, which is 15 or fewer days in a month where a chronic is 15 or more sustained over a three-month period. So by default you make some smaller numbers and episodic for chronic. A significantly larger proportion was 50% reduction in monthly migraine days were again observed in larger two studies with 50% achieving that in 100 mg and 56% was the 300 mg dose, but again over one-third of the population studied was in the placebo group did have that outcome, did achieve a 50% reduction. So over one-third of the population do that. Other studies were not… and that's other study, singular, were not powered so they did not have statistical power, a large enough sample size for efficacy outcomes and making a difference was observed in the days per month in five to eight weeks. For functionality we have only one randomized trial that assessed functionality and it received a GRADE rating of low. There is no significant difference in mean change of the HIT-6 with eptinezumab versus placebo. Slide 27.

Now we're on erenumab versus placebo. We have five randomized controlled trials making up over 2,500 participants and a little bit of a shift here. So we have findings at 12 to 24 weeks. So we went up 24 weeks within this body of evidence for erenumab for episodic migraines. For clinical improvements we have a GRADE rating of moderate again with significantly larger decreases in monthly migraine days. This ranged across the five RCTs from a reduction of 1 day to 2.3 days in the 70 mg dose and 1.6 to 1.9 for the 140 mg dose. So again you see overlap in the affect based on [inaudible] indication that a higher dose is more efficacious. We saw significantly larger proportions with 50% reduction monthly migraine days in the erenumab versus placebo, as well as rescue medication use. For functionality we had four RCTs measured out of the

five body of evidence with a GRADE rating of moderate. We observed significantly larger improvements on various outcomes and that is HIT-6, MPFID and MIDAS. Slide 28.

Now we're back to 12 weeks. So fremanezumab versus placebo two randomized trials plus the 1,200 participants. Clinical improvement received a GRADE rating of moderate and this translates to significantly larger reduction in migraine days per month. This ranged across the two RCTs from 1.3 to .8. Technically that's not much of a range at 1.3 and it's 2.8. But then we do have the dosages to account for in there too. So significantly larger reductions in acute medication use for rescue therapy, as well as symptoms being recorded and a greater proportion of 50% or more in monthly migraine days with fremanezumab versus placebo. So for functionality we have two randomized trials and they both [inaudible] here to a GRADE rating of moderate for significantly larger improvements in the MIDAS score for all doses across studies. Slide 29.

So episodic migraine prevention again galcanezumab versus placebo four randomized trials constituting close to 2,300 participants and we have follow-up at 12 to 24 weeks here as well. So clinical improvement GRADE rating of moderate. We saw significantly larger reductions in monthly migraine days. This ranged from .9 to 2 days across doses and studies. We also saw a significantly larger proportion, again, galcanezumab versus placebo, reporting at least a 50% reduction in monthly migraine days. We also saw significantly larger use of rescue medications in galcanezumab versus placebo and these ranged from 1.6 to 1.8 days, which I think is an error. I don't think this is more of a metric of times of use. Sorry for that. So functionality we have a GRADE rating of moderate and 4 RCTs that capture that with large improvements in galcanezumab versus placebo with MIDAS, MSQL, HIT-6, though all measure were reported by studies and some findings were not significantly different. So some of these did not hit the statistical significance of .05 reduction for galcanezumab versus placebo. Slide 30.

This is just a wrap-up. Unlike the previous wrap-up we do have some difference here. Eptinezumab, which was again approved in February 2020 it was new to this update and for migraine days per month, as well as the reduction of 50% or more in migraine days per month we see a moderate quality of evidence rating was the HIT-6 was a GRADE rating of low. So a little bit lower in quality of evidence, as well as we observed no difference with eptinezumab. All other outcomes got moderate ratings and favoring the CGRP versus a placebo. Slide 31.

We're going to dive into acute migraine treatment. Slide 32, please.

Rimegepant is the first one up. We have three randomized controlled trials with over 3,500 participants. Again, rimegepant compared to a placebo. And also as a reminder we have findings at two hours post dose for acute migraine treatment studies. So clinical improvement is again our outcome. Grade rating of moderate. We saw significantly larger proportion of participants with freedom from pain with an absolute risk difference ranging from 7.6 to 16.2 percentage points and that's in rimegepant versus placebo. We also saw significantly larger proportion of individuals with freedom from most bothersome symptoms, which again is self-reported in the two RCTs that accept that of the three. For functionality we have two randomized controlled trials with a GRADE rating of moderate. We see significantly larger proportions with ability to function normally with rimegepant versus placebo. Slide 33.

We're talking about ubrogepant now. We have three randomized trials with close to 3,800 participants, again, compared to a placebo and findings are at two hours post-dose. For clinical improvement we have three randomized trials GRADE rating of moderate. We see significantly larger proportions of individuals from freedom of pain. This has an absolute risk difference ranging from 7.4 to 16.6 percentage points. So overall it lasts quite nicely with the previous findings with rimegepant. Again, we don't have head-to-head studies so sometimes our eyes have to go across studies in that manner. We have significantly larger proportions of individuals with freedom from their most bothersome symptoms and two randomized controlled trials of the three. For functionality only one of the three RCTs measured this. We have a GRADE rating of moderate with significantly larger proportions of individuals reporting ability to function normally within two hours post dose. ORs of 1.7 and 1.9 for 50 mg and 100 mg respectively and those are significantly different. Slide 34.

So this is just a wrap-up. Both are new because they were approved after the original report. So for rimegepant versus placebo, as well as ubrogepant versus placebo we have moderate quality of evidence across the outcomes and both favor the oral agent versus a placebo. Slide 35.

So now we're going to get into cluster headache prevention. Slide 36.

Starting here we'll talk about some of our findings. So we galcanezumab versus placebo. This is a randomized trial of 106 participants. So a pretty small randomized trials. Galcanezumab, again, is the only CGRP inhibitor with the cluster headache prevention and negation. I captured that in a figure at the beginning of the presentation. So findings up to eight weeks

are recorded for cluster headache prevention connected to galcanezumab treatment. So for clinical improvements we have a GRADE rating of low. So a little bit reduced confidence here and let me explain why. So we have a mean changing frequency of attacks per week at week number three, which is also seen a 3.5 reduction. You can see our confidence interval indicates the statistical significance because we do not have 0 within the confidence interval. However, when we translate the findings to week eight we see an actual increase and 1.3 on average. This was not statistically significant because we do have 0 within our confidence interval, but it is also a worrisome finding. It is a small trial. I do want to talk about that, maybe an additional larger study may find something different, but at three weeks we have a 3.5 mean reduction in attacks per week relative to a placebo and then at eight weeks we actually see an increase in galcanezumab versus placebo. It's not significant, but it's not a direction that's probably desired. And then for functionality none we recorded as far as outcomes were concerned for this one small trial. Slide 37.

Again, this is the only approved indication for a cluster headache and we see low quality of evidence for both outcomes that were assessed for galcanezumab versus placebo and, again, favorable outcomes early on, but those did not hold at a longer term follow-up and it's hard to say long-term follow-up when we're talking eight weeks given that cluster headaches can last for a year in some cases. Basically we need more evidence, longer term follow-up studies and larger samples to better understand this drug. Slide 38.

We're going to now dive into adverse events or harms for CGRP inhibitors. Slide 39.

This is just an overview set up for the body of evidence for chronic migraine prevention. We have six randomized controlled trials with over 3,500 participants. So we have one RCT with eptinezumab, one with erenumab, three with fremanezumab and one with galcanezumab all, again, versus a placebo. I will stop and note here that we looked for observational or cohort studies for harms only and unfortunately did not identify any within our systematic review update so we are just relying on trials to talk about harms and adverse events. As most of you likely know trials are not usually powered, number one, for adverse events and then number two, typically don't have the follow-up necessary to determine long-term consequences. And so for our findings we have serious adverse events GRADE rating of very low. Low for fremanezumab because they had the three RCTs, so a larger sample. Overall rare events cannot be necessarily stablished because of the smaller samples, smaller

follow-up time and the infrequency of the outcomes occurring. So we have very low confidence in three of the four and that translates to no confidence in the findings and in fact a new study would dramatically find our findings is the translation of a very low rating. For discontinuation of adverse events we, again, have a GRADE rating of very low and low for fremanezumab. Unfortunately relationships cannot be determined because of the rare events that are occurring here with discontinuation due to adverse events. Slide 40.

Now we'll talk about episodic migraines. So we talked about chronic on the previous. We'll talk about episodic now. Thirteen randomized controlled trials addressed adverse events or harms with close to 7,400 participants, two RCTs were on eptinezumab, five were on erenumab, two were on fremanezumab, and four were on galcanezumab. For our findings, again, serious adverse events were rare events and a relationship could not be established with a GRADE rating of very low. We also had discontinuation due to adverse events captured within these 13 RCTs at GRADE rating of very low because the events were quite rare and the relationship could not be determined with discontinuation due to adverse events. Slide 41.

So now we're going to talk about acute migraine treatment. Again, rimegepant and ubrogepant. We have seven RCTs, over 8,500 participants, three RCTs analyzed rimegepant, four analyzed ubrogepant. And the same story here with serious adverse events we had a GRADE rating of very low. These were infrequent within the studies and a relationship could not be determined because of that. Slide 42.

So cluster headache prevention, talking about harms here. We had one comparing galcanezumab and placebo and that's that one small trial that we found some different findings versus the rest of the body of evidence. So a sample of 106 individuals, serious adverse events, very low rating, no events were observed, relationships cannot be determined because there are no events in this small 106 trial. Discontinuation due to adverse events was the same story. Very low rating. Rare events did… so there were some discontinuations but not enough to have a meaningful relationship to be determined. Slide 43.

Now we're going to get into key question number 3 and that's on subgroup differences and this can be both for efficacy and adverse events. The spoiler alert is that there is not a lot of evidence out there on subgroups. So let's go onto slide 44 and address that.

There were three studies reported as far as subgroups are concerned. Fremanezumab, again, those three studies that we talked about previously for migraine prevention reported similar efficacy in participants not taking concomitant preventative medications compared to the full study population. There was that one subgroup analysis that was basically done so not a broad or deep analysis here within subgroups and more evidence is needed to better understand this. Slide 45.

We're going to start with our discussion. Slide 46.

We'll get into our details. So we do have some caveats here. It's like limitations of the body of literature, as well as our review. So we captured no head-to-head studies. So one CGRP versus another was not in there. A CGRP versus another treatment like a triptan is not in our report because we cannot find them. There is, again, the one registered ongoing study of topiramate versus [inaudible] inhibitor and that could be forthcoming. All of the included were conflicted. So there's sponsorship in the space by the manufacturers. Some of you may be unaware, but there's a growing body of evidence within Cochrane [inaudible] systematic review indicating that sponsorship of studies is significantly biased in the study in which they are more likely to report a positive effect in a study that is not sponsored by a manufacturer. So that's why I'm talking about that today. We have a growing body of evidence indicating that sponsorship of studies may lead to substantial conflicts with different findings. We also have prevention studies only of 12 weeks duration and that's a pretty small period of time for a condition that effects an individual for their life. So longer follow-up is needed for these studies. The acute treatment studies only effects an individual migraine attack. So they didn't look at a subsequent event, only that single one. The initial acute attack was studied. Nearly all prevention studies required a run-in phase and that run-in phase consisted of an electronic headache diary. We can probably assume not everyone will adhere to that in the real-world setting. So what happens in those trials is as their patient did not adhere to it, they were not enrolled in the active phase of the trial. So the run-in phase we did those potentially out, limiting generalizability of findings. And then mostly excluded patients had clinically significant psychiatric or medical conditions, as well… pregnancy was not studied in any of these and so we don't know about the efficacy of CGRP in pregnancy as well as within individuals with psychiatric or other medical conditions. So in general the populations were fairly healthy that were studied so it is again a note about generalizability. Slide 47.

Continuing on with our limitations here women compared to men do have a higher frequency of migraines. So they report them more frequently, as well as suffers from migraines more frequently. So it makes sense that the study population analyzed more women than men. However, some of the studies looked at only about 90% of women as there was only 10% of men who were studied. So that limits the generalizability of the findings to men with migraines and then furthermore most of the studies did actually not report race or ethnicity so we couldn't discern the demographics or pitching characteristics within these studies, as well because of that. So again a note about generalizability. Few studies, as indicated by key question number 3, addressed subgroup differences and no studies reported on patient reported outcomes such as employment or health care utilization. And then lastly this is a note about our review. We did not request [inaudible] from the manufacturer so as a result we did not report conference abstracts or press releases or oral presentations at conferences so those were not included in our analysis though the body of evidence is growing as you saw based on published literature that is peer reviewed. And we only looked at studies that were published in English. So there are some limitations to our systematic reviews. Slide 48.

Let's start with migraine prevention as far as conclusions are concerned here. So relative to a placebo we see eptinezumab, erenumab, fremanezumab, and galcanezumab were more efficacious, again, relative to a placebo with moderate quality of evidence. Chronic migraine days range from 1.8 to 3.5 fewer within those CGRP inhibitors versus placebo. For episodic slightly lower range, but again there's some overlap here and just a reminder for the third time here episodic migraine 15 or fewer per day or 15 or… excuse me, per month. That would be terrible if that was per day. So it's 15 or fewer per month where 15 or more within that month. You'll see some natural variation by those indications, but we have overlap and reduction in days within the month. So serious adverse events and discontinuation due to adverse events as we've talked about were infrequent. They were rare and as a result relationships could not be determined and that's very low quality of evidence ratings for those. Let's go to slide 49.

We'll transition from migraine prevention to acute migraine treatment now. Again, relative to placebo rimegepant and ubrogepant were more efficacious with a moderate quality of evidence rating and the proportion achieved freedom from pain at least two hours post dose ranged from 6.4 to 16.6 percentage points higher for active doses relative to a placebo. And then for serious adverse events same story as the other CGRP inhibitors that are not oral. We see no relationship that can be

determined because of the rarity of the event. As a result we have very low quality of evidence. Slide 50.

With cluster headache prevention conclusion so galcanezumab was more efficacious in the short-term so that 1 to 3 week range and we gave it a GRADE rating of low, but again at the 8-week period of time there was no significant difference and so this is unclear because the trial with 106 participants was a small trial and there may be power issues. It was in the non-desired direction in which a placebo was actually being favored as 8 weeks. So basically we just need more evidence in this area for cluster headache prevention, specifically galcanezumab which has the FDA approved indication. There are no serious adverse events that occurred and discontinuation due to AEs or adverse events were rare and as a result no relationship could be determined with very well quality of evidence rating. Slide 51.

So this is our last context slide or information slide before I open it up to questions. So there's no direct head-to-head evidence, which we've talked about. One way to potentially get around that is you can look at a network meta-analysis which offers indirect comparisons. We didn't talk about those in our findings today. They are in the discussion section of the report and they do address migraine prevention and acute migraine treatment. And so take a look at those. If you'd like I will tell you just very briefly about this network meta-analyses. Again, indirect comparisons which can be [inaudible]. We don't see substantial differences indicating that one CGRP inhibitor is better than another or another migraine treatment that's not a CGRP inhibitor performing better than a CGRP inhibitor. So essentially there's comparable efficacies across these different treatment. So for preventive therapy Medicaid administrators might think [inaudible] therapy, as well as additional cost. So for instance eptinezumab is intravenous infusion. The others are subcutaneous injections. So these may be relevant things to consider as you walk through this body of literature given the fact that there is comparability in a lot of our findings. So I will wrap up there and I'm happy to take any questions.

Ginni Buccola: Thanks a lot, Curtis. Are there any questions from the committee?

Alex Park: I have three questions if I might. Thank you, Curtis. Wonderfully detailed and thorough presentation and it looks like compared to our last review we have more evidence for eptinezumab so would you say it's safe to elevate that to include that in the motions being safe and efficacious with the other three drugs?

Curtis Harrod: So I think that's something for the committee to decide. What I will say is that eptinezumab as the last time we talked about this report was not approved by the FDA and so the committee may have considered that difference because of that rationale and so I think more discussion should be on with that. They did have comparable findings relative to the other CGRP inhibitors for the most part within our evidence base.

Alex Park: I don't know if it was a type-o or a good point favoring eptinezumab, but they were looking at the 75% reduction versus any of the other studies dealing with 50%. Is that right?

Curtis Harrod: That's not a type-o. They did look at that. It was the one study that raised the bar a little bit from 50 to 75 and they did report 50% as well. They did find significant differences in that 75% reduction.

Alex Park: That's good to know. I think that would help the committee in making that decision. And then my next question is just educational. You know, looking at the accessory report that you sent out—the adverse event rate on some of these studies we can go 40, 50, 60%, which sounds really high to me. But then the serious adverse event rates is quite low, usually single digit. So what kind of adverse events are they seeing and is that pretty typical in this literature?

Curtis Harrod: Yeah, it is really typical in the literature. Adverse events are basically anything that reported by a patient. So in most cases it is an injection site pain for the subcutaneous injection, which as you know is common within any type of literature looking at injectable. For serious adverse events the one that was reported, again, [inaudible] were liver enzyme. So there's some potential concern around liver functionality. They weren't different between, and I want to be clear about that in serious adverse events, they weren't different between the CGRP versus placebo, but these are randomized trials. They did the short-term follow-up and they're not necessarily powered to detect the difference there. So I do want to put those caveats as that might be something to look forward to in an observational study with a larger cohort.

Alex Park: Okay. Thanks. The last question – the oral agents they were only assessed for acute treatment not for prevention?

Curtis Harrod: That's correct.

Alex Park: Okay. Thank you.

Curtis Harrod: Thank you.

Ginni Buccola: Any other questions from the committee?

Leah Marcotte: Hi. I have one question. Do you know of any effectiveness industry files or [inaudible] sponsored trials that are ongoing right now with this medication?

Curtis Harrod: I would have to… let me look at the report real quick. There is the topiramate head-to-head study. I'll pull that up. That is a registered trial. I will note there was a June 2020 completion date, but as everyone knows June is a different month than we ever thought it was going to be. So there might be some delays in that trial of it being completed. We were pretty excited to see that comparative study at least being registered because as we talked about, all the included studies today are strictly placebo-controlled trials. So let me just pause for a second. It is erenumab versus topiramate. So 70 mg and 140 mg of erenumab and 50 to 100 of topiramate. 775 participants are enrolled in this trial and they are looking at episodic migraine.

Leah Marcotte: So that's looking at preventative?

Curtis Harrod: Episodic, correct.

Ginni Buccola: Just making sure everyone got their questions answered. Yes? Curtis, thank you again very much.

Curtis Harrod: Thank you.

Ginni Buccola: We'll move on to stakeholder input. We have three stakeholders, Chelsea Leroue with Biohaven Pharmaceuticals then Tim Wardell with AbbVie and then Carrie Johnson PharmD with Amgen. If there are any other stakeholders I haven't mentioned please go ahead and raise your hand so that we're aware that you're here. Chelsea, are you ready to go?

Chelsea Leroue: Are you able to hear me okay?

Ginni Buccola: Yes we are. You have three minutes for your time. Thank you.

Chelsea Leroue: Thank you. Good morning. My name is Chelsea Leroue and I'm from the Medical Affairs Department at Biohaven Pharmaceuticals. I appreciate the opportunity to present additional supportive information regarding ODT or rimegepant indicated for the acute treatment of migraine with or without [inaudible] in adults. Nurtec OTC is available in a 75 mg orally disintegrating tablet formulation. It dissolves rapidly within seconds

without the need for water and is the only oral CGRP antagonist with a long half-life of 11 hours. Nurtec represents a novel mechanism of action that directly targets the underlying physiology of migraine, treats migraine without the [inaudible] constrictive effects of triptans and is not associated with addiction potential or medication overuse headache. A migraine treatment is considered suboptimal if the patient experiences persistence or recurrence of their headache after taking their medication requiring them to take a second dose or additional rescue medication. A single dose of Nurtec OTC provides rapid release that lasts through 48 hours. The profile of Nurtec OTC achieves the four goals of acute migraine put forth by the American Headache Society including (1) Rapid and consistent freedom from pain and associated symptoms without recurrence. Nurtec treated patients achieved rapid pain relief within 60 minutes as well as freedom from pain and freedom from most bothersome symptom by 90 minutes and all of these efficacy endpoints were sustained through 48 hours with a single dose. (2) Restored ability to function. After taking Nurtec patients returned to normal function by 60 minutes. In a 52-week long-term study Nurtec significantly reduced migraine-related disability and lost productivity time. (3) Minimal need for repeat dosing or rescue medications. Only 14% of patients treated with Nurtec OTC rescue medication within 24 hours. 63% of Nurtec treated patients who were pain free at two hours remained pain free through 48 hours without redose or additional rescue medication. And lastly, (4) Minimal or no adverse events. The most common adverse reaction was nausea, which occurred in 2% of Nurtec OTC treated patient compared to 0.4% on placebo. In the one-year long-term [inaudible] study only 2.7% of patients discontinued due to an adverse event. No serious adverse events were related to Nurtec and no clinically relevant lab abnormalities were observed. In summary, one 75 mg orally disintegrating tablet of Nurtec provides migraine patients with rapid and sustained relief without redose or titration.

Biohaven respectfully asks the committee to consider adding Nurtec OTC as a preferred agent after trial and failure of up to two triptans or a contraindication to triptans is this is in accordance with guidance from both the American Headache Society and the Institute for Clinical and Economic Review or ICER. Thank you for your time and attention. I would be happy to answer any questions.

Ginni Buccola: Thank you, Chelsea. Any questions? We'll move on to Tim Wardell with AbbVie.

Leta Evaskus: Give me a minute while I find him in the list here. Okay, Tim.

Tim Wardell: Thank you, Leta. My name is Tim Wardell. I'm a pharmacist with AbbVie here to discuss ubrogepant brand name Ubrelvy, which was approved in December 2019 and indicated for the treatment of acute treatment of migraine with or without [inaudible] adults. Ubrogepant is an oral CGRP receptor antagonist more similar to erenumab as a receptor blocker rather than a ligand. By blocking CGRP it reduces or prevents vasodilation rather than blocking vasoconstriction like other migraine specific agents. Ubrogepant is an oral 50 or 100 mg tablet taken prn. A second dose can be taken two hours after the initial dose, if needed. The maximum dose within 24 hours is 200 mg and it has been studied in patients who have up to eight migraine or attacks within 30 days. In clinical trials, as Curtis mentioned, efficacy was studied in triptan naïve, contraindicated and non-responders in measurement of pain freedom, absence of most bothersome symptoms at two hours post dose. Both the 50 and 100 mg doses showed statistical significance for both and primary endpoints after one dose. In those that needed to redose grater efficacy was seen after a second dose. Ubrogepant was tolerable as the most common adverse events were nausea and somnolence. Of note ubrogepant has one contraindication related to use with strong [inaudible] theory F1 inhibitors. Has no warnings or precautions included CV or medication overuse headache warnings, narrow long-term safety extension study, no LFT abnormalities were found. The development was born out of a true van market scan analysis which demonstrated the episodic migrainers used two times the amounts of opioids and barbiturates compared to controlled patients. And in concert with the development of ubrogepant as an option for patients that are unresponsive, contraindicated or find triptans intolerable, AbbVie partnered with Optum to better understand triptan dosing patterns in patients with acute migraine. In a retrospect of analysis which was presented at AEN and at AHS of more than 12,000 patients with a match control more than half did not refill their index triptan and of those patients more than 50% switched to an opioid or barbiturate with no improvement in migraine days. Additionally, 22% of patients are contraindicated for triptan use due to the CV risk. With that being said AbbVie is pleased to offer ubrogepant as a non-serotonergic option to acutely treat migraine attacks. We respectfully ask for consideration of access in those patients with CV risk and a single-step edit in those patients who were unresponsive or intolerable to triptans. Thank you. Would be happy to answer any questions if there are any.

Ginni Buccola: Thank you, Tim. Any questions for Tim? Okay. Thanks again. We'll go next to Carrie Johnson with Amgen.

Carrie Johnson: Okay. Hi. Can everybody hear me?

Ginni Buccola: Yes, we can. Thank you.

Carrie Johnson: Thanks so much. My name is Carrie Johnson. I'm a pharmacist with Amgen Medical Affairs. I appreciate the opportunity to provide the committee with an update and testify in support of Aimovig or erenumab. Aimovig is a fully human monoclonal antibody to the CGRP receptor and is indicated for the preventive treatment of migraine in adults. Aimovig can be self-administered using the SureClick auto injector and comes in two dosing options. Of the injectable CGRP products Aimovig is the only one that specifically targets the CGRP receptor. Aimovig has an established tolerability profile. The most common adverse reactions in clinical studies were injection site reactions and constipation. Recent label updates to the Aimovig warnings and precautions include serious complications of constipation updated in October 2019, and new onset or worsening of pre-existing hypertension updated April of this year. Both updates were the result of post marketing surveillance. Please see the full Aimovig prescribing information for further details. The recently published American Headache Society or AHS consensus statement on integrating new migraine treatments into clinical practice provides the following two key recommendations regarding CGRP products. A monoclonal antibody CGRP or to the CGRP receptor may be prescribed after a six-week trial of two class of drugs and secondly patients who have medication overuse despite the use of preventive treatment may require an escalation dose, a change in preventive therapy, or the addition of another preventative treatment. With this recent update excluding patients with medication overuse headache from receiving preventive treatment now differs from AHS recommendations. Two updates specific to Aimovig. Long-term data is available from the Registrational Strive Study in patients with episodic migraine as a 4.5 year interim analysis of this ongoing 5-year study in patients with episodic migraine. Three-quarters of patients receiving Aimovig achieved a 50% reduction in monthly migraine days along with a reduction in pain intensity. Aimovig was generally well tolerated, no increase in adverse events over time, and no new safety signals were observed. Long-term data is also available from the registrational phase to chronic migraine study at one year two-thirds of chronic migraine patients converted to episodic migraine. Injection site reaction and constipation were the most commonly reported adverse events and no new safety signals were observed in that long-term set either.

Migraine pathophysiology is most factorial and complex and migraine is a very heterogeneous disorder. No two patients' migraine experiences or

response to treatment are the same. Aimovig has demonstrated long-term safety and efficacy showing sustained reduction in monthly migraine days, has a unique mechanism of action among the injectables and comes in two different dosing options that can be self-administered. We respectfully request that the committee add Aimovig to the preferred drug list so that the providers have therapeutic options. Thank you for your time and I'm happy to address any questions. The comparative study that was referred to earlier just completed. It was a little delayed because everything… so we're expecting results any time now. Any other questions?

Ginni Buccola: Thank you, Carrie. Are there any questions for Carrie? Okay. Thanks very much.

Leta Evaskus: I have one more stakeholder, Maria Agapova. I have unmuted you.

Maria Agapova: Good day. My name is Maria Agapova. I'm an outcomes liaison at Telepharmaceuticals. Thank you for the opportunity to address the committee this morning. I'm going to be speaking in support of Ajovy fremanezumab injection and providing just additional information atop the DERP report.

First and foremost I want to update the committee that the Ajovy auto injector become available in April of this year making Ajovy the only long-acting self-administered subcutaneous anti-seizure therapy with the option of monthly and quarterly dosing allowing for as few as four times per year either with the auto injector or the pre-filled syringe, which is ultimately very important in this time and day.

I wanted to also provide exploratory analysis looking at that 75% reduction in monthly average migraine days for episodic migraine patients. One in four reached that threshold of 75% in treatment versus 1 in 7 taking placebo and then in chronic migraine 1 in 5 patients achieved 75% reduction in headache days of at least moderate severity compared to 1 in 10 taking placebo. I also wanted to note reductions in acute medications is very important for patients who may be over-using acute medications and then a post hoc analysis of chronic migraine patients taking Ajovy we saw pretty nice reductions in that. In the open label extension study period reversion out of medication over-use endured through month 12 in roughly 60% of patients with acute medication over-use at baseline.

And then I'm going to move on to safety. So we looked at 24 clinical studies of Ajovy in 4,777 patients with migraine exposed to Ajovy and no

additional safety signals were seen across the exposed population. Phase 2 and B and Phase 3 pooled data, that's about 2,500 patients adverse reports were about 48 to 69% as was quoted by Dr. Park. But most of those were mild to moderate severity and serious adverse events and adverse events leading to discontinuation were infrequent and had similar incidence across groups.

I wanted to draw your attention to patient's cardiovascular safety profiles. We saw cardiovascular safety profiles similar to placebo, about 1% of adverse events or patients that had adverse events associated with that, and in patients with cardiovascular medical history—hypertension, hyperlipidemia and those types of risk factors, no new safety signals were detected and long-term open-label blinded extension study hypertension occurred in 2% of Ajovy treated patients. No worsening of hypertension over 12 months in patients with history of baseline hypertension was observed. And then in a post-marketing period hypertension [inaudible] identified as a safety signal. Just a note we did look at the [inaudible] database analysis with normalizing by claims and saw the post-marketing [inaudible] do differ by monoclonal antibody. That was presented recently at [inaudible].

Then moving to constipation…

Ginni Buccola: Your three minutes are up so if you could conclude that would be great.

Maria Agapova: Sure. I was on my last sentence. Again, showing that only 1% of patients reported constipation and that was correlated in the post-marketing data, as well. Thank you. I apologize for the little overage.

Ginni Buccola: No problem. My apologies for interrupting your last sentence. Any questions for Maria? Thank you very much. I believe that concludes our stakeholders for CGRPs and it looks like we can move to the motion.

Alex Park: I'm looking at the motion and I would like to recommend we strike the last paragraph about eptinezumab in light of the new data that Curtis provided. I'm open to discussion from the committee on that.

Ginni Buccola: I would agree with you. It seems like an appropriate change to make.

Alex Park: Thanks, Ginni. Let's see, Leta, if we do that we will probably also want to put eptinezumab into the body of the first paragraph.

Donna Sullivan: Was this a full report? An update?

Leta Evaskus: Yes, it is.

Donna Sullivan: And so are those other two products on the market, do those need to be added?

Leta Evaskus: Yes, if the committee wants them added.

Alex Park: So if we did that do we have to create a separate paragraph, Donna, because it looks like we're talking about the original four drugs in terms of migraine prophylaxis and the other two new agents would be acute treatment.

Donna Sullivan: If you feel that they should be included in the class and if you feel that they should be first line treatment you could put them in there or you could make another paragraph or just add another sentence.

Alex Park: I would be in favor of doing a separate paragraph calling out those two drugs for acute treatment as second line given the short-term single-attack design of the trials and the relative newness of the FDA approval.

Nancy Lee: I would echo that. It's not for chronic migraine is it? Or acute?

Leta Evaskus: Acute. Do you want me to put as a second line agent in that sentence?

Alex Park: I think that would be appropriate. Donna, do we have to say something about interchange for those, as well?

Donna Sullivan: Yes, you should.

Alex Park: Okay. Thanks.

Donna Sullivan: And they would be subject to interchange between the two, not between the entire class.

Alex Park: Yes, that makes sense because of their unique approvals for acute treatment.

After considering the evidence of safety and efficacy for the treatment of migraine prophylaxis, I move that eptinezumab, erenumab, fremanezumab, galcanezumab are safe and efficacious for the treatment of their approved indications. These CGRP inhibitors should be second line agents on the Washington PDL. Erenumab, fremanezumab, galcanezumab and eptinezumab can be subject to therapeutic interchange in the Washington preferred drug list.

After considering the evidence of safety and efficacy for the treatment of acute migraine, I move that rimegepant and ubrogepant are safe and efficacious for the treatment of their approved indications as second line agents on the Washington PDL. Rimegepant and ubrogepant can be subject to therapeutic interchange with each other in the Washington preferred drug list.

Nancy Lee: I second that motion.

Ginni Buccola: All in favor say aye.

Group: Aye.

Ginni Buccola: Are there any opposed? Reiteration of the prior motion carries. Thanks for the expert wordsmithing on the motion. I believe that we are going to go ahead and adjourn the P&T Committee meeting portion of our meeting. It was a quick one this morning and we will convene the DUR Board and we look to Umang Patel to start our review of oncology agents.

Donna Sullivan: Umang, we can't hear you.

Leta Evaskus: I don't see that you are on audio. You may not have put in your audio pin number.

Umang Patel: Can you hear me?

Leta Evaskus: Yes. Now we can hear you. Thank you.

Umang Patel: Okay. Can everyone see… my web cam is on as well?

Leta Evaskus: Yes.

Umang Patel: Okay. Great. So we'll go over some of the topics here today. Just to remind the committee, as we did in June, what we will do is more of an updated review of some of these topics. Any new clinical information, new medications, updates to formulations or strengths, or indications in the last one year will be reviewed. Otherwise anything older than that will not be reviewed. Some of these classes do not have any reviews whatsoever and so there is no information that will be reviewed there. We'll go ahead and get started.

For the first class or large umbrella class will be oncology agents. So if you go to slide 4, Leta. We've broken these down into the subclasses that Apple Health PDL has them divided into. So as you can see here there are going to be 13 different subclasses here. We do have the androgen biosynthesis inhibitors that have no updates. Again, bold on this slide does indicate the specific medication has an update. Antiandrogens oral medications updates for Erleada and Xtandi. The next subclass will be antineoplastic miscellaneous. And we'll have an update regarding Kisquali Femara. We have the Braf kinase inhibitors along with the Cyclin dependent… the CDK inhibitors where we will review Ibrance. FGFR kinase inhibitors and the hedgehog pathway along with the MEK inhibitors do not have any updates there. We'll have the MTOR kinase inhibitors reviewing everolimus and no updates for the multikinase inhibitors. And then or the ADP ribose… the PARP inhibitors we will touch on Zejula, Lynparza and Rubraca. And then there are no updates for the retinoids or topoisomerase inhibitors or the tropomyosin receptor kinase inhibitors either.

So moving on to our first medication here. On the next slide you see Erleada. I apologize for my pronunciation. Some of these are a little bit tough. Again, bold on these slides does indicate pertinent updated information. So in September 2019 the FDA approved expanded indication for the treatment of metastatic castration-sensitive prostate cancer. Previously it was only approved for non-metastatic castration-resistant prostate cancer. Again, the warning and precautions are all the same. I will go over them initially and if there are any differences in different classes then I will highlight those. So there are warning precautions – ischemic cardiovascular events occurred in patients receiving treatment. Fractures have occurred in patients. Falls have occurred in patients receiving patients with increased incidence in the elderly as one can imagine. Seizures occurred in less than 1% of patients receiving treatments. And lastly embryo-fetal toxicity as well. The dosage and availability for the committee's reference. In terms of special populations for patients who are renally-impaired. There are no clinical significant differences in renal or hepatic impairment being mild to moderate and for hepatic that's child [inaudible] A as in Alpha, B as in Beta. The severe renal or hepatic impairment there's unknown effects on the PK on the pharmacokinetics.

On the next slide here we'll pivot over to Xtandi. And in December 2019 the FDA approved expanded indication for the treatment of patients with metastatic castration sensitive prostate cancer. It was already indicated for patients with castration-resistant prostate cancer. The warnings and precautions are very similar to the previous slide so I won't go over them

again. And the dosage and availability, as you can see, are available here. Some of these slides may go faster than others, because these are all kind of lumped in the same class. There are a lot of overlap and just for time sake, since my time is limited for these classes, I will kind of go through them, but if the committee has any questions I'm more than happy to go back or review something specifically, as well.

On the next slide here we do have Kisqali Femara co-pack. So in September 2019 the FDA approved expanded indications for the initial endocrine-based therapy for the treatment of pre and perimenopausal or postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer. Previously this was approved in postmenopausal women only. For the warnings and precautions there are some different ones to highlight here so I'll only look at the ones that are different from the previous. There is a QT interval prolongation. So it's recommended to monitor ECGs and electrolytes prior to treatment. Repeat ECGs approximately day 14 of the first cycle and beginning of the second cycle, and as clinically required. Hepatobiliary toxicity – so there is an increase in transaminase levels. So LFTs… monitoring LFTs is recommended every two weeks for the first two cycles. Neutropenia as one can imagine. It is recommended to perform a CDC before initiating therapy and to monitor them every two weeks for the first two cycles. And lastly, as I mentioned before, embryo-fetal toxicity in a lot of these oncology medications. No update to the dosing and availability. And for special populations with renal impairment and hepatic impairment there's no adjustment in mild to moderate for either of those. There is a dose reduction in the… for both ribociclib portion to 200 mg once daily and no adjustment for letrozole for renal impairment. And to flip it for hepatic impairment there is a reduction in letrozole to 2.5 mg and lower dose for ribociclib as well.

Moving on to the next medication we have is Braftovi. In April 2020 the FDA approved the new indication in combination with cetuximab for the treatment of adult patients with metastatic colorectal cancer with a BRAF V600E mutation, as detected by an FDA approved test, after prior therapy. It is not indicated for the treatment of patients with wild-type BRAF melanoma or wild-type BRAF CRC. And then additionally separately from this, but in April 2020, as well, the FDA approved a companion diagnostic, the therascreen BRAF V600 E RGQ PRCT kit for the approved indication that I mentioned a second ago. It does have other indications as you can see under the indications tab here. The warning precautions are very similar to the previous ones. Some of the newer ones being new primary malignancies cutaneous and non-cutaneous can occur. It is recommended monitor for malignancies and perform dermatologic

evaluations prior to, during and following discontinuation of treatment. Tumor promotion in BRAF wild-type tumors have increased, cell proliferation can occur. And lastly major hemorrhagic events can occur, as well.

Moving on to the next slide here we do have Ibrance and in November 2019 the FDA approved a new tablet formulation. No changes in indications. It was a kinase inhibitor indicated for the treatment of adult patients with hormone receptor positive, human epidermal growth factor reception 2 negative advanced or metastatic breast cancer in combination with an aromatase inhibitor for initial treatment in postmenopausal women or men, or in combination with fulvestrant in patients with disease progression following endocrine therapy.

In terms of warnings and precautions you do see some of the same ones except interstitial lung disease or pneumonitis has been seen. Severe or fatal cases have been reported and it is recommended to monitor for pulmonary symptoms. As I mentioned there was a new formulation of tablets. As you can see the dosing is identical to the capsules. It just now comes in a tablet form.

Moving on to Afinitor. From January 2020 the FDA approved the first generic Afinitor from Par Pharma for 2.5, 5 and 7.5 mg and Teva, again, 2.5, 5, 7.5 and 10 mg and Par and Endo have announced they have launched their products already and this, again, eight months ago. Indications – here you can see postmenopausal women with advanced HER2 negative breast cancer in combination with exemestane after failure of treatment, adults with progressive neuroendocrine tumors of pancreatic origin, and adults with progressive, well-differentiated, non-functional neuroendocrine tumors of GI or lung origin that are unresectable, locally advanced or metastatic. Adults with renal cell carcinoma after failure of treatment with sunitinib or sorafenib and lastly adults with renal angiomyolipoma and tuberous sclerosis complex not requiring immediate surgery.

Again, there is a black box warning with this medication. Only physicians experienced in immunosuppressive therapy and management of transplant patients should prescribe this medication and to avoid nephrotoxicity, reduce doses of the medication when used in combination with cyclosporine.

Dosing and availability, as you can see, are listed below.

Moving onward so next is Zejula. Now in May 2020 the FDA approved a new indication for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy; previously indicated only for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based therapy. Again, no significant different warning or precautions here and dosing and availability is unchanged as well. Dosing is stratified by indication and can be found in the TCRs that are in the web portal for the committee or in the package insert.

On the next slide we have Lynparza. Now there were multiple updates to this medication so I kind of broke it down by significant updates even though the dates are the same. In May 2020 the FDA approved a new indication for the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. In the same month and year the FDA approved in combination with bevacizumab for the maintenance treatment of adults with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency positive status defined by either a deleterious or suspected deleterious BRCA mutation, and/or genomic instability. And lastly in the same month and year, the FDA approved a new indication for the treatment of adults with deleterious or suspected deleterious germline or somatic homologous recombinant repair gene-mutated metastatic castration-resistant prostate cancer in patients who have progressed following prior treatment with enzalutamide or abiraterone.

I reviewed the indications there. With warnings and precautions very similar warnings and precautions coming through. A newer on here, venous thromboembolic events can occur including pulmonary embolism in up to 7% of patients with mCRPC. Monitor patients for signs and symptoms of VTE or PE and treat as medically appropriate.

Now the last medication here we have Rubraca. So in May 2020 the FDA approved a new indication for the treatment of adults with deleterious BRCA mutation germline and/or somatic associated metastatic castration-resistant prostate cancer who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy. The FDA approved test to detect BRCA1/BRCA2 mutations in patients

with the mCRPC, but it is not currently available yet. As you can see the indications are stratified by ovarian and prostate cancer. The update being in the prostate cancer indication with the warning of precautions. A newer one that we are seeing today is MDS/AML so it can occur in patients exposed to treatment and in some cases more fatal. Monitor patients for hematologic toxicity at baseline and monthly and discontinue the medication if it is confirmed.

With oncology agents that concludes the first half of oncology agents. I know according to the agenda there is a break here before we resume the TKIs so I will pause here for the committee chair.

Ginni Buccola: Looking for feedback from the group if you'd like to continue with the oncology agents or take a break? All right. I don't hear any feedback so I'm going to go ahead and stick with the agenda and… hate to be wishy-washy, but we're not at 10:45 yet. So Umang, do you want to go… are you comfortably going ahead?

Umang Patel: Absolutely. I just wanted to make sure that I didn't stray from the agenda.

Ginni Buccola: Oh no. We'll go ahead and finish up that section and then go to break. Thanks!

Umang Patel: Perfect. So on the next slide here you'll see that oncology agents, as I mentioned earlier, were broken down by different subclasses. So here you can see the next class we'll be going over are the TKIs and this a more substantial class. That's why it kind of received its own little category on the agenda. As I mentioned earlier the bold indicates significant clinical information. So we'll be reviewing Calquence, Inlyta, Ayvakit, Alunbrig, Tabrecta, Lenvima, Nerlynx, Turalio, Qinlock, Tukysa and Brukinsa, as well. Again, I apologize if I misprounced any of those.

Moving right along. So the first medication here we have Calquence. So in November 2019 FDA approved a new indication for the treatment of adult patients with CLL, chronic lymphocytic leukemia or SLL, small lymphocytic lymphoma who is already approved for adults with Mantle cell lymphoma, MCL, who have received at least one prior therapy.

Warnings and precautions – serious and opportunistic infections may occur. So it is very important to monitor for signs and symptoms of infection and treat promptly. Hemorrhage, cytepenias as we mentioned being an oncology class that's somewhat expected, and lastly afib and

atrial flutter. So monitor for symptoms of arrhythmias and manage appropriately. No dosing or availability changes here.

Moving right along to the next update, which is Inlyta. So for Inlyta in June 2020 the FDA approved a new indication in combination with avelumab or pembrolizumab for the first-line treatment of patients with RCC advanced renal cell carcinoma. Previously it was approved as a single-agent for the treatment of advanced RCC after failure of one prior systemic therapy. As you can see it does have the other indication I just mentioned, unbolded. In terms of warnings and precautions hypertension and hypertensive crisis are something to monitor with this medication. It has been observed. So blood pressure should be well controlled prior to treatment and obviously monitoring during and after treatment is recommended. Arterial and venous thromboembolic events have been observed as well and can be fatal as one can imagine. So use with caution in patients who are at increased risk for these events. And lastly, cardiac failure. So cardiac failure has been observed in patients taking this and as you can imagine it can be fatal. So monitor for signs and symptoms throughout treatment. Dosing and available – there are no changes here.

Moving right along to Ayvakit. So in January 2020 the FDA approved a new drug indicated for the treatment of adults with unresectable or metastatic GI stromal tumor or GIST harboring a platelet-derived growth factor receptor alpha exon 18 mutation, including PDGFRA D842V mutations. Since this is a new drug I will kind of go through all of the information for this. The warning and precautions intracranial hemorrhage has been noticed with whole treatment for Grade 1 or 2 reactions until resolution and then resume at a reduced dose. Permanently discontinue this for recurrent Grade 1 or Grade 2 reaction or first occurrence of a Grade 3 or Grade 4. There have been some CNS effects, primarily things such as cognitive impairment, dizziness, sleep disorders. It depends on the severity. You can continue this medication at the same dose, withhold it and then resume it at the dose, or just reduce it. Again, it depends on the symptom and the severity of it. And lastly embryo-fetal toxicity as we've mentioned before with other comparable medications. Dosing is 300 mg once daily and available in tablets as 100, 200 and 300 mg. Since this is a new drug here pediatrics there have been no safety and efficacy established for any pediatric patients. In terms of impairment for both rental and hepatic, mild to moderate in both renal and hepatic require no dosage adjustment. In terms of severe the dosage is not yet established.

The next medication is Alunbrig. So in May 2020 the FDA approved a new drug indicated for the treatment of adult patients with anaplastic lymphoma kinase or ALK positive metastatic non-small cell lung cancer as detected by an FDA-approved test; patients should be selected for treatment of metastatic NSCLC based on the presence of ALK positivity in tumor specimens. Now in terms of warnings and precautions there is ILD pneumonitis, which we saw in similar medications previously, hypertension, as well. I'm not going to review if a warning or precaution has already been touched on by a similar medication, I won't review that specifically. Bradycardia. So health care practitioners are recommended to monitor heart rate and blood pressure regularly during the treatment and if patients are symptomatic withhold and then once the bradycardia has resolved you can restart the treatment at a lower dose. And then embryo-fetal toxicity, as well.

The dosage here is 90 mg once daily for the first seven days; then increase to 180 and the availability in tablets is there in front of you. Similarly to the previous medication, pediatric safety and efficacy has not been established in this one and dose reduction adjustment is recommended only for severe renal and hepatic impairment, nothing for mild or moderate in either renal or hepatic.

The next medication here we have Tabrecta. In May 2020 the FDA approved a new kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer whose tumors have a mutation that leads to a mesenchymal-epithelial transition exon 14 skipping as detected by an FDA approved test; and then the FDA also approved the FoundationOne CDx assay as a companion diagnostic test.

Warnings and precautions – as we've seen before ILD pneumonitis and embryo-fetal toxicity. A newer one that we are yet to see hepatotoxicity so it is important to monitor liver function tests. Withhold, dose reduce, or permanently discontinue based on the severity. Dosing is 90 mg once daily for the first seven days and then you increase it to 180 and the availability in tablets is 150 and 200 mg.

The next medication is Lenvima. So in September 2019 the FDA approved expanded indication for the use in combination with pembrolizumab, for the treatment of advanced endometrial carcinoma that is not MSI-H or dMMR, in patients with disease progression after prior systemic therapy and are not candidates for curative surgery or radiation. As you can see it does have a litany of other indications, as well here. The dosage is indication based, as well, as you can see in front of you. And the availability is in capsule form here. In terms of

impairment, very similar to others – severe hepatic or renal impairment does require dose adjustment, mild to moderate does not.

On the next slide here we have Nerlynx. So in February 2020 the FDA approved for the use in combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2 positive breast cancer who received two or more prior anti-HER2 based regimens in the metastatic setting; already indicated as a single agent, for the extended adjuvant treatment of adults with early stage HER2 positive breast cancer to follow adjuvant trastuzumab-based therapy.

As I mentioned earlier with similar medications warnings and precautions here hepatotoxicity, embryo-fetal toxicity.

Dosing – as one can imagine is indication based. So as it is stratified here. And availability is down below.

The next medication is Turalio. And so for this medication here August 2019 the FDA approved Turalio for the treatment of adults with symptomatic tenosynovial giant cell tumor associated with severe morbidity or functional limitations and not amendable to improvement with surgery.

In terms of warnings and precautions there is embryo-fetal toxicity with this, as well and there are some black box warnings that would be fruitful to review. It can cause serious and potentially fatal liver injury. So it's recommended to monitor LSTs prior to treatment and at specified intervals with hold the dose or reduce or permanently discontinue it in case the patient does show signs of hepatotoxic beyond any spectrum. And it is available only through a restrictive program called the Turalio REMS Program.

Recommended dosing is 400 mg twice daily and the availability is in capsules, 200 mg. For this medication, again, safety and efficacy in pediatrics has not been established and only mild to severe renal impairment does require dose adjustment and moderate to severe hepatic impairment does not have established dosage adjustment yet.

The next medication here is Qinlock and so for Qinlock we do see in May 2020 the FDA approved this medication for the treatment of advanced GI stromal tumor who have received at least prior treatment with three or more kinase inhibitors, including imatinib. The warnings and precautions are very similar in embryo-fetal toxicity. Newer ones that we are seeing here are risk of impaired wound healing. So it is recommended to

withhold the treatment for at least one week prior to elective surgery. To not administer for at least two weeks after a major surgery and until adequate wound healing. The safety and resumption of this medication after resolution of wound healing complications have not been established yet. New primary cutaneous malignancies have been observed. So it is recommended to perform dermatologic evaluations when initiating this medication and routinely during treatment. And lastly cardiac dysfunction. It is recommended to assess ejection fraction by echocardiogram or MUGA scan prior to initiating treatment, during treatment, as clinically indicated. And discontinue if the patient has Grade 3 or 4 left ventricular systolic dysfunction.

Recommended dosage is 150 mg once daily and it's available in tablet forms.

Leta Evaskus: Umang, this is Leta. Can we pause here and take a 10-minute break? Ginni, is that okay?

Ginni Buccola: Of course and my apologies for missing that break mark. Thanks, Leta.

Leta Evaskus: No problem. So let's reconvene at 11:00. It's 10:48.

Ginni Buccola: That sounds great.

Leta Evaskus: Okay. Thank you.

Ginni Buccola: Umang, we'll turn it back to you to finish and then we'll go to our stakeholders. Thanks.

Umang Patel: Sounds great. So we'll pick up right where we left off. On the next slide we'll pick up with Tukysa. So in April 2020 the FDA approved this medication for the treatment of adult patients with advanced unresectable or metastatic HER2 positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2 based regimens in the metastatic setting. The warnings and precautions as you can see are very common. In embryo-fetal toxicity we've reviewed. Hepatotoxicity as well. Diarrhea – so severe diarrhea has been seen with this medication including dehydration, acute kidney injury and death have been reported. So it is recommended to administer antidiarrheal treatment as clinically indicated. The recommended dosage 300 mg twice daily with or without food and there's a dose adjustment if a patient is hepatically impaired, as well. The availability in tablets is there, as well.

The next slide, the last medication in the kinase inhibitor class is Brukinsa. So November 2019 the FDA approved Brukinsa in the treatment of adult patients with mantle cell lymphoma who have received at least one prior therapy. This indication is approved under the accelerated approval program based on overall response rate. Continued approval of this indication may be contingent upon verification and description of the clinical benefits based in a confirmatory trial. Warnings and precautions – a lot of these, again, embryo-fetal toxicity we discussed. Hemorrhage, as well. Patients can be at an increased risk of infections. So it is incumbent to monitor for signs and symptoms. Cytopenias as we've discussed before. Secondary primary malignancies – so patients have been observed to have other malignancies including skin cancers. So it is advised to tell patients to use sun protection. And lastly, cardiac arrhythmias such as afib and atrial flutter.

The dosage 160 mg twice daily or 320 once daily. And there's a dose adjustment recommendation for hepatic impaired patients. The availability, as you can see here, is in capsules.

That is the over-arching oncology medications we've gone through, which had various subclasses along with ending it with the TKIs. Any questions at all?

Ginni Buccola: Thanks, Umang. That was a lot of information. We appreciate it. Any questions from the committee? Okay. We're ready to move to stakeholder input. It looks like we have four stakeholders listed. If you don't hear your name called could you please raise your hand and let us know? We will be hearing from Vilasini Ravanam with Pfizer, Mark Balk with BeiGene, Julie Baker with Deciphera Pharmaceuticals, and Long Nguyen with GSK. So we'll go first to Dr. Ravanam with Pfizer and you'll have three minutes for your comments.

Vilasini Ravanam: Thank you. So my name is Vilasini Ravanam with Pfizer Oncology Medical Affairs. I have a PhD in clinical oncology. I'm here to provide the committee with efficacy and safety information for Braftovi in metastatic colorectal cancer. The first and only approved targeted regimen for this population of patients. Based on data and published literature from [inaudible] Society the estimated numbers of patients with metastatic [inaudible] is close to 174,000 and of this about 50% have the mutation. Coming to the indication Braftovi or encorafenib is indicated in combination with isatuximab for the treatment of adult patients with metastatic CRC hovering a [inaudible] new patient as detected by an FDA approved test after prior therapy. Limitations of use is that this drug is not indicated for the treatment of patients with [inaudible]. According to

the current [inaudible] guidelines Braftovi in combination with isatuximab is the only category 2 recommendation in BRAF V600 E mutant patients who had progression on therapy for advanced or metastatic disease and who have not been previously treated. As for the rationale coadministration of Braftovi with isatuximab had a 92 [inaudible] greater than either drug alone in [inaudible] of CRC with this unique mutation the BRAF V600 E. So Braftovi is a kinase inhibitor of BRAF V600 E as well as [inaudible]. Isatuximab is a monoclonal antibody antagonist that binds [inaudible]. The recommended starting dose of Braftovi 300 mg, 475 mg capsule taken orally once daily. The recommended dose adjustment for certain age for Braftovi and as for isatuximab it is advised to refer to the prescribing information for recommended isatuximab dosing information.

Related to efficacy in the randomized space three activity controlled open label trials on patients who were previously treated and with a disease progression of one or two tried therapies this patient was treated in the combination of Braftovi and isatuximab and demonstrated statistically significant improvement in overall survival compared to the control arm showing a medium overall survival of 8.4 months versus 5.4 months on the control arm, which is [inaudible] with isatuximab [inaudible] with isatuximab. The medium fall off for this was 7.8 months.

As for the clinical safety profile the months [inaudible] in more than 25% of the patients who received this combination were fatigue, nausea, diarrhea, dermatitis, abdominal pain, decreased appetite, [inaudible] and rash. Other clinical importance is occurring in less than 10% of the patients where isatuximab was pancreatitis. The most common lab abnormalities greater than 20% are great as compared to the control arm were mainly anemia and lymphopenia.

Ginni Buccola: Dr. Ravanam, I'm sorry to interrupt, but your three minutes are up. If you could conclude.

Vilasini Ravanam: Okay. Just the last sentence that in conclusion adding this combination will offer a new treatment option for this patient. I'll stop here and I can take any questions at this time.

Ginni Buccola: Thank you very much. Are there any questions from the committee? Thank you, again. We'll go ahead and move to Mark Balk with BeiGene.

Mark Balk: Great. Thank you very much. As mentioned, my name is Mark Balk. I'm a PharmD with medical affairs at BeiGene. Thanks, Umang, for doing a good job going through the drug review. So I'm going to talk about

zanubrutinib Brukinsa in a very accelerated fashion. So as Umang mentioned it's been approved as a BTK for treatment of adult patients with mantle cell lymphoma who have received at least one prior therapy for those patients who relapsed refractory and it was approved by the FDA November 14, 2019 and been incorporated into the NCCN clinical guidelines for with mantle cell lymphoma within two weeks later. The efficacy of Brukinsa was assessed in two different studies that are outlined in the package insert so I won't cover those to any great extent except just going on to the primary efficacy endpoint that for both studies the overall response rate assessed by independent review committee was consistent that 84% across both studies, including complete response rate to 59% in the Phase 2 study and 22% in the Phase 1 2 dose ranging study. For safety there are no contraindications to the use of Brukinsa. Warnings and precautions were outlined nicely, again, by Umang and those are by enlarge class effect for the BTK inhibitors. So the most common adverse reaction include [inaudible] count decrease, the cytopenia that Umang had mentioned. So neutropenia, [inaudible] apenia, upper respiratory tract infection, rash, bruising, diarrhea and cough. So some of the other important aspects that Brukinsa can be given in either a 320 mg once daily or 160 mg twice daily regimen can be given with or without food. No clinical significant differences in pharmacokinetics was observed when given with gastric acid reducing agents. No adjust of dose needed for patients with mild to moderate renal or hepatic insufficiency and Brukinsa can be used with dose reductions with strong or moderate CYP3A inhibitors and in patients with severe hepatic insufficiency. One other thing that I'll mention is that the pricing on the drug has been introduced at about 7 to 8% lower than the two competitive agents on the market. Lastly, just the request that given Brukinsa's efficacy and safety profile we'd ask the members of the committee to consider the data presented and allow for patients with relapsed refractory MCL in the state of Washington to have access to Brukinsa. I'll stop there within my three minutes.

Ginni Buccola: Thanks Dr. Balk. Any questions from the committee? Okay. We'll move on. Thank you. Going next is Julie Baker with Deciphera.

Julie Baker: Good morning. My name is Julie Baker with medical affairs representing Deciphera Pharmaceuticals and I appreciate having the opportunity to present some information on Qinlock, which is also known as ripretinib and which was very well reviewed by Unam a minute ago. Qinlock is indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor, also known as GIST who have received prior treatment with three or more kinase inhibitors including imatinib. Recommended dosage of Qinlock is 150 mg orally once daily with or

without food until food progression or unacceptable toxicity. Qinlock has been proven effective in [inaudible], an international multi-center double-blind placebo-controlled trial. One hundred twenty-nine patients were randomized in a two to one ratio to Qinlock 150 mg once daily or placebo. Primary efficacy outcome measures were PFS based on disease assessment by blinded independent functional review using ratified resist 1.1 criteria and the medium PSF was significantly improved by Qinlock compared with placebo, which was 6.3 months versus 1 month. The hazard ratio was .15 and the P value was less than .0001. Most common adverse reactions in 20% or more of patients were alopecia, fatigue, nausea, abdominal pain, constipation, myalgia, diarrhea, decreased appetite, Palmar plantar erythrodysesthesia syndrome or PPES and vomiting. The most common Grade 3 or 4 lab abnormalities in 4% or more were increased by pace in decreased phosphate. Serious adverse reactions that occurred in more than 2% of patients were abdominal pain, anemia, nausea and vomiting. Regarding warnings and precautions with PPES in [inaudible] Grade 1 to 2 PPES occurred in 21% of the 85 patients who received Qinlock and based on severity you should withhold and then resume at the same or reduced dose.

Regarding new primary cutaneous malignancy in [inaudible] carcinoma occurred in 4.7% of 85 patients who received Qinlock with the median time of 4.6 months and a range of 3.8 to 6 months. Melanoma occurred in 2.4% of the 85 patients who received Qinlock. With hypertension in Invictus Grade 1 to 3 hypertension occurred in 14% of the 85 patients who received Qinlock including Grade 3 hypertension and 7%. Do not initiate in patients with uncontrolled hypertension and based on severity withhold and then resume at the same or reduced dose or primarily discontinue. Function in Invictus cardiac failure occurred in only 1.2% of the 85 patients who received Qinlock Grade 3 projection fraction occurred in 2.6% of the 77 patients who received it and who had a baseline at least 1 post baseline echocardiogram. Safety has not been assessed in patients with a baseline injection fraction below 50% and permanently discontinue for Grades 3 or 4 left ventricular systolic dysfunction. Regarding risk of impaired wound healing Qinlock has the potential to adversely affect wound healing. Withhold for at least one week prior to elective surgery and do not administer for at least two weeks following major surgery and until adequate wound healing. Lastly, embryo-fetal toxicity based on findings from animal studies and the mechanism of action Qinlock can cause fetal harm when administered to a pregnant woman and advise pregnant woman of the potential [inaudible] to a fetus. Please refer to the Qinlock prescribing information for complete product information including warnings and precautions. I'll close with a statement that will request based on today's testimony to

Deciphera Pharmaceuticals requests that Qinlock be added to the preferred drug list. I thank you and I will be happy to answer any questions you may have.

Ginni Buccola: Thank you, Julie. Any questions from the committee? Okay. Thanks. Moving next to Long Nguyen with GSK.

Leta Evaskus: Long, I see that you are self-muted.

Long Nguyen: Can you hear me now?

Leta Evaskus: Yes.

Long Nguyen: Great. Thank you everyone. Good morning. My name is Long Nguyen and I am the Health Outcome Liaison at GlaxoSmithKline here to provide you additional comments on Zejula. Prior to the year 2020 [inaudible] inhibitors monotherapy are only indicated for ovarian cancer patients with a BRCA positive status, which compromised of only about 25% of all patients diagnosed with this disease. The other 75% of patients with a BRCA negative status are more difficult to treat with limited options available.

Like Dr. Patel mentioned in his report, Zejula was approved in May as a monotherapy for the maintenance therapy for all patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to first line platinum based chemotherapy in all patients regardless of biomarker status and unlike other PARP inhibitor the indication does not require an FDA approved companion testing. The approval based on the results of the Prema Registration Trial demonstrated a 50% and 60% reduction in risk of progression and death in patients with a BRCA negative and BRCA positive biomarker status respectively. This expanded patient population indication received a Class 2A recommendation as a preferred single-agent in the updated NCCN guidelines in March of this year.

The approval of the Prema Trial also include an implementation of an individualized dosing strategy where patients weighing less than 77 kilos and/or a platelet count of less than 150,000 cells per microliter should initiate Zejula at 200 mg instead of the normal starting dose of 300 mg once a day. The implementation of an individualized dosing regimen reduced the [inaudible] of Grade 3 or more hematologic adverse events seen in the trial by 35 to 59% compared to the fixed dose regimen.

In summary, Zejula is currently the preferred PARP inhibitor on the Washington PDL and Apple Health drug list and with the advantages and Zejula discussed previously over other agents in the same class, I ask that the committee continue to maintain its status allowing more patients diagnosed with this dismal disease to be treated. Thank you so much for your time and attention. I'll be happy to address any questions the committee may have.

Ginni Buccola: Thank you Dr. Nguyen. Any questions from the committee? Okay. Are there any other stakeholders who didn't have a chance to be heard?

Leta Evaskus: I do not see any other stakeholders.

Ginni Buccola: Okay. Let's go ahead and move to the motion.

Marissa Tabile: Sorry to interrupt. I forgot to mention at the beginning you should have gotten a link to the PDL publication so… just because we're all digital now we couldn't offer anything printed. We did offer you guys a link to the publication so you can see what products are preferred and non-preferred. So if you wanted to review any of those particular classes just let me know and we can go through them on the publication if you would like.

Ginni Buccola: Thank you. I'll open it up and make sure the committee gets a chance to chime in now if there is anything specific we should pause to review.

Marissa Tabile: Okay. Sounds great. And you should be able to search for it using the filters at the top. So if anybody has any issues just let me know and we can kind of walk through how to use it.

Ginni Buccola: Great. Committee members, is there any need for time or specific questions about reviewing that document? Does everybody feel ready to move to the motion? Just chime in if you are not ready. Okay. So we'll move back to the motion then.

Leta Evaskus: If you want to tell me when you're ready for the next slide…

Ginni Buccola: Thanks Leta. Let me just bring my camera up to feel a little more active. Yeah, I would go ahead, please and go ahead to the next slide. I'm going to have Leta go ahead. Again, committee, chime in if we are moving too fast or we need to stop. We'll pause here. Next slide.

Connie Huynh: So I move that all products in the drug class as listed on slides 2 and 3 are considered safe and efficacious for their medically-accepted indication

and are eligible for preferred status and grandfathering at the discretion of HCA. Products in these classes may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Jordan Storhaug: I second the motion.

Ginni Buccola: All those in favor please say aye.

Group: Aye.

Ginni Buccola: Any opposed? The motion carries.

Leta Evaskus: Since we're just at 11:22 I would suggest continuing with the ophthalmic agents up until around 12:00 when we can have lunch. Does that work?

Ginni Buccola: That sounds great to me. If Umang is ready to go, let's go for it.

Umang Patel: Absolutely. Okay. We'll go ahead and move right along to the ophthalmic agents, specifically glaucoma agents here. As I mentioned earlier, again, just to remind the committee, we're only focusing on any new pertinent new information in the last year. So older guidelines will not be reviewed. They are found in the TCR that is in the web portal for the committee. Anything in the last 12 months that was new will be reviewed here a little bit.

I want to give a little bit of background here since it is a specific disease state as opposed to the oncology to have numerous different cancers that we reviewed there. For glaucoma agents approximately 2.7 million people in the United States suffer from glaucoma. It's the second most common cause of permanent blindness in the U.S. and most common cause of blindness among African Americans and Hispanics. Risk factors for the development of glaucoma include elevated IOP, advancing age defined as greater than 40 years, family history and African American or Hispanic descent. Increased IOP is common in glaucoma and is believed to contribute to the damage of the optic nerve, which can lead to loss of visual sensitivity and field. However, some patients with glaucoma have normal IOP, and many patients with elevated IOP do not have glaucoma. So therefore IOP alone is no longer considered a diagnostic criteria for glaucoma.

Two major types have been identified—open angle and closed angle. In open angle there is reduced flow through the trabecular meshwork. Open angle accounts for a majority of the cases that you see. And in closed angle the iris is pushed forward against the trabecular meshwork, blocking fluid from escaping. Reduction of IOP may be achieved either be decreasing the rate of production of aqueous humor or increasing the rate of outflow of aqueous humor from the anterior chamber of the eye. And topical ocular hypotensive agents can delay or prevent the development of primary open angle glaucoma in some patients.

The only kind of newer thing to highlight for the committee is for the medication Durysta. So in March 2020 the FDA approved a new formulation of Durysta which is a bimatoprost implant, indicated for the reduction of intraocular pressure in patients with open angle glaucoma or ocular hypertension. The warning and precautions here, again, to highlight the bolding indicates new information, which we do have a little bit of time and I figure I can be comprehensive here. With warnings and precautions there is endothelial cell loss. So due to the possible corneal endothelial cell loss, administration of this medication should be limited to a single implant per eye without retreatment. There's corneal adverse reactions, which has been associated with adverse reactions and risks with multiple implants. Use caution in patients with limited corneal endothelial cell reserve. And lastly iridocorneal angle and this medication should be used with caution in patients with narrow angles or anatomical angle obstruction. For dosage it is an ophthalmic intracameral administration and it should be carried out under aseptic conditions because it is an implant. And like I said it is an implant containing 10 mcg of bimatoprost in a drug delivery system. This medication has not been established in pediatric patients and there is no adequate or well-controlled studies for patients who are pregnant wanting to receive this medication. It is a shorter presentation for the glaucoma agents, but I'll pause here and ask if the committee has any questions.

Ginni Buccola: Thanks Umang. Committee, any questions? Okay. I don't see we have any stakeholders listed. Is that correct?

Leta Evaskus: That is correct and I do not see that anyone is raising their hand. If you'd like to speak, please raise your hand now. I don't see any stakeholders.

Ginni Buccola: For efficiency, or is this too confusing, is it all right if we review the immunomodulators and do both motions at the end? Or is it better we do the motion now, Leta?

Leta Evaskus: I believe the motions are split out so… oh no, they are together. So let's do the immunomodulators.

Ginni Buccola: Okay. Great.

Umang Patel: Okay. So this is kind of the first time we're kind of doing this for Washington State. There are no updates for immunomodulators in the last year. So there is no background information or anything… or new medications to review. Again, the TCRs are posted for the committee members if they wanted additional information.

Ginni Buccola: Okay. That's also very simple for today. Are there any stakeholders. I don't see any listed.

Leta Evaskus: Yeah, there are still no one raising their hand.

Ginni Buccola: Okay. So let's go ahead then and we'll do both of these motions. Again, committee members, chime in if we're moving too fast through any of these slides. Okay? Why don't you advance to slide 8, Leta?

Diane Schwilke: If the committee is ready… can you all hear me? I move that all products in the drug classes listed on slide 6 are considered safe and efficacious for their medically-accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in these classes may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Connie Huynh: I second.

Ginni Buccola: All those in favor?

Group: Aye.

Ginni Buccola: Are there any opposed? Okay. The motion carries.

Leta Evaskus: Since we're just at 11:30 should we continue with the respiratory agents?

Ginni Buccola: Yes, please. Let's keep going.

Umang Patel: Okay. So we'll pivot over to the respiratory agents, specifically pulmonary fibrosing agents here. Again, to give a little bit of background

here, so idiopathic pulmonary fibrosis or IPF is a chronic, progressing lung disease occurring primarily in middle-aged to older adults. It is characterized by progressive fibrosis resulting in decreased ventilation and gas exchange. In the U.S. it is estimated roughly about 132,000 people with approximately 50,000 new cases being diagnosed and over 30,000 deaths per year. Researchers expect this number to rise, due to improvement in accurate diagnosis and longer life-expectancy as disease understanding and management increases. While the cause of IPF is unknown, a primary theory of pathogensis is an inciting factor in a susceptible patient that may cause the initial alveolar damage, provoking a response ultimately leading to fibrosis. Potential risk factors for IPF include smoking, GERD, diabetes, viral infections such as hepatitis C. Possible causes of pulmonary fibrosis include environmental toxins, medications, and genetic predisposition. And most commonly death is due to respiratory failure, but other causes include pulmonary hypertension, heart failure, pulmonary embolism, pneumonia and lung cancer.

There are no updates and guidelines or anything like that. Again, more information is found in the TCRs in the web portal. So the medication Ofev in September 2019 there were multiple updates to this medication. In September 2019 FDA approved expanded indication to slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease or SSc-ILD and in March 2020 the FDA again approved a new indication for the treatment of chronic fibrosing interstitial lung diseases with a progressive phenotype. I had already had, as you can see, it already had a previous indication for idiopathic pulmonary fibrosis. For this medication in terms of warning and precautions there is one for hepatic impairment where this medication is not recommended for use in patients with moderate or severe hepatic impairment. There can be elevated liver enzymes, which kind of ties into the previous notation here and drug-induced liver injury. So ALT, AST, and bilirubin elevations have occurred, including cases of drug-induced liver injury. And lastly prior to treatment initiation it is necessary to conduct liver function tests in all patients and a pregnancy test in females of reproductive potential. I'll touch base on that in a minute. In terms of dosage and availability you can see here there's no update to that. This medication in terms of pediatric patients the safety and efficacy has not been established. In terms of pregnancy, which I was speaking of a second ago, based on findings from animal studies and its mechanism of action it can cause fetal harm when administered to a pregnancy woman and has a category D right now for pregnancy. Something unique to note with this medication is particularly with patients who are smokers. So smoking was associated with a decreased exposure to OFEV, which may

alter the efficacy profile. So it is encouraged for clinicians to instruct patients to stop smoking prior to treatment of this medication. This is the one and only update to the idiopathic pulmonary fibrosis class. I'll pause here for any questions from the committee.

Ginni Buccola: Any questions committee members? Okay. I see one stakeholder, Michael Horton with Boehringer Ingelheim Pharmaceuticals. So Michael, when you're unmuted and ready you'll have three minutes to share.

Michael Horton: Good morning. My name is Michael Horton. I'm a senior associate director for the clinical development and medical affairs team for the [inaudible] lung disease program at Boehringer Ingelheim. As you know, in September of this year as he just pointed out… or September of last year, Ofev was indicated for the slow of rate of decline in pulmonary function in patients with systemic sclerosis associated with interstitial lung disease. Based on the efficacy in a Phase 3 randomized double-blind placebo-controlled study of 580 patients who had systemic sclerosis interstitial lung disease and this trial included patients with both diffuse cutaneous and limited cutaneous systemic sclerosis. The primary endpoint was the [inaudible] decline in [inaudible] over 52 weeks and it was significantly reduced by 41 mls compared to placebo, which corresponded to a relative treatment effect of 44%. The most common adverse event was diarrhea, which was reported in 75.7% of patients in the Ofev group compared to 31.6% of patients in the placebo group. Then in March of this year we did receive approval for the treatment of chronic fibrosing interstitial lung diseases in patients with a progressive phenotype in a, again, based on a Phase 3 randomized double-blind placebo-controlled trial of 663 patients. I also meant to note in the package insert this is referred to as Study 5. The trial for the systemic sclerosis interstitial lung disease is referred to as Study 4 in the package insert.

This trial is a little bit different in that the inclusion criteria included patients with a clinical diagnosis of chronic fibrosing interstitial lung disease based on the presence of fibrosis and the HRCT in who presented with signs of progression, which was defined by worsening of PFTs or a combination of worsening of PFTs, worsening of imaging or worsening of symptoms. In addition, patients were required to have progressed despite management deemed appropriate in clinical practice by investigators for the patient's relevant interstitial lung disease and this progression and treatment had occurred in the 24 months prior to randomization for the trial.

I did want to note that the underlying clinical interstitial lung disease diagnosis represented in the trial included hypersensitivity and [inaudible], all immune interstitial lung disease, idiopathic non-specific interstitial pneumonia, unclassifiable idiopathic interstitial pneumonia, as well as some other interstitial lung disease. However, it should be noted that this indication is not based on an underlying interstitial lung disease but is based on a phenotype and that phenotype being people have a chronic fibrotic lung disease that is progressive in nature. Similar to other trials the primary endpoint was the [inaudible] declining [inaudible] over 52 weeks and in this instance it was a reduction of 107 MLs representing a 57% relative reduction and then in terms of adverse effects everything we saw was similar to what we've seen in the earlier trials with IPF and systemic sclerosis. So I realize three minutes is a short period of time and that was a very brief overview, but if there are any questions I'd be happy to answer those.

Ginni Buccola: Thank you very much. Any questions from the committee? Okay. Thank you. Are there any other stakeholders that we weren't aware of?

Leta Evaskus: I don't see any other stakeholders.

Ginni Buccola: Okay. Thanks. Let's go ahead and move to the motion then for pulmonary fibrosis agents. I think you're okay to advance to slide 10.

Alex Park: Can I ask a question, Donna? Can I ask you a question, Donna?

Donna Sullivan: Sure. Go ahead.

Alex Park: These are probably pretty pricy drugs and it's in a very difficult condition that has pretty chronic progressive decline for most folks and the data is kind of not super elevating for either of them and you have a meta-analysis I was reading in the TCR, that Umang provided. It's pretty old and both drugs are pretty similar. How would HCA decide which drug gets to be preferred?

Donna Sullivan: That's a great question. If the data is relatively poor on both of them then one doesn't kind of like rise to the top of the more effective. We would usually look at the cost. I'm not 100% sure off the top of my head what our current status is on these particular drugs so I'd have to look that up. Hang on. Give me a minute.

Marissa Tabile: Donna, both are preferred on the PDL.

Donna Sullivan: Thank you.

Alex Park: That's very generous. That's great.

Donna Sullivan: Are you recommending we do something differently?

Alex Park: No. I was just… we are ahead of schedule and I was just curious how that works. I've had a couple patients on these drugs and they are extremely expensive. So I was just curious how HCA handles that. It's nice that they have made the decision for the time being to make those preferred.

Well, if the committee is ready then I move that all products in the respiratory agents' pulmonary fibrosing agents drug class are considered safe and efficacious for their medically-accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products with the same medication before a non-preferred drug will be authorized unless contraindicated and not clinically appropriate where only one product is preferred.

Diane Schwilke: I second.

Ginni Buccola: All those committee members in favor, please say aye?

Group: Aye.

Ginni Buccola: Are there any opposed? Okay. The motion carries. I would propose that we continue to move forward and do smoking deterrents before lunch.

Umang Patel: Absolutely. Smoking deterrents is similar to the immunomodulators. So there are no updates in guidelines or new medications, formulations or anything like that in this class so there ultimately is nothing new to review in this class. I'll pause here for the committee, as well.

Ginni Buccola: Thanks Umang. We have one stakeholder and that's Piao Ching with Pfizer. When you're ready to go you will have three minutes.

Piao Ching: Good morning. My name is Piao Ching. I'm a pharmacist with Pfizer Medical Affairs team. I want to thank you for allowing me to provide information about Chantix in support of Pfizer's request to retain Chantix on Apple Health Preferred Drug List. Chantix is indicated as an aid to smoking cessation treatment in adults. The recommended dose of Chantix is 1 mg twice daily following a one-week titration of .5 mg once daily on days 1 through 3 followed by 5 mg twice daily 4 to 7. The

following information pertains to recent guidelines created to smoking cessation. The 2018 ACC expert consensus decision possibly on tobacco cessation treatment is applicable to anyone who smokes tobacco cigarettes by giving special emphasis to individuals with cardiovascular disease. Cigarette smoking is a chronic, relaxing substance use disorder caused by addiction to nicotine. Most smokers are [inaudible] to repeat the cycles of short-term abstinence followed by relapse to smoking before achieving a long-term tobacco abstinence. This requires clinicians to adopt chronic business management strategy similar to other diseases such as hypertension and diabetes. All patients should be asked about tobacco use at all clinical encounters and smokers should receive clear advice to stop tobacco use. Every smoker should be offered treatment rather than ask if they are ready. All smokers should be offered proven pharmaceutical smoking cessation aids and proactive connection to evidence-based behavioral support. Any [inaudible] models allow clinicians to offer smoking cessation treatment to every smoker with patients having the option to refuse treatment. In 2018 the ACC expert consensus [inaudible] recommends Chantix as a first line pharmacotherapy option for smoking cessation. The American Corrective Society or ACS practice guidelines on initiation of pharmacologic treatments in tobacco-dependent adults was released on July 15th of this year. The guidelines did not address all possible pharmacotherapy options and did not address all the potential clinical [inaudible]. The guidelines are not intended to supply clinician with such [inaudible].

Two key recommendations include the following: for tobacco-dependent adults in whom treatment is being initiated, Chantix is recommended over a nicotine patch and over bupropion. In tobacco-dependent adults who are not ready to discontinue tobacco use it is recommended that clinicians begin treatment with Chantix rather than waiting until patients are ready to stop tobacco use. In closing, I would like to thank the committee for listening to my testimony and again ask you to consider Pfizer's request to retain Chantix on Apple Health's Preferred Drug List. I would be happy to respond to any questions you may have. Thank you!

Ginni Buccola: Thanks very much. Are there any questions from the committee? Okay. Thanks again. And just confirming there are no other stakeholders?

Leta Evaskus: No, there are no others.

Ginni Buccola: We'll go to the motion then for smoking deterrents. It's okay to advance to the next slide.

Virginia Buccola: I'll go ahead and make the motion. I move that all products in the smoking deterrents miscellaneous – other drug class are considered safe and efficacious for their medically-accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization for medical necessity. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Connie Huynh: I second.

Ginni Buccola: Again, all those in favor please say aye.

Group: Aye.

Ginni Buccola: Any opposed? And the motion carries. That brings us to the end of the… it seems like a good pausing point for lunch. We're right at 11:48. So why don't we come back in 32 minutes to continue. Is that okay?

Woman: 12:20.

Ginni Buccola: Okay. Thanks everyone.

Leta Evaskus: I'll leave the meeting up so you don't have to log out.

Ginni Buccola: Thank you.

Leta Evaskus: Ginni, are you on the line?

Ginni Buccola: Yes, I'm here.

Leta Evaskus: Okay. Great. Let's get started again. I just have a note really quick that you can delete Shirley from the stakeholder list. Marissa, are you on?

Marissa Tabile: Yes, I'm here.

Leta Evaskus: Great. I'm going to change presenters to Marissa and she's going to go through the policies.

Marissa Tabile: Thank you. Can you see the cytokine and CAM policy up on the screen?

Leta Evaskus: Yes.

Marissa Tabile: Okay. Great. We can go ahead and get started with the cytokine and CAM antagonists' policy. Ryan Taketomo will be going through it and then Ryan I will be guiding you so if you need me to scroll down or switch to the form just let me know.

Ryan Taketomo: Thanks, Marissa. So starting off this afternoon with the cytokine and CAM antagonists' policy. This is the third iteration of the policy and so, again, to summarize the purpose of this policy was to provide coverage criteria for the [inaudible] indications, which these agents are prescribed in the Apple Health population. Key changes from the previous version include update to the drug list to incorporate new drugs to market, updates to the dosing and quantity limits and we did update an age limit for [inaudible]. In addition, based off stakeholder feedback we did add a new clinical indication for non-radiographic axial spondylitis. If you could scroll down to that section, please.

Based off feedback they requested that this indication be included. This indication is treated similarly to the ankylosing spondylitis so the criteria is almost 100% as that. That comes from the American College of Rheumatology guidelines. You will note one difference with criteria 2C with ankylosing spondylitis we require trial and failure of both of our preferred products which are Humira and Enbrel. However, for the non-radiographic axial spondylitis indication we are only including Humira and that is because only Humira is currently recognized in Micromedics, which is a recognized compendia for Medicaid. So other than that the criteria for NAS will be the same as anchylosing spondylitis.

We can scroll down to the dosing and limitations section. Just to point out that I did recognize that there are two new agents for which the non-radiographic axial spondylitis indication is not included. Currently it's included for Humira and Cimzia, however, Cosentyx and Taltz also have that specific indication. So I will be… the plan is to add those after the DUR meeting. And with that we can move down to the pen form.

So this is the pen form, which we send to providers that request the information to kind of facilitate the prior authorization process. Pretty much the only change was the addition of the non-radiographic axial spondylitis indication. So with that I'll leave it up to the committee to see if there are any questions.

Ginni Buccola: Thanks Ryan. Anybody on the committee have any questions? Okay. Then we'll go ahead and move to stakeholders. We have three stakeholders Carrie Johnson with Amgen, Bobbi Bentz with Eli Lilly and

Bob Reemts with UCB. And so Carrie as soon as you're unmuted you'll have three minutes to share your comments.

Carrie Johnson: Okay. This is Carrie Johnson. I'm a pharmacist with Amgen Medical Affairs. Thank you for the opportunity to speak in support of Otezla or apremilast. Otezla was FDA approved in 2014 for the treatment of adult patients with active psoriatic arthritis, adult patients with moderate to severe psoriasis who are candidates for phototherapy or systemic therapy and now in July 2019 for the treatment of oral ulcers associated with Behcet's disease in adult patients. Warnings and precautions include diarrhea, nausea, vomiting, depression, weight decrease and drug interactions. Please see the full prescribing information at Amgen.com for further information.

Some important reminders about Otezla, Otezla is not a biologic and recent public guidelines place it in a separate category. It is an oral small molecule that works intracellularly to inhibit [inaudible] 4 with a unique mechanism of action and it reduces the cell's reduction of pro inflammatory cytokines and increases the production of anti-inflammatory cytokines further distinguishing it from biologics.

Importantly, Otezla has no black box warning and no requirement for pre-medication screening or laboratory monitoring and as an oral small molecule it does not induce the production of anti-drug antibodies.

Four key updates – there were two label updates for this past year. The first in July of 2019 Otezla became the first FDA approved therapy for the treatment of oral ulcers in adult patients with Buhcet's disease. This is a rare, chronic, multi-system inflammatory disease that effects approximately 5 in 100,000 people in the U.S. [inaudible] also occurs in more than 98% of patients and can be significantly painful and impact quality of life. In the Phase 3 release study Otezla demonstrates significant improvement versus placebo at week 12 and the number and pain or oral ulcers associated with Buhcet's disease. Most commonly reported adverse events include diarrhea, nausea, headache and upper respiratory tract infection. The second label update in this past year scalp psoriasis occurs in greater than 90% of psoriasis patients and it is considered a difficult [inaudible] aspect of psoriasis. In a Phase 3 style study Otezla demonstrated significantly greater improvement in scalp psoriasis, scalp and whole body itch, and quality of life versus placebo at week 16 with improvements continuing out to week 32. Most common adverse events diarrhea, nausea, headache and vomiting. These data are fully published and were added to the label this year. The third update, long-term data is published now up to five years in psoriatic arthritis and

over three years in psoriasis and they show no increase in incidence or severity of adverse events and no new safety signals over time. The fourth update is recently fully-published claims now [inaudible] added demonstrate that biologic-naïve patients with psoriatic arthritis who initiated Otezla had situate similar to biologic users and significantly lower health care costs regardless of treatment switching. In summary, Otezla is not a biologic. It is placed in a separate category. In recent guidelines Otezla does not have a black box warning and has no requirement for pre-medication screening or laboratory monitoring, has no warnings or precautions related to infection or malignancy, and as an oral small molecule it does not induce the production of anti-drug antibodies. Otezla represents an important oral non-biologic option for your adult patients with moderate to severe psoriasis, active psoriatic arthritis and now for oral ulcers associated with Buhcet's disease. Thank you for your time and I'll take any questions.

Ginni Buccola: Thanks, Carrie. Any questions from the committee? Okay. We'll move to Bobbi Bentz.

Bobbi Bentz: Hello. This is Bobbi Bentz. I'm an outcomes and evidence liaison with Eli Lilly and Company, which manufactures Taltz also known as ixekizumab. This is an IL17 inhibitor. It was originally approved for the treatment of plaque psoriasis, but has since been approved for psoriatic arthritis and ankylosing spondylitis and was most recently approved for pediatric psoriasis in non-radiographic axial spondyloarthritis.

As you have reviewed this drug before, I really just wanted to take a moment to provide two updates of research that were completed since your last review. First is a completion of a study called [inaudible]. This was a randomized controlled trial comparing Taltz with Tremfya in patients with plaque psoriasis. In this study Taltz showed superiority to Tremfya on the primary outcome measure, which was a complete clearance of skin lesions. The other update is the completion of a trial on [inaudible] H2H and this study compared Taltz with Humira in participants with psoriatic arthritis. In this study Taltz demonstrated superiority to Humira on the primary outcome measure, which in this study was actually a simultaneous achievement of ACR50 which is a 50% reduction in disease activity and then similarly to the other study a completion of skin clearance or a PASI 100 score. That's really all I wanted to share today briefly and just thank you for letting us provide some of these updates. As we kind of always suggest to review the packet insert for all the safety details and I'm happy to try and answer any questions you might have or provide follow-up as needed. Thank you!

Ginni Buccola: Thanks very much. Any questions from the committee? Okay. Then we'll go to Bob Reemts.

Bob Reemts: My name is Bob Reemts and I am one of the medical outcomes specialists for UCB and want to thank the committee to Washington State Health Care Authority to present the significant [inaudible] updates to UCB certolizumab pegol or Cimzia. Now Cimzia was the first and that's the only TNF alpha blocker FDA approved for the treatment of non-radiographic axial spondyloarthritis or [inaudible] with objective signs of inflammation. Cimzia received FDA approval for [inaudible] in March of 2019. Now to summarize [inaudible] painful and debilitating inflammatory arthritis predominantly affecting the spine or sacroiliac joints and in contrast to AS or ankylosing spondylitis, which patients have evidence of structural damage on x-ray NRX SPA patients do not, but that burden of disease is similar and additionally NRX SPA effects equally a distribution between males and females. Now the PI, which now includes the significant indication for NRX SPA, which is supported by the… our clinical development program AS006 and AS001 and the dosing in four NRX SPA for [inaudible] is 400 mg initially at weeks two and four followed by 200 mg every two weeks and four weeks. We also have data in the PI now that reflects our pharmacokinetic studies in women of child-bearing age, which includes CRIB, which was a prospective post-marketing multi-center PK study which evaluated [inaudible] transfer of Cimzia describing [inaudible] to low [inaudible] transfer from mother to fetus and CRADLE, which was a prospective post-marketing study that evaluated the concentration of Cimzia and human breast milk, which found minimal transfer into the milk during lactation.

The adverse drug reaction profile now reflects that study with NRX SPA, which the safety profile reflects similar results to patients exposed in RA category and previous experience with Cimzia. I want to thank the committee for the time and I'll answer any questions. Thank you.

Ginni Buccola: Thank you. Any questions from the committee members for Bob? All right. Thanks very much. Are there any other stakeholders?

Leta Evaskus: There are no other stakeholders.

Ginni Buccola: Okay. Let's go to the motion.

Marissa Tabile: I have the motion up for the committee.

Leah Marcotte: I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 66.27.00-3 as recommended.

Nancy Lee: I second that motion.

Ginni Buccola: All those in favor say, please say aye.

Group: Aye.

Ginni Buccola: Are there any opposed? Okay. The motion carries. And we'll on to Apple Health policy hormone treatment for gender dysphoria.

Marissa Tabile: Okay. Good afternoon everybody. This is Marissa from the Health Care Authority. I will be presenting the hormone therapy for gender dysphoria policy. Just to give you guys a little bit of background, I did work on this in collaboration with Luke, our other pharmacist. He'll be presenting his other policies as well. So if you hear him chime in don't be surprised. He did work on this policy with me, as well. So just to give you a little bit of background on the policy, how this policy came about was we had the testosterone policy which was just recently approved in June at the DUR meeting and we identified that the testosterone policy did not address or give any guidance to our NCOs on how to address hormone therapy for gender dysphoria. So we thought it would be advantageous to create a policy that would be all-inclusive of all the hormone therapies used. So testosterone, estrogen and GnRH agonists into one policy and have it be the hormone therapy for gender dysphoria policy. So as we were working on this policy we did consult with our internal nurse consultant who oversees the transgender program here at the Health Care Authority just to make sure that as we were drafting the policy that it was aligned with our wax we have in place and also that it didn't create any additional barriers for patients. We also consulted with a pediatric endocrinologist at Seattle Children's Hospital and then as well as with some providers at UW Medicine who specialize in transgender care. So we were able to collaborate with a lot of different people just because we want to make sure that this policy is not restricting any access or creating any barriers for patients to get their medication.

As we were drafting this policy we did use the [inaudible] Professional Association for transgender health at W pack guidelines, as well as the Endocrine Society guidelines for general dysphoria and we modeled the criteria after those recommendations. So just to give you a little bit of background on the disease state.

So gender dysphoria involves the conflict between a person's physical or assigned gender and the gender for which he/she/they identify with. Gender dysphoria can cause individuals to experience significant distress and problems with functioning associated with the conflict that they experience between how they feel and think of themselves and their physical or assigned gender. So treatment of individuals with gender dysphoria varies between change in gender expression or body modifications are also bold. So for this particular policy in general we're really only addressing really the change in gender expression just because it's really only addressing the hormone therapy. It's not addressing any surgical modifications that patients can undergo, but for hormone therapy it is pretty common for even patients that are wanting to do body modification to really undergo hormone therapy first and then do the surgical modifications. So it is a pretty common process for patients with gender dysphoria and the hormone therapy that they can undergo is either masculinizing or feminizing. So masculinizing therapy includes medications that increase testosterone levels in the body and that causes masculinizing changes to occur. And feminizing therapy is just the opposite. So that includes medications that will decrease the levels of testosterone in the body while also using estrogen to reduce the feminizing changes.

This policy also addresses puberty suppression. So for those adolescent patients that want to undergo puberty suppression the most common way is using the [inaudible] releasing hormone agonist. For this sake I'm just going to say GnRH agonist to help suppress endogenous puberty. And usually those adolescent patients that do undergo GnRH therapy end up transitioning to using either testosterone or estrogen depending on if they identify as female to male or male to female.

Just to go through the policy here we broke it up into different sections. So we have the testosterone therapy in one section, the estrogen therapy in its own section, and then the GnRH agonist therapy in another section. So it is split out that way just for your reference. Just to go through some of the criteria, the criteria for the testosterone and the estrogen are pretty similar. The only things that really differ are really the risks associated with those medications and I'll point those out as I go through the criteria, but it's pretty large for the same amongst the two. The criteria for testosterone would be a diagnosis of gender dysphoria as defined by the DSM5. The patient identifies as female to male or non-binary. We got feedback from a provider to include the non-binary just because some patients that do undergo hormone therapy don't necessarily want to transition to, you know, or they don't identify as female as male. They identify as non-binary so we included that to be all-

inclusive. The next criteria is the patient has been informed of the irreversible effects including the potential loss of fertility. Documented informed consent is given for the treatment of dysphoria so patients understand the treatment that they are about to undergo. They attest to agreeing to that. If the patient is less than 17 years old, informed consent was given by the parents or their legal guardian as applicable and a pediatric endocrinologist or other clinician that is experienced in pubertal assessment has determined that the hormone therapy is appropriate for patients less than 17 years of age. The patient is not pregnant or breastfeeding. The patient's risk has been evaluated. So these are the risks that differ between the testosterone and the estrogen criteria. So here we have been evaluated and treated if necessary for breast cancer, if they have elevated hematocrit, untreated severe obstructive sleep apnea, uncontrolled or poorly-controlled heart failure, if they've had a major cardiovascular event in the past six months, or unstable coronary artery disease. So if they meet all the criteria then the request would be approved for 12 months and then the authorization criteria would just be the same criteria that I discussed above and then that would just be approved for 12 months, as well.

For the estrogen criteria it's pretty largely the same like I said. The only thing that differs is this number 6 right here. So the risks are different of course with estrogen versus testosterone so the risks for the estrogen therapy would be history of breast cancer, venous thromboembolism, cardiovascular disease if they have a risk for that, cerebrovascular disease, severe liver dysfunction, history of migraines, and they have been evaluated, or seen if they have had any prolactinoma. Also this request would be approved for 12 months if they meet the criteria and then the reauthorization criteria this should actually be changed and I will actually change it now because we don't have a seventh criteria. It should only be six. So if they meet all criteria 1 through 6 and if they do it will be approved for 12 months for estrogen.

For puberty suppression or GnRH agonists therapy the criteria is different than the testosterone and the estrogen criteria. So I'll just walk through it a little bit. So of course they have to have the diagnosis of gender dysphoria like above. For those that are adolescents the patients have to have documentation from the provider that the physical changes of puberty have arrived so at least Tanner Stage 2 and then also documentation of puberty is ongoing and they have not completed puberty or gotten to Tanner Stage 5. We consulted with the Seattle children's provider who did tell us that those patients that are seen and are less than 17 years old usually have to be followed for mental health services so we wanted to keep that included in the criteria. For this one

it would be confirmation from a mental health professional that all of the following true: that they have coexisting social and medical or psychological problems that have been managed to allow successful initiation of treatment. The client has sufficient mental capacity to make fully informed decisions. And the behavioral health provider specializes in the treatment of gender dysphoria in adolescence. The criteria also has they have been educated about the possible adverse effects of course and then that they have informed consent was given by the patient and the parents so that they know exactly what their treatment regimen is going to be and know the risks and benefits of it. The GnRH agonist therapy in the treatment of gender dysphoria. I'm sorry, I should have separated that. The top tier that I was just explaining was for puberty suppression and the bottom criteria is for the treatment of gender dysphoria. So in gender dysphoria it is just that the diagnosis by the DSM-5 and that the patient identifies as male to female or non-binary. Typically GNIH therapy is used for those patients that are transitioning from male to female so we didn't put anything for female to male and then the patient meets the criteria that is above in the estrogen therapy. So that is listed here and follow with the estrogen criteria above. So for those the requests would also be approved for 12 months if they meet all the criteria and then for re-authorization criteria it would be that they have a positive clinical response. So we would want to see if it is used for puberty suppression and if the puberty… if they are able to suppress the endogenous hormone and then if it's used for puberty suppression documentation of ongoing need and then of course informed consent through the parents and the patients. For the reauthorization it would be approved for 12 months, as well.

Going down here to the dosage and quantity limits. So it's a pretty comprehensive list. We wanted to make sure that we included all of the products that are actually being used in clinical practice. Right now these products that we as preferred and non-preferred on the PDL. So this here is all the testosterone products that we've listed with their dosages. So we have injections, we have gels, we have patches, implants listed for the testosterone products. And then for the estrogen products we have of course the Estradiol tablets, the oral tablets, we have the Estradiol transdermal patches, the Estradiol injection, and I believe we actually need to add the gel on here. That was something we got from a provider. So I apologize it's not on here. But I will make sure to add that into the estrogen section now that I think about that. So estrogen gel will be there.

Then for GnRH agonist therapy we have the Histrelin implant, the Leuprolide injections, Triptorelin and Goserelin injections and implants listed as well.

These are the coding for this policy. The HCPCS code for some of the products and then the references are here as well. And then I'll go ahead and move over to our authorization form. One thing to note about how we plan to manage… how this policy will be implemented is for this particular policy, because we don't really want to create more barriers for the patients that are undergoing hormone therapy for gender dysphoria, we thought it would be best to handle the request by what we call expedited authorizations. So what the expedited authorization will do will at the point of sale the pharmacist who's… or the pharmacy that is filling the claim will get like a rejection and they will put in one of those EA codes and then it will override the PA requirement if there are any EA requirements on the drug. The only caveat to that is that the EA codes will not override the preferred or non-preferred statuses of these drugs. So if the doctor is trying to request for a non-preferred product and they try to put in an EA code… the pharmacist tries to put in an EA code it won't work or they might get a rejection to try a preferred product first. So there is a little caveat to that so that then we're still keeping in line with preferred and non-preferred products on the PDL. So this form that you're looking at here would pretty much be used for like those non-preferred products just so that then we can make sure that it's being utilized correctly. So this is pretty much a regular authorization form that we have. It hasn't been tailored to the clinical policy. So it's pretty general questions that we're asking. Of course the diagnosis, any alternative…

Amy Irwin: I'm so sorry to interrupt you. This particular form would actually be used if the pharmacy was not aware that the client met the EA criteria.

Marissa Tabile: Oh, got it. Okay. Thank you, Amy, for clarifying. I apologize for misspeaking. So like I was saying the authorization, the questions that we ask on here are pretty general questions. It's not anything too specific. So what were the outcomes? Is there any other prescribers? Brand versus generic? If the patient has tried a generic and they have to get the brand name product. And then any justifying comments that any providers want to put in there. They can write in there. This is the authorization form for it. If any of the committee members have any questions I would be happy to answer any. But I will go ahead and hand it over to you, Ginni.

Ginni Buccola: I do have a question. It's about the section under puberty suppression. It was #4 C. It was laid out so clearly around… my concern about access is that it is very difficult to find a behavioral health provider who specializes in children and adolescents, period, especially for our citizens who live remotely to find someone who specializes in gender dysphoria is going to be pretty hard. I'm wondering about language that might be more inclusive to a behavioral health provider willing to consult with a specialty team or… I'm not sure.

Marissa Tabile: Yeah. I would say the behavioral health complaint of this policy has been the hardest, I think, for us to draft just because, like you said, we have examples of… it's hard to get a provider. We did get feedback from some providers that not necessarily all providers, even in adult care, require their patients to see a behavioral health specialist. So we were trying to think of how we should word it. And so I'm open to any feedback if you want to wordsmith it right now. We can certainly do that.

Ginni Buccola: And I would say that would be standard of practice at the clinic, the FQHC that I work in that does a lot of gender firming care. It does not, again, they do not predominantly do adolescence, but there are some. There are some that might meet these criteria. My thought would be, and I'm certainly open to any other word ideas, would be a behavioral health provider with the capacity to address the impact of treatment for gender dysphoria in adolescence. I think it's also going to be difficult to quantify who is a specialist and how do they… and that's a whole other layer of sort of paperwork.

Marissa Tabile: Do you think it would be better for us to add what you've recommended into one of the letters or would you like us to reword C?

Ginni Buccola: I would prefer re-wording C just so we remove the requirement that that behavioral health provider be a specialist.

Marissa Tabile: Okay. Thank you for the recommendation. I will admit this was a very tough section for us to draft because we were trying to figure out how exactly how to word it. So any feedback is good feedback.

Ginni Buccola: I think it looks really good and it's a very challenging… it's very challenging to find… yeah. Thank you. Are there any questions from any other committee members?

Alex Park: Thank you, Marissa. It's obviously a huge amount of research and a lot of guidelines out there. You have done an amazing job kind of incorporating all of it. I think it would be kind of good for practitioners to have access

to the policy, because it sort of tells them exactly what to do. I think the only thing I would think about adding is the monitoring component under the female to male and male to female gender dysphoria. For instance on number 7 under the female to male section. All those health issues; the cancer, etc., etc. are very important, but maybe something like patients risk of an evaluated and treated and monitoring plan established for the following, etc. That would be consistent with Endocrine Society guidelines for monitoring for those conditions, as well.

Marissa Tabile: Perfect. I'm going to reword it right now. I'm sorry, Dr. Park, could you…

Alex Park: Oh, sure. We could say like monitoring plan established.

Marissa Tabile: Okay. How does that look?

Alex Park: That looks great.

Marissa Tabile: Okay. I'll go ahead and add that to the estrogen section.

Alex Park: Super. Thanks, Marissa.

Marissa Tabile: No. Thank you for the feedback, Dr. Park.

Leta Evaskus: I have a question from Petra Eichelsdoerfer. There are some additional estrogen products that are not included in the list in the policy. For example, estradiol topical spray. Does the HCA intend for the list of products included in this policy to be inclusive of all that are currently available?

Petra Eichelsdoerfer: There are some products out there that aren't used very often and they are generally not preferred items, but there are other products that aren't listed on there and since that list is including quantity limits and is likely to be interpreted as showing what products are actually coverable for gender dysphoria the question arises, do you want to include those products as possibly coverable for this diagnosis?

Marissa Tabile: That's a really great question, Petra. So we could definitely add it in, but we were thinking, as we were drafting the policy, of really only including products that are actually being used in clinical practice right now. We thought that might make the most sense. The providers that we did speak to didn't make any mention of… I think it's a spray that you said, but if the committee… if you recommend to add it or if you think it might get confusing to leave it off, I'm open to any suggestions that you might have.

Petra Eichelsdoerfer: Yeah. My suggestion would be if you want to focus just on products that are currently being used in clinical treatment you add some kind of a statement about that. You know? That other products are also coverable and whatever caveats you want to have, because approach to treatment changes over time and our ability to change the policies is usually behind, you know, it lags a little bit behind and that means we're going to get those requests potentially before the policy gets updated to include those products.

Marissa Tabile: Got it. Yeah, I think that's actually a great idea to add like maybe a note there noting that the products listed are clinical practice products that are being used and that as things change, you know, we can certainly update it to include those other products in the policy.

Petra Eichelsdoerfer: Right. And then maybe some kind of a statement around quantity limits that you want to put on those products or if you don't want to. I mean you just… there needs to be some guidance around how to handle a request for this diagnosis for a product that's not listed. Because as I said ultimately we're going to see a request before the policy gets updated, just because of the way these policies get updated.

Marissa Tabile: Thank you, Petra. I'm making it now.

Petra Eichelsdoerfer: And I apologize. I have to leave the conversation for a little bit for another meeting. So if you have any additional follow-up questions for me, if you can let me know later. Reach out to me via email.

Marissa Tabile: Okay. No problem. Sounds great. Thank you so much.

Ginni Buccola: While Marissa is finishing that up, I just want to open it back up to the committee and see if there are any other comments or any other questions for us from you, Marissa?

Marissa Tabile: I guess do you guys think that that would be a great idea what Petra recommended about adding the statement for the products listed in clinical practice or… I just want to see from the provider perspective if it would be confusing not adding those on or if we should add them on?

Nancy Lee: I would suggest maybe saying products that are used in clinical practice based on current practice guidelines. Like associate it with the current practice guidelines. So as the practice guidelines get updated some of the products could be updated too, I guess.

Marissa Tabile: Okay. I can go ahead and do that.

Donna Sullivan: Nancy, I'm a little concerned about saying stuff like that because clinical practice guidelines aren't necessarily based in evidence. They are not… unless we have a particular practice guideline that we like and feel as strongly based in evidence, I hate to have something out there that just says in general we'll follow general clinical practice guidelines because we all know there's lots of guidelines out there and they are not always supported in the evidence.

Nancy Lee: What about changing it to like high quality clinical practice guideline? I mean we kind of use clinical practice guidelines for other things too. And we've consulted specialists for this, as well. So I don't know…

Donna Sullivan: What are you trying to accomplish?

Nancy Lee: I guess used in clinical practice. So sometimes clinical practice and guidelines don't necessarily go hand in hand.

Donna Sullivan: Yeah. I don't think we need to wordsmith this here. I think we can come up with a way to incorporate these new… these other agents in there. There's already a note that says if any drug, you know, comes to market with a new indication that would fall under this policy it would be covered for that indication. So we'll work on getting this addressed and making sure that it is clear that products that are indicated for this treatment or supported in the compendia would be approved.

Marissa Tabile: Okay.

Ginni Buccola: Do we feel ready to move to a motion?

Alex Park: Yes.

Ginni Buccola: All right.

Marissa Tabile: I have the motion up for you.

Alex Park: I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 24.00.00-1 as recommended.

Constance Huynh: I second.

Ginni Buccola: All in favor say aye.

Group: Aye.

Ginni Buccola: Any opposed? Okay. The motion carries. We're scheduled to take a break right now, but since we are moving so quickly I will propose that we just keep on going.

Leta Evaskus: The break is actually scheduled for 1:45 so let's keep going.

Ginni Buccola: I'm just looking in order not at the time slot. So we'll go to the migraine agents. The CGRP receptor antagonists with Luke.

Luke Dearden: Good afternoon. The purpose of this is to discuss the new Apple Health policy regarding oral calcitonin gene-related peptide or CGRP antagonists. This policy highlights two medications that we did discuss earlier this morning, ubrogepant or Ubrelvy and rimegepant or Nurtec ODT. Both of these are indicated for the acute treatment of migraine headaches in adults. So background, and I apologize, if this is a little bit of a refresher from Curtis' presentation earlier, but you Ubrelvy was approved by the FDA in December 2019 and Nurtec was more recently approved in February 2020. Both agents were evaluated in very similar Phase 3 randomized-controlled trials that included patients who had experienced between two and eight migraine episodes per month for the proceeding three months. Notably a very large majority of these patients studied were women, which is reflective of the disease state and had attempted other abortive treatment previously, most commonly NSAIDs. Both Ubrelvy and Nurtec ODT increased pain freedom at two hours and decreased bothersome symptoms, which included photophobia, phonophobia and nausea compared to placebo. They did so in a statistically significant manner. One key difference between products is that Ubrelvy allows for a second dose two hours after the first dose where Nurtec ODT allows for a single dose per 24 hours.

We'll discuss the clinical criteria very briefly. These are based primarily on the clinical trials and also the product labeling and a high level summary… I'll go through high level summary of these criteria, which include (1) Appropriate diagnosis of migraine. (2) At least two migraine episodes per month. (3) There has to be an evaluation for medication overuse headaches. (4) Is trial and failure of at least two triptans including at least one triptan that is used in combination with an NSAID and at this time we wouldn't allow these oral agents to be used in combination with a preventative CGRP antagonist. And then finally, (5) Client is an adult or 18 years or above.

The reauthorization criteria, which mirror the primary outcomes studied in the clinical trials and reauthorization would be allowed if effectiveness is demonstrated either by reduction in pain or reduction in bothersome symptoms. So you can keep scrolling down.

You've got the dose and quantity limits there, which notes that Ubrelvy may be used twice in a 24-hour period and Nurtec once. And then brief evidence review below that. And then we can head down to the penned form, as well, for your review.

Marissa Tabile: I'm pulling it up right now.

Luke Dearden: Great. So this is the form that the prescriber fills out to ensure that the prescribing aligns with the policy and feel free to take some time to review it and then I'm happy to accept any questions about this policy.

Ginni Buccola: Thanks Luke. Are there any questions from the committee members? All right. So we're going to go ahead and move to stakeholders then. We have two stakeholders, Chelsea Leroue with Biohaven and Tim Wardell with AbbVie. So Chelsea when you are unmuted, please go ahead with your three minutes.

Chelsea Leroue: Okay. This is Chelsea Leroue from the medical affairs department at Biohaven Pharmaceuticals with Nurtec ODT or rimegepant. I just had a few comments to make in addition to the comments that I made earlier in the day. Regarding the dosage and administration the reason for the maximum dose in a 24-hour period being that one single dose is due to the long half-life of 11 hours that Nurtec has and in our clinical trials we saw sustained benefits through 48 hours with a single dose. And then regarding the concomitant use the [inaudible] as acute migraine treatment with a CGRP monocronal antibody or labs for preventive treatment there is no contraindication and once those labs were FDA approved they were allowed as concomitant preventive medication in the 52-week long-term safety study with Nurtec and two recently published analyses of this cohort of patients using Nurtec and either erenumab, fremanezumab or galcanezumab suggest that Nurtec may be used acutely to relieve a tax without tolerability or safety problems in those patients receiving preventative CGRPs. I will stop there and answer any questions you might have about Nurtec.

Ginni Buccola: Any questions from the committee? Okay. Thank you, Chelsea. We'll move to Tim.

Tim Wardell: Hi. It looks like I'm unmuted. Similar to Chelsea just a couple of key points. Looking at the criteria one more time that would be different from what we discussed this morning, I wanted to make it clear a key differentiation that we had in our clinical trials program was the outcomes assessed in those triptan-contraindicated and non-responders in measurement of pain freedom absence of most bothersome symptoms at two hours post-dose was that in addition about 25 of the patients in our clinical trials program maintained their pre-enrollment preventative medication use while in the trial, as well out through the long-term safety study extension trial. As mentioned earlier in the long-term safety study no adverse for large… or significant adverse events, which I know was a question earlier today were to be found, particularly around LFTs as that had been a measurement that precluded their approval about five or six years ago. So with that being said I think we covered most of it this morning. I'd be happy to give my time back.

Ginni Buccola: Okay. Thanks, Tim. Any questions from the committee? All right. Any other stakeholders that were not on the list?

Leta Evaskus: I don't see any other stakeholders.

Ginni Buccola: Okay. Let's go ahead and go to the motion then.

Alex Park: Can I ask you a question, Luke?

Luke Dearden: Sure. Yeah.

Alex Park: I was just looking at the reauthorization criteria. What are you looking for from providers when you say clinically-meaningful reduction? As opposed to just reduction?

Luke Dearden: Um, that's a good question. So I wanted to kind of purposely be vague just to provide access to the medication if the patient had reported basically any sort of pain reduction that improves their quality of life to a significant degree then I wanted to allow them to try the medication. Does that answer your question?

Alex Park: Yes. I mean there's a whole field of how we define what is clinically meaningful in pain reduction in the literature and it's a pretty hot topic. Sometimes it means certain severity scales or statistical mumbo jumbo was used to quantify what is happening, but I think what you're saying is that's not what you're looking for and I just wanted to make sure that we weren't limiting access by forcing providers to use one of those prescribed measuring sticks. Thank you.

Luke Dearden: Yeah. I just saying reduction in pain I wouldn't be opposed to that. However, just saying reduction in pain doesn't necessarily mean that is really improving anybody's quality of life [inaudible] and still be…

Alex Park: Thank you. Donna, I noticed on the other policy we're listing preferred and non-preferred, but we're not on this. Is that okay? And/or is there a reason for that?

Donna Sullivan: Um, it's probably just an oversight that we would list… we just need to list which are preferred and non-preferred. Also, I think because we reviewed the drug class and there's new drugs we might not have a complete list yet, but we'll get that added.

Alex Park: Okay. Thank you.

Marissa Tabile: Ginni, this is Marissa. Did you want me to move back to the motion slide?

Ginni Buccola: Thank you.

Alex Park: I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 67.70.10-1 as recommended.

Leah Marcotte: I second.

Ginni Buccola: All committee members in favor, please say aye.

Group: Aye.

Ginni Buccola: Any opposed? And the motion does carry. That will take us to our next topic, migraine agents and calcitonin gene-related peptide receptor agonists.

Luke Dearden: I'll now be discussing an update to the Apple Health policy regarding subcutaneous calcitonin gene-related peptide receptor antagonists for the prevention of migraine. This policy was previously published in 2019 and I'm seeking feedback or approval on the few updates. As far as preferred options go the Emgality remains the preferred medication in this class. So first for the minor updates the primary indication for these medications remains prevention of migraine headaches. The clinical criteria for approval for this indication has remained similar although there are a couple notable changes and Marissa if you could scroll down

a bit to the clinical criteria for prevention of migraines that would be great.

The ICHD-3 diagnosis criteria was added to the appendix of this policy just for completeness and to provide a general reference for the diagnosis criteria. And then if I can draw your attention to criteria #4 which discusses the medication classes that have to be tried prior to approval for these agents. We removed calcium channel blockers as an option so now criteria 4 directs trial and failure of at least one agent from two out of the following three classes—anticonvulsants, antidepressants and beta blockers. And that removal was because there's not great compendia support for use of calcium channel blockers in the setting of migraine prevention.

Calcium channel blockers is not listed there anymore. Under the antidepressants nortriptyline was removed for similar reasons and under beta blockers timolol and nadolol were added. Those are the minor updates to this policy. The largest update to this policy is the addition of a new indication – cluster headaches for Emgality. Emgality gained approval after demonstrating safety and efficacy in a Phase 3 randomized placebo-controlled trial. In the trial 49 patients taking two doses of Emgality 300 mg one at baseline and one after four weeks were compared to 57 similar individuals taking placebo. Each patient had between four and eight headache attacks per day at baseline. During weeks 1 through 3 Emgality reduced headache frequency compared… Emgality reduced headache frequency compared to baseline by a mean of 8.7 attacks per week compared to 5.2 weeks per week for placebo, which was statistically significant. One note that Curtis brought up this morning is that the benefit of Emgality did not extend to the eight-week mark. However, that could be because of the nature of cluster headaches as a disease state where they often just spontaneously resolve after a month or so. So that could certainly be a factor here. Once again, I'll provide a high level summary of the clinical criteria for medication and approval, which includes, again, an appropriate diagnosis, a valuation of medication overuse headache, and then trial and failure of an adequate verapamil dose, which is 360 mg daily and then the patient has to be an adult age 18 or older. Upon initial approval a maximum of two doses of Emgality can be approved for cluster headaches and it may be reauthorized with continued need; meaning that the cluster headache episode is still ongoing and demonstration of effectiveness.

Outlining the dosage and quantity limits – the dose of Emgality is different based on indication and then there's the appendix as the

diagnosis criteria for cluster headache and also migraine. We can head on over to the penned form, as well for the committee's review.

Similar to before cluster headaches were added as a possible indication, and please review and I'm happy to answer any questions.

Alex Park: There was one new drug that we elevated on our work at the P&T this morning. It's epti something. Eptinezumab. Do we need to add that to the drug list on the policy?

Luke Dearden: That's a really good question and I guess I would defer to Marissa and Donna for that question.

Donna Sullivan: Yes. I think these are… these are for treatment of… was it one of the new ones for preventing chronic migraine or for treating? Because this was for prevention, this policy.

Alex Park: I think it was one of the preventive CGRPs.

Donna Sullivan: If it is one of the preventive ones it would be added as a non-preferred.

Alex Park: Okay.

Luke Dearden: I did check that on the PDL on that drug and I couldn't find it on there.

Donna Sullivan: We'll look to see if it's in the drug file yet. If it's on the market yet or not. It might not have… depending on how new it is, it might not have gotten into the drug file yet.

Alex Park: Thanks for checking.

Leah Marcotte: This is very minor, but [inaudible] is misspelled in the policy a couple of times. Right there in the second column.

Luke Dearden: Thank you.

Donna Sullivan: There's another instance of a misspelling in the criteria for reauthorization, as well.

Ginni Buccola: I'm just chiming in to make sure no members have any additional questions. Okay. Thanks, Luke. We have one stakeholder and that's Carrie Johnson from Amgen.

Carrie Johnson: Hi. This is Carrie Johnson. I provided full testimony on Aimovig. I'm the pharmacist with Amgen Medical Affairs. I provided testimony on Aimovig this morning and I'll give back my time unless there's any questions.

Ginni Buccola: Any questions? Okay. Thanks very much, Carrie. Any other stakeholders?

Leta Evaskus: I don't see any other stakeholders.

Ginni Buccola: Okay. Then why don't we go ahead and go to the motion.

Leah Marcotte: I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 67.70.20-2 as recommended.

Alex Park: I second.

Ginni Buccola: All in favor?

Group: Aye.

Ginni Buccola: Are there any opposed? Okay. The motion carries. And we will move to antipsychotics, the second generation specifically Vraylar.

Ryan Taketomo: I can see it. Thanks, Marissa. So this policy will specifically be for Vraylar, a second generation antipsychotic and the purpose of this policy is to ensure appropriate use given the number of agents in this class.

Moving down to the clinical criteria. Criteria is pretty much the same throughout the three indications listed—common ones being that the client is 18 years or older, that they meet one of the following for number 2 A that would be a trial and failure of three of the listed oral atypical antipsychotics or that there is documentation that the client has been taking Vraylar and is stabilized on the requested dose. Criteria number three being that they have adequate renal function and criteria four should be client has no history of liver disease or no severe liver disease. Differences between the indications mainly revolve around the agents which are listed in criteria 2 A. That would be the main difference between each of the indications and I would recommend reviewing that list. Other than that the initial authorization criteria is fairly consistent throughout and the same applies to the reauthorization criteria.

After that it's pretty much just the dosing and limitation section for Vraylar and then we have the pen form, which again facilitates the prior authorization process. With that I'll give the committee some time to

review the policy and the pen form and if they have any questions, feel free to ask.

Ginni Buccola: Thanks, Ryan. Any questions from the committee? Okay. We'll go to stakeholders and we have two. We have Phillip Jennings from AbbVie and Paul Thompson from Alkermes.

Phillip Jennings: My name is Phillip Jennings. I'm a senior medical science liaison with AbbVie and thanks for the opportunity to briefly review Vraylar with you today. It's indicated for schizophrenia in adults and treatment of manic [inaudible] depressive episodes of bipolar 1 disorder in adults. It has boxed warnings regarding suicidal thoughts and behaviors and increased mortality in dementia-related psychosis and as well as the same warnings precautions as the other [inaudible] psychotics in the class. I'm not going to have time to review all of those today so please refer to the PI for that.

The most common adverse effects are akathisia and [inaudible] symptoms so discontinuation due to these side effects is about 2% or less than registrational studies. I'd like to address the challenges presented by your current proposal to require three steps through other antipsychotics before allowing Washington Medicaid patients to receive Vraylar. This policy replaced some of the most vulnerable patient populations at risk by requiring prescribers to use some medications that have not been proven safe or efficacious in these populations prior to using FDA approved Vraylar. Specifically, the bipolar 1 disorder mixed manic episodes category has a branded drug, lurasidone or Latuda, as a potential step before Vraylar. However, Latuda is not FDA approved for this indication. In the depressed bipolar 1 disorder category olanzapine is listed as one of the three steps. However, as monotherapy olanzapine is not FDA approved for this indication. This should be of concern to the committee and the mental health prescribing community, as well as most importantly to Washington residents.

Vraylar does have several characteristics which distinguish it from other drugs in this class. First of all the precise mechanism of action is unknown. Vraylar is unique amongst atypical antipsychotics having the highest affinity for the dopamine D-3 receptor. It is the only D-3 preferring antipsychotic available. Activity of the D-3 receptor stopped to be beneficial for mood and cognitive deficits and that's one of the reason it is used. Second, Vraylar has the longest half-life of the orally available antipsychotics and this long half-life suggests that there may be some continued effect that persists after discontinuation of Vraylar and this may be beneficial in preventing rapid onset of relapse in cases of intermittent adherence. Then finally, Vraylar has a neutral metabolic

profile of minimal risk of weight gain and sedation, which is common to some of the other antipsychotics or required steps for Washington Medicaid patients to receive Vraylar. Vraylar is unique in its class with the highest affinity of the D-3 receptor, the long duration of effect, and the tolerability profile is also a potential benefit. Vraylar is one of only two monotherapies that are FDA approved for the treatment of the full spectrum of bipolar 1 disorder including manic, mixed and depressive episodes and it's the only treatment for the full spectrum of bipolar 1 disorder that is considered metabolically neutral with minimal risk of weight gain or minimal sedation. Prescribers choose Vraylar to treat some of their most complex patients for many of the specific reasons I've mentioned here. Vraylar is commonly not a first line drug for bipolar schizophrenia patients and many Medicaid programs recognize this by requiring only a single or a double step. Requiring these additional steps in front of Vraylar make it difficult for your mental health providers to provide the best possible care for their most vulnerable patients. Thank you for your time and attention. I appreciate it.

Ginni Buccola: Thanks very much. Any questions from the committee? Okay. We'll move to Paul Thompson.

Paul Thompson: Thank you. My name is Paul Thompson. I'm a psychiatric pharmacist and senior medical science liaison at Alkermes. Thanks for the opportunity today to provide testimony on Aristado Initio, which was approved in July of 2018. It is an extended release injectable suspension for intermuscular use. I will highlight a few clinical points today. First, Aristado Initio has a black box warning for increased mortality in elderly patients with dementia-related sycosis. I will refer you to the full PI for complete boxed warning and additional info on those. Aristado initio along with a single 30 mg oral aripiprazole dose is part of a one-day initiation regiment given in conjunction with the first dose of Aristado and is indicated for the initiation of Aristada when used in the treatment of schizophrenia in adults. The main formulation difference between Aristada and Aristado Initio is the particle size of the aripiprazole lauroxil crystals in the injection suspension where Aristada is comprised of micron size particles that is chosen for slow dissolution and is approved for monthly, every six-week or every eight-week dosing intervals. Aristado initio has much smaller size particles in the nanometer range and after injection releases aripiprazole faster than Aristada and is only to be used as a single dose. The smaller size particles of Aristado Initio reduced the time to achieve therapeutic levels of aripiprazole relative to Aristada. The one-day initiation regimen could be used to start with any dose of Aristada including the two-month dosing intervals. Aristado initio is only available in a single strength 675 mg and is only used as a single-dose and not for

repeated dosing and it is not interchangeable with Aristada due to the different pharmacokinetic profiles. Aristado initio is administered intramuscularly by a health care professional in the deltoid or gluteal muscle. For patients who have never taken aripiprazole tolerability should be established with oral aripiprazole prior to initiating Aristado Initio. Aristado initio should be avoided in patients with non CYP2D poor metabolism or concomitant strong 2D63A4 inhibitors or inducers or with any hypertensives or benzodiazepines. This is because there are no dosage adjustments available to Aristado Initio since it is the single dose.

The only contraindication is hypersensitivity to aripiprazole and in pharmacokinetic studies the safety of Aristado Initio was generally consistent with that observed in Aristada. Aristado initio is available in a pre-filled syringe and does not require refrigeration. It should be stored at room temperature and not frozen. In closing, Aristado Initio alongside with a 30 mg dose of oral aripiprazole is part of a one-day initiation regimen given in conjunction with the first dose of Aristada and is an option for patients to the previously-approved 21-day oral initiation regimen. The one-day initiation regimen provides comparable plasma concentrations to the 21-day oral initiation regimen and although Aristada and Aristado Initio are both suspensions containing the same molecule, aripiprazole lauroxil, the drug particle size of Initio is smaller and therefore the formulations are not interchangeable.

I would like to thank the committee for the valuable time today and also respectfully request you considering adding Aristado Initio to the Washington Preferred Drug List. Does the committee have any questions for me?

Ginni Buccola: Thank you, Paul. Any questions committee members? Okay. All right. It looks like we will go ahead and move to our motion. I should double check, there are no other stakeholders, I believe?

Leta Evaskus: There are no other stakeholders.

Woman: I have one question. Can we move back to the policy? There is warning around the patient that doesn't have cirrhosis or [inaudible]. That makes sense to me. So if the patient does have cirrhosis [inaudible].

Ginni Buccola: Any other questions?

Alex Park: Can I ask why we chose to limit the access to Vraylar versus some of the other second generation antipsychotics that are listed? I've just been looking at some of the data and it's actually quite convincing medication,

certainly compared to aripiprazole and some of the others that are needed to be tried first. So I just wanted to understand the thinking behind that.

Ryan Taketomo: I will probably have to defer that one to Marissa or Donna.

Donna Sullivan: State that one more time.

Alex Park: I was just asking why we're singling out Vraylar in this policy as second line as opposed to other drugs in the same class?

Donna Sullivan: Great question. I'm thinking it's just one of the brands that is still out there and wondering if it has a different definition. Alex, that's a very good question.

Marissa Tabile: The reason why this policy [inaudible] was because the other products that are listed are [inaudible] with the restrictions on them. Vraylar is the only one that has a [inaudible] medical necessity and we have [inaudible] of a particular product. So we don't really have a policy [inaudible] policy that provides [inaudible].

Ginni Buccola: I'm sorry, but your voice was breaking up a little bit and I was curious to hear what you had to say. I don't know if you could try and say it again?

Marissa Tabile: Yeah. So the reason why Vraylar has its own policy instead of it being [inaudible] policy was because the other products in the class pretty much [inaudible] no resolution [inaudible], but right now Vraylar is [inaudible] requirement on it for medical [inaudible]. So we just needed to [inaudible] for authorization [inaudible] on how to approve or deny this medication.

Ginni Buccola: Just adding a comment as a psychiatric prescriber, while I don't foresee [inaudible] with Vraylar since I primarily work with people who receive their insurance through the state, and I would say that among my colleagues would be a standard to use it as an agent that has a few more [inaudible] miles on it. I lost my train of thought. I do want to say [inaudible] are medication-naïve presenting to me that as long as I have access to the metabolically neutral agents I would prefer to keep everybody on an agent that is generic so that [inaudible] needed to pay for this out-of-pocket for whatever reason they would have the option of using a generic option first. Not to say that this agent isn't appropriate at times, or won't become, you know, more… as it becomes more accessible won't be more useful. That's just a comment from practice.

Marissa Tabile: Yeah, thank you for that comment. The reason why it does have PA is because there's so many other generic antipsychotics on the market. So that's really the reason why, you know, the PA and we want to make sure that it is being used for the right indication.

Ginni Buccola: Any other questions? Are we okay to move to the motion? Okay. We can go ahead and bring the motion up then.

Jordan Storhaug: I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 59.40.001.18-1 as recommended.

Leah Marcotte: I second that motion.

Ginni Buccola: All in favor?

Group: Aye.

Ginni Buccola: Any opposed? Okay. The motion carries. I'll pause briefly. We're at 1:51. We're scheduled for a break, but we also only have two more topics to cover. So I propose we continue to move on unless there's any need to take a pause?

Nancy Lee: I second that motion to continue forward.

Ginni Buccola: Leta, is there any need for a break right now?

Leta Evaskus: Nope. We can keep moving.

Ginni Buccola: Okay. Let's go back to Ryan for gout agents.

Ryan Taketomo: This will be the first presentation of a policy for gout agents. It contains agents for both the [inaudible] and then [inaudible]. The purpose of this policy is of course to ensure appropriate use of the agent included in this policy. So we can go down to the first clinical criteria. This is for colchicine specifically Gloperba, which is the oral liquid formulation of colchicine and so ultimately we just want to make sure that first, that colchicine is being prescribed appropriately and safely and that there is some particular reason on why the liquid is being prescribed versus the tablets or capsules, which are available. And reauthorization criteria just wants to make sure that that status that the patient can't take the capsule and tablets is continuous.

The next drug is febuxostat or Uloric. This is a urate lowering medication and the purpose for some of these clinical criteria is to ensure that there

are more cost-effective agents that have been tried prior to the use of this medication. Primarily, medications such as allopurinol. This medication also has some cardiovascular adverse events potentially. So some of the criteria include… reflect that and just want to make sure that the patients and prescriber are aware of those cardiovascular risks. Can we move to the reauthorization criteria, please?

With the reauthorization criteria I just want to make sure that they have documented positive response when using this medication and that the patient has not experienced any cardiovascular events.

And then the second urate lowering agent is Krystexxa or pegloticase. Similar to the Uloric criteria, because of the cost for this drug we do require prior use of Uloric before this medication can be accessed. Other than that a lot of the criteria is the same as Uloric, however, there is no cardiovascular risk with this medication, in particular.

With the reauthorization criteria I just want to make sure, again, that there is a positive clinical response when using this medication. And so with that we have our dosage and quantity limits and then our penned form.

So this penned form, again, is to help facilitate the prior authorization process. With that I'll give the committee some time to review and ask any questions.

Ginni Buccola: Thanks, Ryan. Committee members, any questions? So it doesn't look like we have any stakeholders for gout agents.

Leta Evaskus: There's no stakeholders.

Ginni Buccola: And I hear a question.

Leah Marcotte: Could we just scroll down so we can see the rest of the form? Thank you so much.

Ginni Buccola: Any need for more time or any questions? Let's go ahead, Marissa, and bring up the motion. And when the committee is ready go ahead and consider that.

Diane Schwilke: I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 68.00.001-1 as recommended.

Ginni Buccola: I second that motion. All those in favor?

Group: Aye.

Ginni Buccola: Any opposed? Okay. The motion carries. We'll move to the last policy for the day, the tyrosine kinase inhibitors with Ryan. Thanks, Ryan.

Ryan Taketomo: This policy is specific for the oral tyrosine kinase inhibitors. The purpose of this policy is to provide blanket criteria, not necessary criteria specific to a drug or its indication, but to ensure that appropriate documentation is captured to support the clinical use of these agents.

So we have our list of all the agents. Some stakeholders have brought to our attention that some oral TKIs or tyrosine kinase inhibitors are missing. So after this we do plan to go back and review the list of oral TKIs and add them if they are missing.

So moving to the criteria, again, this is sort of a blanket policy and we want to make sure we capture clinical piece of information just to support appropriate use of these drugs. These include an appropriate indication recognized by compendia or NCCN guidelines for oncology agents specifically. We also want to make sure that we're capturing appropriate tests. So if a drug is specific for a particular genotype then we would want to collect that information as well. We also want to make sure that the medication is prescribed by or at least in consultation with a specialist who can treat the requested medication in its indication.

And so for the reauthorization criteria essentially we just want to ensure that the patient or client is tolerating the medication well, that there is a documented positive response that the medication is working either it is keeping the disease stable or making their condition better, and that it is continued to be used for… in combination if it's like part of a regime to be used appropriately.

And so with that we have our dosage and quantity limits and then the pen form, which will be used to help facilitate the prior authorization process. And, again, for the dosing and limitation section we do recognize that there are some oral TKIs that are not included and that we will be going back to review that list and add them if they are missing. So with that I'll give some time for the committee to review the pen form and the policy and open it up for questions.

Ginni Buccola: Thanks again, Ryan. Any questions from the committee members for Ryan? I thought I might have heard a question. Okay. Doesn't look like we have any stakeholders. So if the committee feels ready to entertain the motion we could go ahead and bring that up.

Nancy Lee: I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 66.27.00-3 as recommended.

Leah Marcotte: I second.

Ginni Buccola: All those in favor?

Group: Aye.

Ginni Buccola: Any opposed? And the motion carries. And that completes our work for today. So the DUR Board is adjourned. I hope everybody stays safe and healthy and as happy as can be under the circumstances until October. I'll turn it over to Leta in case there are any last minute announcements.

Leta Evaskus: Thank you, Ginni. You did a great job. Thank you all the presenters and we'll see you guys in October.