Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
P&T Meeting Notes
August 15, 2018

Lisa Chew: Hi, this is Lisa Chew, good morning. We're going to convene the Washington State Pharmacy and Therapeutics Committee. I want to remind everybody that this is a recorded meeting. So, please speak into the mic and state your name before speaking. Why don't we start with introductions on this end of the table?

Lorena Wright: I'm Lorena Wright from Coordinated Care.

Frances McGaugh: Fran McGaugh, CHPW.

Petra Eichelsdoerfer: Petra Eichelsdoerfer, United Healthcare.

David Johnson: David Johnson, Molina Healthcare.

Amber Figueroa: Amber Figueroa, committee member.

Susan Flatebo: Susan Flatebo, committee member.

Catherine Brown: Catherine Brown, committee member.

Dale Sanderson: Dale Sanderson, committee member.

Lisa Chew: Lisa Chew, committee member.

Virginia Buccola: Virginia Buccola, committee member.

Jordan Storhaug: Jordan Storhaug, committee member.

Leta Evaskus: Leta Evaskus, Health Care Authority.

April Phillips: April Phillips, Health Care Authority.

Umang Patel: Umang Patel, Magellan.

Ryan Pistoresi: Ryan Pistoresi, Health Care Authority.

Amy Irwin: Amy Irwin, Health Care Authority.

Jose Zarate: Jose Zarate, Health Care Authority.

Lisa Chew: This is Lisa Chew. Leta, do you have some announcements?

Leta Evaskus: Yeah. First on the phone, who do we have?

Curtis Harris: This is Curtis Harris with the Center for Evidence Based Policy.

Leta Evaskus: Hi Curtis. It's really hard to hear you.

Curtis Harris: Okay. Is that any better?

Leta Evaskus: No.

Curtis Harris: Okay. Let's try a portable mic. Is that any better?

Leta Evaskus: That's a little bit better. I'll try turning this up too. Is there anybody on the phone from Labor and Industry? Okay, not yet. Okay, one announcement is, I had two other handouts on top of your binders. This one is the very last section in your binder, the Apple Health PDL, and then this is stakeholder input for the Apple Health policy. So, you can just stick it in the right place.

Lisa Chew: Thanks Leta. Is Brittany on the phone?

Brittany Lazur: Hi, this is Brittany Lazur from the Center for Evidence Based Policy.

Lisa Chew: Yeah, hi Brittany. We're going to go ahead and start with long-acting insulins and your slides are up and showing.

Curtis Harris: This is Curtis Harris for the Center for Evidence Based Policy. I was hoping I could just jump in for a quick 30 seconds to update the committee. So the Center for Evidence Based Policy, which houses the

DERP project, the Drug Effectiveness Review Project, recently switched research vendors, so we've tried [inaudible] from the Pacific Northwest Evidence Based Practice Center to other research vendors. So, a couple of the projects that we will be talking about today were completed by the EPC. We have oriented ourselves to the material and will be presenting them today. However, there may be an instance where we need to have a follow-up, in which we hope to be able to electronically communicate with the head of the committee who can share the material with the rest of the group.

Lisa Chew: Thank you, Curtis. Okay, Brittany you can go ahead and get started.

Brittany Lazur: Thanks so much. So, I will be presenting the findings of the recent long-acting insulins report for type 1 and type 2 diabetes. This is the second update report on this topic. And this report was produced by the Pacific Northwest Evidence Based Practice Center for the Drug Effectiveness Review Project.

So to give a brief overview of this presentation, I'll be going first through some background, delving into our key questions, inclusion criteria, and method for this report. Then delving into the findings, and then wrapping up with a brief summary.

So, as you well know, diabetes is a common, chronic disease, which affects over 30 million people in the United States. Approximately 3% of those have type 1 diabetes. In addition to the daily challenges of managing diabetes, this disease can lead to serious long-term consequences, such as cardiovascular and renal diseases and blindness. Long-acting insulins were created to mimic the insulin that is naturally produced in the body. However, excessive amounts of insulin at any given time can lead to hypoglycemia. These long-acting insulins are available in pen and vial or syringe rapid administrations. The ADA standards of medical care and diabetes suggest that a reasonable hemoglobin A1c goal for many non-pregnant adults is less than 7% for both type 1 and type 2 diabetes.

In this report we focused on two key questions. The first key question dealt with the efficacy, effectiveness, and harms of long-acting insulins.

There were numerous comparisons of interest, including comparing one long-acting insulin to another, comparing delivery methods, so pen versus vial, comparing follow-on or bio-similar insulin to their originator insulin, and comparing long-acting insulin concentration; so more concentrated compared to less concentrated. The second key question pertains to efficacy, effectiveness and harms by subgroups; and these subgroups include demographics, comorbidities, and potential for drug-drug interactions.

This is slide 4. In this report, the authors included evidence on adults and children with type 1 or type 2 diabetes and included evidence on the six long-acting insulins that are listed in this slide. Comparators included other eligible long-acting insulins and their formulations and outcomes of interest included micro and macrovascular disease, mortality, glycemic control and harms including hypoglycemia, withdrawals due to adverse events, and malignancy, such as cancer.

This slide provides some additional detail on the drugs included in this report. In the first column, you will see the generic drug name. The drugs are grouped with a glargine formulation first and then degludec and then degludec [inaudible] combination product and then finally detemir. The trade name for each drug is in the second column and then in the third column you will see the formulation, so pen or vial, and then finally the frequency of administration in the last column.

This report follows standard systematic review methodology outlined by the Drug Effectiveness Review Project. Briefly, literature searches, including Medline and the Cochran Library databases, were conducted, and these were conducted through February of this year. The authors rated the methodological quality of each individual study, as well as the overall GRADE quality of evidence rating for each outcome of interest, and the authors conducted narrative and quantitative syntheses of the evidence conducting that analyses were possible.

The authors rated the methodological quality of each study using methods outlined for the Drug Effectiveness Review Project. Quality ratings range on a spectrum from good to poor based on the clarity with which the study authors recorded method and the efforts taken to

prevent potential biases. So, a good quality study has a clear reporting of methods, and steps were taken to mitigate potential biases and conflicts of interests. Fair quality studies are typically the middle of the spectrum and have incomplete reporting of methods and other limitations, and then finally a poor quality study has poor reporting of methods and clear methodological flaws that could introduce significant bias.

Finally, we will go over the GRADE Quality of Evidence ratings, as you will see these throughout the presentation. The authors used GRADE methodology to summarize the overall quality of evidence for each outcome of interest. The GRADE system defines the overall quality of a body of evidence for your outcome as high, moderate, low, or very low. A rating of high quality evidence indicates that the raters are very confident that the estimate of effect of the intervention on the outcome of interest is close to the true effect. For moderate quality evidence, the raters are moderately confident that the effect of the intervention on the outcome of interest is close to the true estimate; however, it may differ. Low quality evidence, excuse me, the raters have little confidence of the estimates of the effect of the intervention on the outcome. The true effect may be substantially different from this estimate, and this may change with additional studies. Finally, at a rating of very low quality evidence, the raters have no confidence in the estimate of the effect of the intervention on the outcome and the true effect is likely very different from the estimate.

So, next we will delve into the findings of this report.

As mentioned this is the second update report on this topic. Across all reports on this topic the authors have included 71 total studies. Of these, 12 studies are new to this update report. These new studies include nine randomized controlled trials, one which is rated good, five rated fair, and 33 rated poor methodological quality. This report also includes three covert studies, two that were rated good and one that was rated fair methodological quality, and the authors also included eight extension studies or subgroups analyses in that inclusion criteria for this report. Of all trials included since the original report, sample sizes ranged from 15 to over 7,000 patients. Study duration ranged from 16 weeks to two years, and most trials are funded by industry. Of all observational studies

included since the original report, the total number of patients included in these studies is nearly 430,000.

On this slide, we have a breakdown of the 12 new studies by the comparison evaluated, the design of each study, and the population included. The most new evidence was found for the comparison of degludec versus glargine, for which we included five trials of adults and one trial of children. The comparison with the second greatest amount of new evidence was for detemir versus glargine, and this included one trial in adults, as well as three cohort studies in adults, and there were two studies that included a fixed dose combination product, the degludec/aspart, one trial in which the combination product was compared with glargine in adults and one trial in which this combination product was compared with detemir in children.

So one overarching finding that became apparent when looking across studies in this report is that there is largely no significant difference in glycemic control for a number of comparisons evaluated in this report. When we refer to glycemic control, we mean the level of hemoglobin A1c and also the percentage of patients achieving hemoglobin A1c target of less than 7%. This table is divided into comparisons that were evaluated in patients with type 1 and type 2 diabetes. In the first column, you will see the drug comparison. The second column includes the information on the population, so adults or children, and the third column includes the GRADE rating for the quality of the body of evidence. For patients with type 1 diabetes, the finding of no significances difference in glycemic control was based on low quality evidence for the majority of drug comparisons. However, the authors identified moderate quality evidence of the comparison of degludec versus glargine in adults. For patients with type 2 diabetes, the authors identified high quality evidence of no significant difference in glycemic control between degludec and glargine in adults. They also identified moderate quality evidence of no significant difference in glycemic control between degludec and glargine in adults and between glargine U300 and glargine U100 in adults.

We are on slide 13, and the rest of the slides all highlight other findings, such as hypoglycemia and adverse events for the drugs listed here, and we will first start with the degludec comparisons.

Authors found a very low quality evidence of severe hypoglycemia, nocturnal hypoglycemia, and withdrawal due to adverse events for the comparisons of degludec versus detemir in adults and children with type 1 diabetes, and this finding was largely due to few events occurring in the included studies for this comparison.

In adults with type 1 diabetes, patients treated with degludec experienced fewer episodes of nocturnal hypoglycemia compared with [inaudible] treated. Authors were able to pull four studies, yielding a pulled estimate of 0.68. This was considered to be moderate quality evidence.

We are on slide 16. There was very low quality evidence of severe hypoglycemia and withdrawals due to adverse events in adults with type 1 diabetes treated with degludec or glargine, and again this was also due to few events occurring in the included studies for this comparison.

In adults with type 2 diabetes, degludec was found to have lower rates of both nocturnal and severe hypoglycemia compared with glargine. These findings were both moderate quality of evidence. However, there was low to moderate quality evidence of no significant differences in cardiovascular events, cancer, mortality, and withdrawals due to adverse events.

We are on slide 18. This forest plot is a visual representation of what you saw on the last slide, in which patients treated with degludec have lower rates of nocturnal hypoglycemia compared with patients treated with glargine. This was a pooled analysis of nine studies and again the authors rated this moderate quality evidence.

So, next we will move onto evidence of the fixed dose combination product degludec/aspart.

The authors found very low quality evidence of no significant differences in severe or nocturnal hypoglycemia or withdrawals due to adverse events in adults with type 2 diabetes who received either the fixed dose combination product degludec/aspart or degludec alone, and again, this

is due to very few episodes of these outcomes, and it led to a very low quality rating.

There was also very low quality evidence of no significant differences in severe or nocturnal hypoglycemia or withdrawals due to adverse events in adults, adolescents, and children with type 1 diabetes. Again, this was largely due to few episodes occurring in this study for this comparison.

We are on slide 22. There were conflicting findings in terms of the rates of nocturnal hypoglycemia in adults with type 2 diabetes treated with the fixed dose combination product degludec/aspart and those treated with glargine. One trial found statistically significantly lower rates of nocturnal hypoglycemia with the fixed dose combination product than with glargine. However, a second trial found no significant difference in the rates of nocturnal hypoglycemia between these groups. These studies were too heterogenous to pool, and the authors rated them very low quality evidence. There is also very low quality evidence of severe hypoglycemia and withdrawals due to adverse events in these groups and there were few episodes of these outcomes.

So, next we will be moving onto the findings for detemir comparisons.

So, on slide 24, there was no significant difference in rates of severe and nocturnal hypoglycemia or withdrawals due to adverse events in adults with type 1 diabetes treated with detemir or with glargine. These findings were very low to low quality evidence. However, there were conflicting findings in terms of the effect of detemir or glargine on neonatal harms, such as perinatal mortality, adverse effects of neonatal birth weight, and neonatal hypoglycemia. One study found neonatal harms were worse with detemir, while another found that these harms were worse with glargine, and these studies had a number of methodological limitations and small sample sizes, and this led to the very low quality of evidence rating for this outcome.

In adults with type 2 diabetes, there was no significant difference in rates of any chapter between patients treated with detemir and those treated with glargine. However, evidence was unable to show a clear difference in rates of breast cancer between detemir and glargine treated patients.

This finding was based on three studies, one large study that found no difference, one small study that found an increased risk with glargine but not with detemir when compared to MPH, but the study did not directly compare the insulins, and one study that found no increased risk of breast cancer with either insulin. These studies used different methods of analysis and different comparisons in these studies, leads to an overall rating of low quality of evidence and no increased risk of breast cancer. The authors found low quality evidence of no significant difference in severe or nocturnal hypoglycemia between adults with type 2 diabetes treated with detemir or glargine. However, there was moderate strength evidence that more patients withdrew due to adverse events while using detemir. The results are only statistically significant in two trials but the finding is consistent across these trials leading to moderate strength quality of evidence. The reasons for having withdrawal in the detemir group is unclear.

Finally, we will go into the findings for the glargine comparisons.

So, we are on slide 27. The authors found a very low quality evidence of severe and nocturnal hypoglycemia, as well as withdrawals due to adverse events in adults with type 1 and type 2 diabetes who received follow-on or biosimilar glargine compared to those who received standard glargine. Again, this finding is due to few episodes of these adverse events occurring in these studies.

In adults with type 1 diabetes, there was no difference in severe or nocturnal hypoglycemia, as well as withdrawals due to adverse events between patients treated with glargine U300 and those treated with glargine U100 after 2, 6, or 12 months of treatment. These findings ranged from low to moderate quality evidence.

In adults with type 2 diabetes, patients treated with glargine U300 experienced less hypoglycemia over 2 to 6 months of treatment compared with patients who were treated with glargine U100. This finding was from pooled evidence of three trials with a pooled relative risk of 0.74. This finding was considered moderate quality evidence. However, there was no difference in severe hypoglycemia and

withdrawals due to adverse events over 6 or 12 months between patients treated with glargine U300 and glargine U100.

In adults with type 2 diabetes, patients who were treated with glargine pen experienced fewer episodes of sever hypoglycemia compared to patients who were treated with glargine vial and syringe. In a pooled analysis of six observational studies, the odds ratio was found to be 0.74, and one additional observational study that was not included in the meta-analysis had consistent findings, and this is considered low quality evidence.

So, in summary, there were largely no significant differences in glycemic control between long-acting insulins included in this report. There were some differences between insulins in terms of adverse events, namely that degludec had a lower risk of nocturnal or severe hypoglycemia than glargine in type 1 and 2, and type 2 diabetes respectively. Detemir had more withdrawals due to adverse events than glargine in patients with type 2 diabetes. There was less nocturnal hypoglycemia in patients treated with glargine U300 than with U100, although this finding was with short-term treatment, and there was no significant difference at 12 months in patients with type 2 diabetes. Finally, glargine pen had a lower risk of severe hypoglycemia than glargine delivered via vial and syringe, and this was based on observational evidence in patients with type 2 diabetes. Finally, evidence on other harms, such as cancer and neonatal effects or harms with the fixed dose combination product degludec/aspart were very low quality.

This is the end of the presentation. I'd be happy to answer any questions you may have. Thank you.

Lisa Chew: Thank you, Brittany. [22:24 J] Any questions from committee members?

Dale Sanderson: I'm curious, it seems like dosing of these insulins would be a significant confounder when you're comparing one to the other. Is there... was there any attempt to look at that?

Brittany Lazur: That's a really good question. I think we'll need to delve a little bit further into the report, and we'll be able to get back to you offline about

that. I believe that that was something that was considered in this report, but I would need to take a closer look.

Lisa Chew: Any other questions from the committee members? Okay. We have two stakeholders. We have Dr. Zweber and Dr. Irani. If you can come up to the podium. Please state your name, who you represent, and you will have three minutes for your comments.

Sally Zweber: Hi. My name is Sally Zweber. I'm an internist, and I am a medial liaison with Novo Nordisk. So, I'm here today to talk to you about insulin degludec or Tresiba. First, I just want to point out that was a very nice thorough review, a lot of information there that she just gave, but the FDA has mandated that by design, studies of insulin head to head, they have to be what are called noninferiority studies, which means that you try to achieve similar glycemic control in both arms of the study. So, if you have, for instance, Lantus versus Tresiba and you have a group of people on Lantus and a group of people on Tresiba, and you bring all their A1c's down, you're supposed to aim for the same A1c lowering so that you cannot focus so much on that, but focus on the other safety measures, such as hypoglycemia, which you saw a lot of data about hypoglycemia today. I just want to be clear about that. We don't expect to see differences in glycemic control in insulin studies. In fact, we really shouldn't see differences. The studies are all supposed to be designed to provide the same glycemic control in both arms of the study. I just wanted to highlight one thing, and with Tresiba, we've had a label update this year, and basically information was included in our label about the Devote trial, and she did mention that on the presentation. I just want to emphasize that the Devote trial, it was the largest randomized head to head trial comparing Tresiba and glargine U100, and there were 7600 patients in the trial, and it was really primarily to evaluate cardiovascular safety. The primary endpoint was actually achieved because we wanted to show that Tresiba was as safe as glargine U100 in terms of cardiovascular events, and that was achieved. There were similar numbers of cardiovascular events in both arms of the trial. Additionally, secondary endpoints included safety endpoints, such as hypoglycemia. Then, compared to glargine U100, 27% fewer patients in the placebo arm reported severe hypoglycemia. In patients that were treated with Tresiba, there were 40% fewer total episodes of severe hypoglycemia.

So, this data is now in the Tresiba label, as of March of this year. Though not included in the label but consistent with the label, in addition to the 40% overall reduction in severe hypoglycemia, patients that were on Tresiba experienced a 53% fewer episodes of severe nocturnal hypoglycemia. So, overnight when we expect basal insulin to be really the active and important insulin in your system. So, I would ask that you continue to provide access to patients for Tresiba. It's also the only basal insulin that is approved for use in patients down to the age of 1 with both type 1 and type 2 diabetes. So, it's been on your preferred drug list, and I hope that you are able to maintain access to it. Thank you.

Lisa Chew: Thank you, Dr. Zweber. Any questions for Dr. Zweber? Okay. Thank you.

Boman Irani: Good morning. Thank you for the opportunity to comment on the use of Toujeo in patients with diabetes today. My name is Boman Irani. I am the medical liaison with the field base medical affairs department at Sanofi U.S. Today, what I'm going to do is briefly discuss the use of Toujeo in patients with diabetes. We have seen some data already about the ADA guidelines and effective basal insulin, the aim is to closely mimic pancreatic basal insulin secretion and have a longer non-peaking profile, which in turn could cause lowering of hypoglycemia. What we've seen is, patients with type 2 diabetes who experience hypoglycemia after starting basal insulin therapy do have a higher risk of discontinuation of the therapy. So, Toujeo, which is also referred in today's talk by glargine U300 is a long-acting human insulin analog indicated to improve glycemic control in adults with diabetes. One of the things which we've looked closely with Toujeo and comparing it to glargine is pharmacokinetic and pharmacodynamic studies. So, although it is the same glargine molecule, the U300, which is one-third the volume of the U100, it has shown that once you inject Toujeo, it releases much more gradually from the subcutaneous tissue than Lantus or U100 glargine does. What that does, it gives a more constant peaking profile, and a prolonged duration of action beyond 24 hours. What that does, it takes a little longer to reach steady state, to reach a steady state in five days. You, obviously, as we saw today, we looked at the efficacy and safety of Toujeo, and what this longer peaking profile would mean in terms of clinical studies, and these have been described in the edition one to four studies. I'm not going to go into much detail, as some of those studies were presented today, but

one of the pooled analyses showed, which was presented today, is in the main secondary endpoint, which was hypoglycemia, you get especially less conformed severe nocturnal hypoglycemia from weeks nine to month six. This was one of the standouts of this study, as we saw the... and as Sally mentioned, in terms of efficacy or reaching that primary endpoint and [inaudible] A1c, but what really stood out is this nocturnal hypoglycemia with Toujeo versus glargine. We also recently compared Toujeo with Tresiba, which is the two new basal insulins, which have been approved, and which were not included. We actually, the publication was published yesterday in Diabetes Care. So, it is really new, and it was presented at the ADA this year. This study's name, the Bright study, which compared these two new insulins head to head in a clinical trial in patients with type 2 diabetes who are insulin naïve. The primary efficacy endpoint, like many of the other trials we saw today, was reductions of the A1c from baseline to week 24, which was achieved for both glargine U300 and degludec 100, and we met the noninferiority endpoint, which is both the product shows similar [inaudible] reduction at week 24. We saw similar readability in 24 hour self-monitored plasma glucose and fast states self-monitored plasma glucose for both these new insulins. There was a small and similar weight gain for both groups, and a slightly higher mean daily insulin dose of glargine U300 than placebo at the end of the study. For the 24 week study period and the maintenance period, which is once the patient has titrated those and remain stable, the insulin sedimentation rate for nocturnal at any time of the day confirmed hypoglycemia was similar between glargine U300 and degludec 100; however, during the titration period, the insulin of the event rate at any time of day confirmed hypoglycemia and rate of nocturnal confirmed hypoglycemia was lower with glargine U300.

Lisa Chew: Please, Dr. Irani, if you could wrap up your comments, please.

Boman Irani: Yeah. So, what I want to just conclude by saying is that we have these two new insulins out on the market and in terms of A1c reduction, which we've seen compared to glargine U100, albeit similar. What we feel Toujeo offers is much more better 24 hour peaking profile and less hypoglycemia compared to glargine U100, as well as now we have seen this with Tresiba, even in the titration phase, which is an important phase especially for insulin naïve patients that are starting insulin early on, and

they don't want to get hypoglycemia and discontinue. And I'll just take any questions if you have them.

Lisa Chew: Thank you Dr. Irani. Any questions?

Amber Figueroa: I forgot to ask when we reviewed, what is the criteria for severe hypoglycemia? Is that less than 60? Less than 50?

Boman Irani: So we actually, the Bright study, which was the head-to-head versus Tresiba, we looked at less than 70 and less than 50 for both. And then in both those we found, especially in the titration phase, both of those numbers were less. Thank you.

Lisa Chew: Thank you. So I'm going to direct the committee members to the motion. It's on the last page of the section in your binder. I guess we have an option to either reiterate the prior motion based on what we heard today or make a new motion.

Amber Figueroa: There's nothing in here distinguishing the different concentrations with the U200 and U300. Do we need to include that, or is that assumed that sequel efficacy, or what's the plan here?

Ryan Pistoresi: No, we traditionally have not had different strengths for other medications. Like we haven't had the lisinopril5/10. I think it is understood in the previous motion that the U100 and the U300 are included in here, but if you weren't to make part of your motion a recommendations specifically for one of those, then you could call it out, but I think because it is the same ingredient it is being captured in the current motion.

Susan Flatebo: I move that we reiterate the prior motion.

Jordan Storhaug: I second.

Lisa Chew: All of those in favor say aye.
Group: Aye.

Lisa Chew: Any opposed? The motion carries. We are going to be moving onto Hepatitis C. The Hepatitis C scan and Susan Carson are you on the phone?

Susan Carson: Yes, I'm here. Can you hear me okay?

Lisa Chew: Yes we can hear you.

Susan Carson: Okay. Okay, I'll go ahead.

My presentation today is based on a scan that was completed in May of this year by staff at the Pacific Northwest Evidence-based Practice Center.

This is an overview of my presentation and all of the scans that we're presenting today will follow a similar outline. I'll show the history of the topic, the PICO and key questions used to guide the most recent report, give a brief overview of our scan methods, and then present the findings and the summary.

This report was last updated in December 2017 with searches through July 2017. This is the first scan since that report.

The included populations were adults and children with Hepatitis C virus infection, all geno-types and disease stages were included.

This table shows the included interventions by generic and brand names and the date of their FDA approval, with the newest drug shown at the top. The newest drugs are Mavyret and Vosevi, FDA approved in August and July of 2017. For adults, the PICO specified that regimens with at least two direct acting antivirals were included, and for children and adolescents any approved regimen was included.

For the report, studies were included if they compared one direct acting antiviral to another, so head-to-head studies. The same regimen with and without ribavirin or the same regimen given for different duration.

Efficacy and effectiveness outcomes were clinical health outcomes sustained viral response either at 24 weeks or if 24-week results weren't available then at 12 weeks, relapse or reinfection with Hepatitis C virus and serious extrahepatic manifestations. Harms included withdrawals due to adverse events, specific adverse events and hepatitis B reactivation.

The key questions focused on comparative benefits and harms both overall and in subpopulations and the association of sustained viral response to longterm clinical outcome.

So now we are on slide 8. Here are the methods used for the scan. To identify randomized control trials and systematic reviews, the authors conducted searches of Medline, the Cochran Library, and the websites of AHRQ, CADTH, and VA Evidence Synthesis Program (ESP). To identify new drugs, indications and serious harms the authors searched the FDA website, CenterWatch and conducted a limited internet search. Studies were selected if they met inclusion criteria outlined in the PICO's and if they were published in July 2017 or later.

So now I'll present the scan findings.

No new drugs, indication, or serious harms were identified for this scan.

There were 4 new head-to-head trials, including one trial of the newest drug, Mavyret, compared to sofosbuvir plus ribavirin. One trial compared response in a tailored regimen that was of a tailored duration, to a duration of 12 weeks, and two trials compared regimens with or without ribavirin.

Additionally, there were identified five secondary publications from randomized controlled trials that were previously included. Three of these were of the newest drug, Mavyret. Two were full publications of trials that were included in update three in abstract form that are now fully published, and three provided new data on viral logic resistance.

So to summarize, since the last update report there are no new drugs, indications, or serious harms and no new comparative effectiveness

reviews. There are four new head-to-head trials, one of which is of the newest drug, Mavyret. There are five secondary publications and three of which include Mavyret and there is no new evidence on Vosevi.

And that's the conclusion of this presentation.

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

Okay, we have two stakeholders, Mr. Stuart O'Brochta and Ms. Margaret Olmon. If you could please come up to the podium, please state your name and who you represent and you will have three minutes.

Stuart O'Brochta: Thank you. My name is Stuart O'Brochta with Gilead Sciences and I've seen many of you before, so thank you for the opportunity again. I want to thank you for your continued placement of Epclusa on the PDL in Washington and Vosevi, and I just want to just highlight a few things. You've reviewed the clinical data before, and you have reviewed the information and we've done that. So, really some reasons why I believe that you should continue to maintain this. Basically, the key attributes of Epclusa are really simplicity and there are a few things to that simplicity that I would like you to remember. Number one is, One. It is one tablet, once a day, one duration. Three p's, so its pangenotypic and panfribotic, panfribotic meaning all fibrosis stages, and its PI free leading to its simplicity of lack of drug interactions, or limited drug interactions and lack of food requirements. These have all led to high cure rates of 97-99 percentage you've seen before in the SVR's where the proven retreatment strategy in Vosevi that has been studied extensively in our trials. This has the most real world data confirming the clinical trial results, as you have seen in your population as well. So, why does this matter? The one pill, once a day especially in a population that potentially has adherence issues or housing issues you don't need to deal with multiple pills and one pill, once a day avoids that dosing confusion and less potential for storage or loss or diversion within a population that could have housing issues.

The three p's, the pangenotype, panfibrotic and PI free, it also covers the majority of the HCV infective population including patients with very advanced liver disease, as you know. The one exclusion is the small

number of patients that have advanced renal disease of any GFR below 30, which has been predicted to only be about 2% of the population.

So, in summary, Epclusa having this very favorable clinical profile and administration profile, it could potential maximize the treatment outcomes in a population that could have adherence, housing, and food scarcity issues, could be a very ideal regimen to treat that population and get the most benefit for your treatment dollars. So just in summary, to remember the one pill, once a day for one duration for all patients and that this is a pangenotypic and for all patients panfibrotic with the ease of a protease free regimen. So, basically that's what I would like to leave you with and encourage you to maintain this as one of your pangenotypic options for Hepatitis C patients in Washington. Thank you for your time.

Lisa Chew: Any questions? Okay, thank you.

Stuart O'Brochta: Thank you.

Margaret Olmon: Good morning, I'm Dr. Margaret Olmon from Medical Affairs at Abbvie. I appreciate the committees' time to review Mavyret as a pangenotypic treatment for the option for treating patients with HCV and respectively request that Mavyret can continue to be available for the Medicaid patients in Washington. Mavyret is the only once daily pangenotypic ribavirin-free regimen, now FDA approved to treat chronic Hepatitis C virus across genotypes 1-6 including those who do and do not have cirrhosis, having treatment experience with HIV, and chronic kidney disease. Up to 95 of patients with HCV can be treated with Mavyret and the vast majority of patients awaiting treatment are eligible for an 8-week course of treatment. Relative to safety, Mavyret carries a box warning regarding the risk of Hepatitis B reactivation in patients co-infected with HCV and HBV, as do all the direct acting antivirals. Mavyret also has two contraindications, one for patients with severe hepatic impairment, Child-Pugh C, and the other for patients taking concomitant [inaudible] or rifampin. The most common adverse reaction in clinical trials in greater than 10% of patients were headache and fatigue, and the AE's were comparable among the patients with compensated cirrhosis and without cirrhosis. Mavyret is well tolerated, requires no liver monitoring or resistance testing, and no dosage or duration adjustments

are needed for patients with HIV coinfection nor for any level of renal impairment, including patients on dialysis. This has only been a short summary. I appreciate all of the information on the clinical trial that's already been provided and you know that full prescribing information and complete safety information are available online at RXAbbvie.com. I want to thank you very much for your time and consideration, and I can answer any questions you might have at this time.

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

Margaret Olmon: Thank you.

Lisa Chew: I'm going to direct the committee members attention to the last page of the section with the motions. I think we have two action items. One is whether or not the scan is adequate or whether we are requesting a more updated class review and then whether we want to reiterate the prior motion or make a new motion. So let's start with whether we accept the scan as adequate.

Amber Figueroa: I move that we accept that the scan is adequate.

Lisa Chew: Second. All of those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Then the motion carries.

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

Dale Sanderson: Second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Okay, we're going to move onto the Multiple Sclerosis scan, again we have Susan doing the presentation.

Susan Carson: Okay, thank you. So this next scan was completed by EPC staff in June 2018.

So I'll follow the same outline as in my previous presentation.

The last full update, the last full report on this topic was completed in May 2016 with searches through January of 2016. Since then, there have been two scans, with the most recent having searches through November 2017.

The included population for this report were adults with multiple sclerosis or a clinically isolated syndrome.

The included interventions are shown here, with the most recently included drugs listed first.

So, direct comparisons of included drugs were included for the report.

Efficacy and effectiveness outcomes included disability, clinical exacerbation/relapse, quality of life, functional outcomes, persistence, and for patients with a clinically isolated syndrome progression to a multiple sclerosis diagnosis. Harms outcomes were withdrawals due to adverse events, serious adverse events and specific adverse events.

The key questions addressed comparative effectiveness and comparative harms, overall and in subgroups, and the relationship between neutralizing antibodies and outcomes.

For this scan, searches were conducted in the second week of May 2018 and studies published since November 2017 were included. For effectiveness and harms, head-to-head controlled trials and good quality comparative systematic reviews were included. I'll note that placebo controlled trials were included in the last report for a network meta-analysis and for new drugs or formulations with no head-to-head evidence in a given population, but placebo-controlled trials were not included in this scan.

I'll present the scan findings now.

Although no new drugs were identified for this scan, there have been two new drugs that were approved since the last full update, ocrelizumab and daclizumab. There have been new edits to existing FDA warnings as well. For daclizumab, there was an edit to add acute liver failure and fatalities to an existing warning on hepatic injury, and for teriflunomide, a boxed warning on the risk of teratogenicity was edited in November 2016; however, this risk was already known at the time of that drug's approval.

There were no new comparative effectiveness reviews, since the last scan, but two have been published since the last update report. One of these compared glatiramer to beta interferon and another compared different glatiramer dosing strategies.

The current scan identified one new head-to-head trial of fingolimod versus interferon beta-1B in patients with relapsing-remitting multiple sclerosis.

In this scan, 11 new secondary analyses were identified, bringing the total of new secondary analyses since last update to 21.

In summary, since the last scan one new head-to-head trial is found and 11 secondary publications of previously identified trials have been published. No new drugs were approved and no new systematic reviews were identified. Since the 2016 update report, two drugs have been approved, ocrelizumab and daclizumab, and two systematic reviews have been published. Accumulatively, there are two new head-to-head trials; however, neither include the newest drugs.

Thank you and I would be happy to respond to any questions.

Lisa Chew: Thank Susan. Any questions from committee members? Okay, we have two stakeholders. We have Dr. Lynda Finch and Terrie Paine. Please come up to the podium, state your name and who you represent, and you will have three minutes.

Lynda Finch: Good morning, I'm Lynda Finch and I'm a medical liaison for Biogen. Biogen manufactures four therapies for MS., Avonex, Plegridy, Tecfidera and Tysabri, and I'm going to focus my comments on Tecfidera today.

So Tecfidera is the most frequently prescribed oral medication for MS in the US. It's been used now by over 300,000 patients worldwide and it is the most prescribed oral MS treatment for Washington Medicaid patients with MS currently. It's currently in a preferred position with your formulary with Washington HCA, and my request today is that you keep Tecfidera as the preferred product on your PDL, so that patients are able to use Tecfidera firstline when they're newly diagnosed or naïve to MS treatment. So I'm going to share some data with you today from our pivotal trials and our longterm extension that looked at this subgroup of newly diagnosed MS patients that supports your current formulary placement. So, newly diagnosed MS patients in our pivotal trials experienced a 56% reduction in your analyzed relapse rate and this was statistically significant at 2 years versus those newly diagnosed patients that were place on placebo. They also had a statistically significant 54% reduction in the proportionate patients who experienced a relapse, and then newly-diagnosed patients were those that were defined as having been diagnosed in the year prior to entering the study that hadn't been on any treatment other than symptomatic corticosteriods. Most significantly I think most meaningful for patients, is newly diagnosed patients experience a 71% reduction in confirmed disability progression compared to those that were on placebo. So, this is really meaningful data for MS patients. They also had statistically significant reductions across all of the MRI parameters with 88% in decrease in the mean number of T2 lesions, 68% reduction in number of T1 lesions, and 84% reduction in Gad-enhancing lesions.

Now not all newly diagnosed patients are easy to treat, some of them have highly active disease right from the beginning. So, we also looked at this subgroup of patients, and these are patients who had two or more relapses in that first year that they were diagnosed before coming into this study, and this group of highly active, newly-diagnosed patients also experienced a 56% reduction in their annualized relapse rate and a 56% reduction in the proportion of patients who experienced a relapse at 2 years compared with the patients on placebo. So comparable to the

overall population, we were able to control these patients. Longterm, these newly-diagnosed patients do very well. We have 8-year data now from our original study and more than half of the patients that were newly diagnosed and put on Tecfidera have had zero relapses and no disability progression, so that's really outstanding data and very consistent over the longterm. So just to conclude, Tecfidera has shown a very consistent efficacy profile that's been characterized now in over 3,000 clinical trial patients and 300,000 patients worldwide and the combination of its unique MOA and its well-defined safety and efficacy profile supports Tecfidera is a preferred product for all of your patients with MS. Thank you and I'm happy to take any questions.

Lisa Chew: Thank you very much. Any questions from the committee? Okay, thank you.

Terrie Paine: Hello, my name is Terrie Paine and I'm here on behalf of people living with multiple sclerosis. I was diagnosed 20 years ago, actually I just had a birthday, it's been 21 years now, with relapsing/remitting multiple sclerosis. Since then, I have been on three different therapies as my condition has changed and changes in therapy were recommended by my neurologist. For the first 13 years after I was diagnosed, I was on subq injections of Copaxone and my diseased appeared stable, and I was basically asymptomatic, but a routine MRI showed that I had a significant increase in brain lesions at which point my neurologist recommended a change in therapy. The next 5 years I spent on monthly infusions of Tysabri and when I started that therapy I was John Cunningham or JC Virus negative but 5 years later I seroconverted with very high antibodies titers, which put me at a much greater risk for PML and that's a brain infection which can cause significant negative or even fatal outcomes, and so based on that increased risk my neurologist changed my therapy. I spent the last two and a half years on oral Tecfidera, so as you can see the changes in my clinical picture occurred, my neurologist was able to quickly change therapies, which has resulted in good control of my disease and that's a better quality of life. I am a believer that patients and physicians should have the opportunity to choose the best therapy at a given time for a given patient, including those who are treatment naïve. My ability to change therapies at different times has led to the better

outcomes for me after 20 years with this progressive neurologic disease. Thank you and I'm happy to take any questions.

Lisa Chew: Thank you Ms. Paine. Any questions? Alright thank you. Okay, for the committee we are going to direct our attention again to the motion, it's on the last page of this section. Again, there are two action items here. One is whether or not we accept the scan as adequate or want a more updated class review, and then second is whether we want to reiterate the prior motion or make a new motion.

Susan Flatebo: I move that we accept the scan as adequate.

Dale Sanderson: I second.

Lisa Chew: All of those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Okay, the motion carries.

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

Susan Flatebo: I second.

Lisa Chew: All of those in favor say aye. Any opposed? Okay, the motion carries. Alright we will be moving onto the antiemetics scan and Beth, are you on the line?

Beth Shaw: Hi, yes I am.

Lisa Chew: Okay, great, your slides are up.

Beth Shaw: Thank you. So I'll take you through the scan on new antiemetics.

If you move to slide 1, please, you will see the overview of the presentation, which you've seen already.

In terms of the topic history, the original report on newer antiemetics was published in January 2006 with a full update in January 2009. Since then, there's been a series of scans culminating into scan 8.

So in terms of the background, nausea and vomiting can be significant concerns and we're focused here on three groups of patients. The people undergoing chemotherapy and radiation, people postoperatively, and pregnant women and these therapies can be used both to treat the nausea and vomiting but also to prevent it in the first place. So, this review simply describes the amount and nature of new research since the last full update in January 2009.

So, on slide 4, you can see the PICO that we've applied in the reports and the scans. So in terms of the population, it's adults and children and those populations are highlighted before. I'll take you through the intervention, which you'll see on the next slide, and in terms of comparatives, we were really focusing here on active comparatives, so direct head-to-head comparisons of the new antiemetics. Where there was a lack of evidence in that head-to-head arena, we included all of the comparisons of drugs or placebo-controlled trials. In terms of outcomes, we were really focusing on the impact on nausea and vomiting but also people's quality of life, patient satisfaction, and adverse events associated with treatment.

So in terms of the included interventions, you will see on the left hand side, we have the generic name, the middle column we have the brand name of each of those drugs, and then the drug class to which they belong.

And in terms of the key questions that we were trying to address, we've been looking at effectiveness for treating or preventing nausea and vomiting, the tolerability and safety of these drugs, and whether there were subgroups of patients or clinical situations in which there was potential for greater benefit or greater harm.

Our methods for this scan, which you've seen already, I'd like to focus that we conducted this search for this scan, looking for trials published between January 2017 and May 2018.

Now I'll take you through the findings and we'll first look at the new drugs or formulations.

So since the last update reported in 2009, we have identified 11 new antiemetic drugs or formulations, four of which are identified in this scan. We found one first generic approval for the combined drug for sure in pregnant women, and we found three new formulations of the drugs listed here; Aprepitant, Netupitant/palonosetron combination and Rolapitant all of which were IV infusion.

So I'll also take you through some information that we found on new prescribing information and safety warnings.

So since the last scan in 2017, we have found some new prescribing information on the use of Fosaprepitant IV and this was mainly around the use in children, but also some information on how to manage and identify hypersensitivity and infusion site reactions. Similarly, Rolapitant, IV and oral, we found more information on dose regimen and some more information on contraindications and interactions. For Rolapitant, we also found a new serious harm that resulted in a manufacturer's warning letter that was around anaphylaxis, anaphylactic shock and other serious hypersensitivity reactions associated with the use of injectable emulsion.

So what did we find in terms of systematic reviews?

So this is slide 13 and since the last update report in 2009, there have been four systematic reviews identified. The majority of these focus on the use of antiemetic medication in chemotherapy-induced nausea and vomiting. We didn't find any new systematic reviews in this new scan.

What we did find was that one Cochran review on the use of these drugs for postoperative nausea and vomiting had been withdrawn in 2017. This was a substantial review, it included over 60 antiemetic drugs and around 730 studies. At the time of writing the review, 67 of those included 737 studies had been retracted and are underway of investigation undergoing for the studies. We're not able to fully understand the impact this might have on your report and your scans, that would need further work to

explore that, but some of those publications that have been withdrawn were included in the 2006 report.

In terms of randomized trials, since the last update report in 2009, we found 76 relevant trials, 34 head-to-head trials, 22 trials comparing the addition of an NK1 agonist to standard therapy, and 20 placebo-controlled trials, and in this scan, well since February 2017, we have identified five new trials. One is a head-to-head trial and four add-on trials.

So here on slide 17, you can see the details of each of those trials, the one head-to-head comparison, and then the four add on trials. They're all in adults and they're mainly comparing it with ondansetron, IV or oral, and you can see the outcomes there on the left hand side.

We also found since the last update report in 2009, seven secondary analysis. So that's four subgroups analyses of published trials and three pooled analyses of published trials, and in this scan we found four new secondary analyses, two subgroups and two pooled.

So here's the details of the analyses in terms of subgroups. They've looked at all of the people undergoing chemotherapy and also patients with breast cancer undergoing chemotherapy, and in terms of the pooled analysis Barbour et al., 2017 focused on the safety of people, so the effect these drugs in people undergoing chemotherapy, and Chasen et. al., 2017 focused on the impact on daily life and the quality of life associated with these interventions.

So in summary, since the last update report we've identified three newly-approved drugs, eight new formulations or first generic approval, 76 trials, five of which are new in this scan, and seven secondary analyses published RCT's, again four in this scan. Thank you.

Lisa Chew: Thank you, Beth. Any questions from the committee members? I actually have one. I have a question about the harm, the serious harm for Rolapitant. Do we know how common that is and which patients are at risk for the severe hypersensitivity reactions?

Beth Shaw: We can pick out the details for you.

Lisa Chew: Thank you. Any other questions from the committee members? And there are no stakeholders for this drug class. So for the committee members, again, we're looking at the last page of the section looking at the different motions. Whether we want to accept the scan as adequate and then whether we want to reiterate the prior motion.

Dale Sanderson: I would move that we actually accept the scan as adequate.

Diane Schwilke: I second.

Lisa Chew: All of those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries.

Susan Flatebo: My only issue with the motion is the very last sentence that says ". . . for patients receiving highly emetogenic chemotherapy and radiation therapy" shouldn't that be changed to ". . . and/or. . . "because certain high dose radiation therapy regimens can cause a lot of nausea as well?

Lisa Chew: Just other thoughts from the committee regarding the harm associated with Rolapitant, whether we know enough about the harm and the prevalence and which patient populations are at risk. Whether we want to continue to include that on the PDL.

Susan Flatebo: I don't have any experience with Rolapitant but it would probably be given in an infusion center, chemotherapy infusion center, who would have access to emergency kits if needed. I mean I guess it would depend on again the incidents of the anaphylaxis or HSR.

Amber Figueroa: I don't feel like... this is a drug that I don't deal with at all either, so I don't feel like the presentation includes enough information for us to make a decision either way. Could we request that somebody gather the information and present it back to us?

Ryan Pistoresi: I will note that when we meet with DERP again, just to let them know that there is some interest in getting more information about this serious adverse event and so we will bring it up with other states too, since other states may be interested in that, so we will make a note. Thank you.

Amber Figueroa: I guess one other discrepancy looks like they brand it as a moderately emetogenic or highly emetogenic and our motion only implies that the NK1 antagonist is available for the highly emetogenic but it looks like they are studying it in both of these groups. Do we want to adjust that or leave it?

Ryan Pistoresi: This is just saying that the preferred drug list must include one of these drugs for the patients receiving the highly emetogenic chemotherapy and/or radiation therapy. It doesn't say that it is necessarily excluded for those patients, but if you want to change that so that way that drug is available for both of those groups, you certainly can, but it's just saying that one of the drugs on the preferred drugs needs to be from that specific drug class.

Susan Flatebo: I agree with this verbiage. It's just saying that an NK1 antagonist should be included for patients getting highly emetogenic chemo or radiation therapy. So if you're on a moderate chemo regimen and you did not get an NK1 antagonist yet, you are having a lot of nausea, I don't think this is saying that you can't have that added on with future treatments, it's just typically not given with maybe the initial dose.

Are we comfortable with leaving Rolapitant in the motion or should we say that we're maybe delaying including that for now until safety information has been gathered?

Dale Sanderson: Do we know how many people use this? Do you have any kind of number?

Ryan Pistoresi: So, no I don't have any utilization data that I can present today, so I am not sure how many people are using it. However this is one of the new formulations that has since come out since the last scan. So, I would anticipate that it's not very much relative to the other antiemetics, but I

can't say with any confidence how many patients within our populations are using it, at least today.

Lisa Chew: I'm kind on the fence now whether to keep it or not. If we took it off, would patients still have a wide range of choices or access to these meds, if we were to remove that, I suspect probably. I guess I tend to take it off until we have more information, but I'm interested in other people's thoughts.

Male: I would agree. The other question I have is, is there anything unique about that agent that would call for its use compared to the others?

Ryan Pistoresi: So what I'm hearing you talk about is whether it should be eligible to be preferred or not preferred. That means it could still be eligible for patients in unique situations, in which that medication may be available to them, but it would not necessarily be one of the firstline preferred drugs on the preferred drug list. So, the way that you may want to phrase the motion is that it's not eligible to be a preferred. It will still be available through the programs, but it would not be considered one of the firstline treatments, as would some of the drugs within that drug class. Is that direction the one that you're thinking about? Or are you thinking about a different direction for that?

Leta Evaskus: You can exclude it from the PDL, which means that it's not available preferred or non-preferred, and currently it is non-preferred on the Washington PDL.

Virginia Buccola: I just want to say that it sounds like I'm hearing a lot of, I'm seeing a lot of heads kind of shaking up and down wondering what to do, my question might be that if we deferred making a decision to our next meeting, how does that impact the clients that we're serving if we waited to have more information?

Ryan Pistoresi: So your question is about what would happen if we delayed making a motion today? We would continue to have the same preferred, non-preferred status until there was a new recommendation. So the current, old motion would still be in effect, and our current PDL as it is would continue to stay the same.

Virginia Buccola: It would be helpful for me to make a decision to have a little more information. Some of the questions that weren't able to be answered today just because time is needed to find the data.

Ryan Pistoresi: So what I'll do is that I'll mention to DERP and to the other states that there is some interest from out P&T committee to get more information, specifically about the Rolapitant. So, we'll see when we can get the new evidence prepared for you, as was mentioned at the beginning of this meeting we are getting some new vendors. So, we may be getting some evidence in a little bit faster or in different formats or different types of reports. So, we'll see what we can do in regards to that.

Male: Would it be appropriate to withdraw that this scan was adequate? Since it doesn't seem like it was adequate.

Ryan Pistoresi: I don't see why not. I mean after this discussion if you would like to go back and change that to say that the scan was not adequate because it didn't necessarily answer that question. However, the purpose of this scan is not to provide new evidence. It's mainly to look at what is available out there as a way to guide whether we need a new report or not. So, the scan does not necessarily have a lot of new information. What it did though is identify that there is this new serious harm that has been identified, which is the purpose of the scan, and then the purpose of this discussion, I think, is to say we need more information, which could then lead to an expanded scan or a report or whatever the other DERP participants recommend. So, from my perspective, I do think the scan is adequate, because it did identify this and it did kind of spur this conversation, but I think the preferred course of action is to then recommend to DERP and to the other states that we do need more information in the form of an expanded scan or an update to this report.

Male: So be it.

Ryan Pistoresi: Okay.

Amber Figueroa: I agree that the scan is adequate. I think we should leave it the way it is, and I think we shouldn't make any motion on the antiemetics at this point so that the current one stands until we get more information.

Lisa Chew: Does the committee feel comfortable with that? I don't have to make a motion.

Ryan Pistoresi: So, the only thing that you did mention and at the very beginning was changing the very last sentence to be "and/or", is that something you would still want to consider at this time, the "chemotherapy and/or radiation therapy" or are you looking to remove that for now and then have the old motion?

Susan Flatebo: I think it should have "and/or" in there, included.

Lisa Chew: So does it seem reasonable to revise this motion to include that change and then delay the decision on whether we want to keep Rolapitant on there or not at a later time?

Ryan Pistoresi: I think what you can do is you can change the motion to have the "and/or" and then you can have a note, like what Leta added at the bottom, to request more information on the harms of Rolapitant. We have done that in the past, most notably for the insomnia class two years ago, which you said did not have enough adequate information about the use of these drugs in children. So, we then went back and had a new report that focused more on children that we presented last year in 2017. So, this helps us to keep track of some of the conversations, some of the concerns that you have so that way when we revisit this and hopefully have that information at that time, we can remember why we made that decision. I think what is currently up there satisfies what I'm hearing from the committee today.

Lisa Chew: Does anybody want to read that motion?

Amber Figueroa: After considering the evidence of safety, efficacy, and special populations I move that Aprepitant, Doxylamine/Pyridoxine, Netupitant/Palonosetron, Fosaprepitant, Granisetron, Ondansetron, Rolapitant, Dolasetron, and Palonosetron are efficacious for their FDA

approved indications. The preferred drug list must include at least one medication that includes alternate routes approved in both adults and children. The antiemetics can be subject to therapeutic interchange within their mechanism of action in the Washington PDL. The preferred drug list must include a neurokinin 1 antagonist for patients receiving highly emetogenic chemotherapy and/or radiation therapy and that a request for more information on the harms of Rolapitant.

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

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Okay, and then we have our last topic here, the antiplatelet scans. Susan, are you back with us?

Susan Carson: Yup, here I am. Thank you.

Lisa Chew: Great. Your slides are up.

Susan Carson: Awesome. Okay. So, this scan was conducted by staff here at the Center for Evidence-based Policy.

So, here is the same overview of my presentation, you've seen multiple times today.

This report was first done in 2005 and has been updated several times since. The most recent update was conducted in August of last year with searches through the end of March 2017.

The population was adults with acute coronary syndrome, coronary revascularization via stenting or CABG, previous Ischemic stroke or transient ischemic attack, or symptomatic peripheral artery disease.

The interventions are shown here in the table by active ingredient and brand name on the right hand column. Note that two formulations were excluded, ticlopidine tablet and cangrelor infusion.

For the last report the comparators were antiplatelet drugs compared to each other, so head-to-head comparisons, unless there was no head-to-head evidence for a drug. Then placebo or aspirin comparators were included.

The outcomes for effectiveness and efficacy were the clinical outcomes all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, and failure of an invasive vascular procedure. For safety, included outcomes were overall adverse events, withdrawals and withdrawals due to adverse events, and serious adverse events.

The key questions focused on the comparative effectiveness and efficacy and harms overall and in subgroups and differences between drugs based on the duration of therapy.

So, we used the usual methods for this scan. For this scan, we included studies published after March 31, 2017.

I will now present our scan findings. So, we identified no new drugs, no new formulations, indications or serious harms.

We identified one systematic review, which focused on ticagrelor versus other antiplatelet or placebo for stroke prevention specifically. So, this review had a limited scope.

We also identified four subgroup analyses of randomized control trials that were previously included in the report. The Trilogy ACS trial, this is a subgroup analysis in patients with or without diabetes, either type 1 or type 2, and that Trilogy ACS trial compared aspirin plus prasugrel versus aspirin versus clopidogrel in acute coronary syndrome. The second subgroup analysis was in from the TRA 2 P-TIMI 50 trial, which compared vorapaxar versus placebo in MI or peripheral artery disease, and this subgroup analysis compared patients with previous CABG or who were undergoing CABG. The Euclid trial compared ticagrelor to clopidogrel in coronary artery disease, and this subgroup analysis looked at patients specifically with critical limb ischemia. Then finally a subgroup from the Plato trial, which compared ticagrelor to clopidogrel in acute coronary syndrome, and this subgroup analysis compared early versus late

angiography, and they define those as less than three hours and greater than three hours.

Finally, we identified four new head-to-head trials in this scan. These had primary outcomes though that were biochemical or intermediate outcomes, but they did also report short-term harms between ten and thirty days as secondary outcomes.

So to summarize, since the last update report we identified no new drugs, indications, or serious harms. We identified one new systematic review of randomized controlled trials of Ticagrelor for stroke prevention. We also identified four new subgroup analyses and four head-to-head trials that had intermediate outcomes but also reported short term harms.

So that's the presentation and thank you.

Lisa Chew: Thank you, Susan. Any questions from the committee members? There are also no stakeholders for this class and again we go to the motion. We have two actions again to accept the scan as adequate and either we want to reiterate the motion or make a new motion.

Catherine Brown: I move to accept the scan as adequate.

Amber Figueroa: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Okay, the motion carries.

Susan Flatebo: I move that we reiterate the prior motion.

Catherine Brown: I second.

Lisa Chew: All of those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Okay and the motion carries. Okay, so the P&T committee is now adjourned and we'll take a 15, like 10:45? Okay, great. Thanks everyone.

Alright we're going to go ahead and get started and we are now convening the Drug Utilization Review Board. We have Umang Patel who is going to be doing a presentation.

April Philips: Before Umang jumps into his presentation, I wanted to point out, some of the classes that we'll be discussing are really old. There haven't been new products in these classes for years. Since the Apple Health PDL is supposed to be an all-inclusive, we are reviewing those classes, bringing them to you. So, there may not be clinical information, you know, necessarily on those products. We just want to let you know that they will be included in the PDL.

Umang Patel: Just as April alluded, I will kind of point out when we get to those classes when there isn't robust information like the other ones. We'll just look at the medication that fall under there and it will just be like that.

So, on the next slide, just as we normally do, each topic will be divided into the disease state, the indications, the dosage and formulations, and guideline updates, if there are any.

The first category we'll go under is cough and cold.

So just a quick overview of the disease state; the common cold is a viral illness that affects persons of all ages prompting frequent use of OTC and prescription medications and alternative remedies. Adults in the US experience two to four colds per year. The common cold is the most common reasons for physician visits, with cough being a common presenting symptom. At least 200 identified viruses are capable of causing the common cold, and the viruses often implicated are the rhinovirus, coronavirus, parainfluenza virus, respiratory syncytial virus, adenovirus and enterovirus. Although histologic effects on the nasal epithelium may vary, any of the viruses can cause vasodilation and

hypersecretion leading to the common cold syndrome, which includes nasal congestion, nasal discharge, postnasal drip, throat clearing, sneezing, and cough. Acute cough can be characterized as a cough that's lasting three weeks or less and the causes of acute cough include the common cold or other respiratory tract infections and allergic rhinitis. A subacute cough lasts three to eight weeks and this can remain after the initial cold or respiratory infection is over. Lastly, a chronic cough can last over eight weeks, and the causes of this can include asthma, bronchitis, and chronic obstructive pulmonary disease or COPD. The cough may also be associated with factors such as GERD, medication side effects, pulmonary embolism, smoking, lung cancer, and cough due to these conditions will not be addressed in this class review.

So just a quick additional overview, cough and cold formulations are available in use of the treatment of the sign and symptoms of the common cold, sinusitis, allergies, and cough. They come in various combinations, from simple cold combinations, narcotic cough and cold formulations, as well as non-narcotic cough and cold formulations. The cold formulations are available as prescription generics, which are combined in one of the following manners with several of the available ingredients. We'll have antihistamine only, antihistamine with decongestant, decongestant with expectorant, and expectorant only. There are many narcotic cough and cold formulations as prescription generics, which are combined in one of the following manners with several of the available ingredients: antitussive-anticholinergic, antitussive-antihistamine-decongestant, antitussive-decongestant-expectorant, and lastly antitussive-expectorant. Lastly, there are many non-narcotic cough and cold formulations that are available as prescription generics such as antitussive-antihistamine, antitussive-antihistamine-decongestant, antitussive-antihistamine-decongestant-expectorant, antitussive-decongestant, antitussive-decongestant-expectorant, and lastly antitussive-expectorant. Just to take quick step back for a little bit of a clinical background, for the anticholinergics, how they work is they competitively block the muscarinic receptors, which will help kind of dry the mucus membranes. The antihistamines competitively antagonize the effects of the H1 receptors in the GI tract, the uterus, the large blood vessels and bronchial smooth muscle, which help with the overall symptom relief. Antitussive in terms of opiates,

they directly act on receptors in the cough center in the medulla. These agents also have a drying effect on the respiratory tract and increase the viscosity of bronchial secretion. For the antitussive non-opiate, dextromethorphan is a non-competitive antagonist of the MNDA receptor in the brain and spinal cord, so it acts on the cough center in the medulla to raise the threshold of coughing by decreasing the excitability of the cough center. And the last for the expectorants, it loosens and thins the sputum and bronchial secretions to ease expectoration.

So, here we have the dosing availability. Now, as always we have the dosing stratified between adults and children and the availability as well. So, while you take a second to look at this, I will say that for pediatrics many of the products in this category are approved for use in children as young as 2 years of age. The use of prescription opiate cough and cold products are limited to adult patients aged 18 years and older due to the risks of these medication outweighing the benefits. For pregnancy, pregnancy category depends on the component ingredients. Many are pregnancy category C, but it is recommended to consult the individual package insert for the product information.

On the next slide, we have the antihistamines, the previous slide we had anticholinergics and antihistamines. Here we are continuing with the antihistamines where we have seven of the antihistamines here. Again with special populations, such as patients who have a renal disfunction, dosage adjustments may be warranted; however, specific guidelines in the renal impairment are not available. It is recommended to refer to the package insert as well.

Here we have the antihistamines along with the antitussives, which are the opiates. In terms of hepatic impairment, very similar to renal impairment, patient-specific dosage guidelines are not available, and it is recommended to refer to the specific package insert.

And lastly, here we have the antitussives that are non-opiate, the decongestants and the expectorants. The last special population to consider are the geriatric populations. The elderly are more susceptible to the anticholinergic effects of antihistamines, so reduced initial dosages may be needed.

Here we have just the guidelines, the American College of Chest Physicians (ACCP) Evidence-based Clinical Practice Guidelines on the Diagnosis and Management of Cough back in 2006 stated that patients with an acute cough associated with common cold can be treated with a first generation antihistamine and decongestant preparation.

That concludes this topic. Are there any questions?

Lisa Chew: There are no stakeholders.

April Phillips: For the Apple Health PDL, our cough and cold classes divided up into several subclasses, the decongestant systemics, the decongestant internasals, the antitussives, the expectorants, miscellaneous, which includes like your saline, and your miscellaneous combinations, which are the combinations which include Tylenol or aspirin. So, our recommendations is to continue coverage of the cough and cold products in accordance with the Federal Laws. All of the products within each subclass are considered safe and efficacious within that subclass and are eligible for a preferred status and grandfathering at the discretion of HCA and all non-preferred products require a trial of two preferred products within that subclass with the same indication and different active ingredients before a non-preferred drug will be authorized, unless contraindicated, not clinically appropriate or only one product is preferred.

Amber Figueroa: I move that the Apple Health Medicaid program implement the limitations for the cough and cold drug class listed on slide 12.

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

Group: Aye.

Lisa Chew: Any opposed? And the motion carries.

Umang Patel: The next class we'll discuss are the Macular Degeneration Agents or the Ophthalmic-Angiogenesis Inhibitors.

Just a quick overview, age related of macular degeneration or AMD is the most common cause of irreversible vision in the United States. It is divided into two subtypes, the first being dry or non-exudative. In dry AMD, drusen, which is a yellow deposit of lipid and fatty protein, form on the extracellular material beneath retinal the pigment epithelium. Dry AMD may progress to wet AMD in approximately 20% of patients, in which pathologic choroidal neovascular membranes grow under the retina, and then the second being wet or exudative, or neovascular. There is also retinal vein exclusion RVO, which can cause macular edema. The exact pathogenesis of RVO is unknown, multiple factors have an impact on closure of the retinal vein. Occlusion of this vein leads to back up of retinal blood flow and increases blood flow resistance, leading to retinal damage. VEGF is hypothesized to be increased in retinal damage, stimulating neovascularization and capillary leakage resulting in macular edema.

We'll also discuss for macular edema, diabetes is the leading cause of new blindness in the US. Without appropriate eye care, diabetics have a 20-30% risk of moderate vision loss. Thickening of the retina within two disc diameters of the center of the macula and is a consequence of microvascular changes to the retina, resulting in leakage of plasma constituents and leading to retinal edema. Lastly, degenerative myopathy is also referred to as pathologic myopia. It's the seventh leading cause of blindness in the US. It's common with prevalence in developed countries ranging from 11-36%, and approximately 27-33% of the myopia populations are classified as degenerative myopia. Of the patients with degenerative myopia, up to 10% of that population may develop choroidal neovascularization, a condition where blood vessels begin to grow in the choroid area into the retina. Advanced states CNV can appear as a macular scar where retinal atrophy is present and can lead to vision loss.

So on the next slide we'll look at three medications that make up this class here. We have Eylea, Macugen, and Lucentis. Note, none of these are generic and for Eylea it is indicated for new vascular or wet, age-related macular degeneration. It is indicated for RVO, for diabetic macular edema, and for diabetic retinopathy in patients with DME. Macugen is associated with nonvascular wet age-related macular

degeneration, and lastly, Lucentis is indicated for AMD, RVO, for diabetic macular edema, diabetic retinopathy and lastly myopic choroidal neovascularization. To take just a step back clinically, so the mechanism of action for these, the VEGF that I mentioned earlier, is a protein that induces angiogenesis and creates permeability in inflammation and so that's associated with the neovascularization. Eylea the first medication here, is a soluable decoy receptor that binds to VEGF. Macugen is a pegylated, modified, nucleotide that's a VEGF antagonist. And lastly, Lucentis is a humanized recombinant monoclonal antibody that inhibits VEGF. So they all work in one manner or another with the VEGF.

On the next slide here, you'll see the dosing and availability. Firstly, for Eylea, as you can the dose is stratified by its indications. There is also administration comments. I would usually keep those in the classes that have specific instructions, and lastly dosage forms. For specialized populations, for pediatric safety and efficacy of Eylea, Macugen, and Lucentis have not been studied of patients under the age of 50 years of age. In terms of patients who are pregnant, all three of these should be used during pregnancy only if needed, when the potential benefit justifies the risk to the fetus. Lastly, in terms of geriatrics, geriatric patients and patients with renal dysfunction, there's no difference in efficacy or exposure seen in patients greater than 65 years of age, and for renal patients there is no dosage adjustment needed. Lastly, for patients with hepatic impairment, safety and efficacy of these three medications have not been studied.

And lastly, here we have Macugen and Lucentis with a dose, again stratified by their indications, administration comments, and dosage forms.

In terms of guideline, Age-Related Macular Degeneration Preferred Practice Pattern by the American Academy of Ophthalmology state that intravitreal vascular... they state that intravitreal VEGF inhibitors, such as the three mentioned here, should be used as firstline, as they are the most effective agents to manage neovascular AMD. For retinal vein occlusion, the American Academy of Ophthalmology states, 2 years of treatment with an intravitreal VEGF inhibitor are safe and effective in macular edema associated with central or branch RVO. Vision related

quality of life was improved at 1 month and 6 months after the therapy. There is limited data in preferring one over the other agent in this class. In terms of macular edema, the American Academy of Ophthalmology states that for clinically significant macular edema, laser surgery has been the traditional treatment. Current data indicates that intravitreal anti-VEGF therapy is more effective for center-involving CSME than monotherapy with laser surgery. They recommend anti-VEGF therapy as a preferred initial treatment for center-involving macular edema, with or without laser therapy. For nonproliferative diabetic retinopathy, they say that anti-VEGF may sometimes be used in patients of an NPDR, that is mild, moderate, or severe with clinically significant macular edema or in patients with clinically significant macular edema and proliferative diabetic retinopathy who are now considered high risk for vision loss. And lastly, for patients who have proliferative diabetic retinopathy, it states, patients who have PDR without macular edema but are a high risk for vision loss recommend anti-VEGF therapy. They also recommend this therapy in patients with any amount of macular edema regardless of whether it is considered clinically significant, as those treatments have been shown effective in center-involving DME.

Lastly, the American Diabetes Association states, they recommend ophthalmic assessment in general for patients with Type 2 diabetes at the time of diabetes diagnosis and within 5 years of diabetes onset in adults with Type 1 diabetes. If exams are negative for one or more annual examination, then assessment may occur every 2 years. It also states that intravitreous therapy with anti-VEGF agents is currently the standard in management of central-involved DME as monotherapy or in combination with laser therapy. Based on their assessment data, suggests Eylea may be most effective at improving visual acuity for eyes with CIDME and acuity levels of 20/50 or worse. For eyes with CIDME and visual acuity of 20/40 or better they found that the efficacy of anti-VEGF was similar for all agents. And lastly, anti-VEGF therapy may be a suitable alternative to panretinal laser photo therapy in patients with PDR through at least 2 years. Any questions?

Lisa Chew: Any questions? There's no stakeholders.

April Phillips: Our recommendation is all ophthalmic angiogenesis inhibitors are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of the Health Care Authority. All non-preferred products require a trial of two preferred products with the same indication and different active ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Dale Sanderson: I move that the Apple Health Medicaid Program implement the limitations for the ophthalmic and angiogenesis inhibitors listed on slide 22 as recommended.

Virginia Buccola: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Then the motion carries. Okay, move onto antiparasitics.

Umang Patel: Next topic will be antiparasitic or antihelmintic. Please bear with me with this one. There are numerous parasitic disease states I do have to cover and so just bear with me.

Helminths are worm-like parasites such as flukes and nematodes, for example roundworms, tapeworms, whipworms, and hookworms. Roundworms with Trichinella subspecies and Anisakis subspecies and tapeworms as well. These are the most common foodborne parasites in the US. Symptoms of foodborne helminthic infections include abdominal pain, diarrhea, muscle pain, skin lesions, malnutrition and weight loss. It's transmitted by water, soil, or person-person contact and pets, particularly roundworms and hookworms. For roundworms, strongyloides species, it's prevalent in tropical areas including the southern US. Often found in rural areas, institutional settings, and lower socioeconomic groups. The larvae in contaminated soil penetrate the skin and migrate to the small intestine by various routes, such as lung or connecting tissues, where the adult female worms lay eggs. Symptomatic case includes GI, dermatologic and pulmonary symptoms. For pinworms,

generally not responsible for serious health concerns; however, this can spread easily from one child to another, by a transfer of eggs, which are swallowed. Once hatched, the pinworm travels to the anus, where it deposits eggs. Pinworm infections are characterized by itching around the anal and vaginal area at night. Before I go, just a quick sub note with this, it is very important with these parasite agents to cause death of the helminths. So, it's important that the anthelmintics are selectively toxic to the parasite and not the host. So, products in this review will include the oral anthelmintics agents only.

Next we'll go over hookworms. Once widespread in the US, particularly the southeastern region, but improvements in living conditions have greatly reduced infections. It is mainly acquired by walking barefoot on contaminated soil. The larvae penetrates the skin, migrates to the small intestine and then it is passed in the feces. Most people infected with hookworms have no symptoms but some may experience GI symptoms. Most serious effects are blood loss leading to anemia, in addition to protein loss. Tapeworm infections, here both parasites, are found in dogs, therefore are referred to as dog tapeworm. Cystic echinococcosis in humans are asymptomatic, however harmful, slowly enlarging cysts in the liver, lungs and other organs can develop unnoticed if untreated for years. Alveolar echinococcosis is rare in humans but if contracted it can lead to parasitic tumors in the liver, lung, brain and other organs as well. If it is left untreated, it can be fatal. For neurocysticercosis it is a parasitic infection that is targeted by the CDC for public health action. There are an estimated 1,000 new hospitalization for this in the US each year, most frequently reported in New York, California, Texas, Oregon and Illinois, caused by pork tapeworm, which can infect various parts of the body leading to cysticercosis, or larval cysts. The most serious form is neurocysticercosis, which affects the brain and can lead to death, and it can be transmitted by ingesting contaminated food and is prevented by proper handwashing, particularly by food handlers.

The last overview, we have onchocerciasis, which is caused by the parasitic tapeworm. It is also nicknamed the River Blindness because the blackfly that transmits the infection lives near rivers and streams and the infection can result in blindness. These infections are found in tropical climates, most prevalent in sub-Saharan Africa, and limited in the

Americas and Middle East. People who become infected are usually long-term travelers to the areas. Once infected the adult parasite typically resides in the nodules in the subcutaneous connective tissues for approximately 15 years, and symptoms include rash, pruritus, skin nodules, and vision changes. For schistosomiasis, it is not typically found in the US. It occurs after contact with fresh water contaminated with the schistosoma parasite, which penetrates the skin typically when wading, swimming, bathing, or washing. Over several weeks, the parasites migrate through host tissue and develop into adult worms inside the blood vessels of the body. Parasite eggs that do not pass out of the body can become lodged in the intestine or bladder causing inflammation or scarring. Without treatment, schistosomiasis can last for years and lead to increased risk of bladder cancer. And lastly, signs and symptoms of chronic schistosomiasis include an abdominal pain and large liver, blood in the stool or urine, and difficulty urinating. Lastly, there are liver flukes, which are usually found in Asia or an Asian immigrants transmitted by eating raw or undercooked fresh water fish. It can infect the liver, gallbladder and/or bile duct. Symptoms are related to inflammation and intermittent obstruction of the biliary duct, and if left untreated, inflammation may lead to cancer.

We have the medications, they're the generic form and indications. We have the five here. We have Albenza, stromectol, Emverm, Biltricide, and Pin-X or Reese's Pinworm, and please note that Stromectol is the only generic available. As you can see, all of these have numerous indications, I won't go through each and every one of them, but it is based on the specific type of parasite.

We'll start with the first three and their dosage and availability. In terms of special populations: so for pediatrics, OTC pyrantel is indicated in patients as young as 2 years of age. Praziquantel, the safe use of this in patients less than 4 years of age has not been determined. Mebendazole, the safety and efficacy has not been established in patients younger than 2. Ivermectin has not been established in patients less than 15 kilograms. And lastly, Albenza, the safety of it is similar to that of adults. In terms of pregnancy, please not that they all have varying pregnancy categories, either B or C. Praziquantel is category B, Pyrantel Pamoate the product labeling advises against it unless

conducted with a physician, Mebendazole there is developmental effects of it have been observed in animal studies but there is inadequate information associated with human studies, and ivermectin and albendazole are both pregnancy category C.

And here we have the remaining two.

So in terms of guidelines, again please bear with me, albendazole, mebendazole, and ivermectin target parasitic worms that infect the small intestine. These types of infections are transmitted through human fecal contamination of soil, which lead to consumption of contaminated plants. Pyrantel Pamoate is available over the counter to treat pinworms, which is easily spread among children. Praziquantel is more limited in its actions and is used to treat schistosomiasis. However, it is not active against nematodes, and then tropical medicine, mass chemotherapy program with anti-parasite, such as ivermectin, have played an important role in controlling parasitic infections.

In terms of roundworms, according to the CDC firstline therapy is ivermectin as a single dose for 1-2 days. As an alternative, albendazole daily for 7 days is an appropriate alternative. In patients with hyperinfection or disseminated cases, ivermectin is recommended until stool and/or sputum are negative for 2 weeks. For pinworms, treatment is with mebendazole, pyrantel pamoate, or albendazole. Keep in mind that albendazole is an off label. Pyrantel pamoate does not reliably kill pinworm eggs. It is recommended as one dose initially and then repeated 2 weeks later. Physicians may advise treating other family members, as well, to prevent reinfection as well as washing under clothes, bed clothes, and sheets. For hookworms, albendazole and mebendazole are taken for 1-3 days and is the drug of choice for the treatment of hookworm infections.

For tapeworm infections, surgery is the most effective treatment to remove cysts; however chemotherapy, cyst puncture, percutaneous aspiration, injection of chemicals, and reaspiration have also been used. Albendazole is FDA approved to treat cystic hydatid disease of the liver, lung and peritoneum. For neurocysticercosis, it is prevented by proper hand washing, particularly by food handlers. Practice guidelines for this

are under development by the IDSA right now. For onchocerciasis, the recommended treatment is ivermectin, which kills the larva but not adult worms. Ivermectin is given every 6 months for the life span of the adult worms or for as long as skin and ocular symptoms persist. For schistosomiasis, the recommended treatment is praziquantel taken for 1-2 days. And lastly, for liver flukes, per the CDC recommendations, praziquantel or albendazole are the drug of choice to treat.

I now open the floor for any questions, and I apologize for doing this right before lunch.

Lisa Chew: Thank you. I need to stop eating sushi but there are no stakeholders.

April Phillips: The recommendation is all products are considered safe and efficacious and are eligible for a preferred status and grandfathering at the discretion of the Health Care Authority. And all non-preferred products require a trial of two preferred products with the same indications and different active ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Amber Figueroa: Kind of off the subject, but in the past when I've tried to locate these drugs, they are very difficult to find. What's the deal? Pharmacies don't stock them or, and I didn't even know there was an over-the-counter pinworm treatment.

David Johnson: Is there a specific product that. . .

Amber Figueroa: I mean, in my experience its mebendazole or albendazole, they are hard to locate.

David Johnson: Well, mebendazole was off the market for a long time. I mean it used to be cheap and it came back as Emverm and it's probably $700 for a course. Albenza only comes in a 2-count bottle now and that's $500 or $600, and the pyrantel, or like the Reese's Pinworm or something like that, it's cheap, but stocking may be an issue. Availability isn't necessarily due to manufacturer changes necessarily, and there was a little bit of a

short spike for a while but it's pretty readily available now. It can be ordered next day.

Female: Also, just from the pharmacy side, to answer your question too, I think it comes down to they expire, and they're not all that cheap to stock on the shelf. So, like you said, they're available. They're just not usually stocked same day. So patients just have to wait a day for the pharmacy to order them, and then they can start their therapy.

Amber Figueroa: I move that the Apple Health Medicaid program implement the limitations for antiparasitic and anthelmintic drug class listed on slide 34 as recommended.

Dale Sanderson: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Alright we'll move onto the penicillins.

Umang Patel: This is one of the, I believe, six classes that April was alluding to early, where there will not be clinical information. There is not a whole lot of updates of penicillins, and so we'll have the list of the medications that fall under this class and that will be all. Could you pull up the Penicillin Appendix? Now this was also on the shared drive on the website as well.

I know this may seem a little atypical, but these are all of the penicillins that are essentially under this subclass. If there's any...

Leta Evaskus: There's a tab called appendixes in your folder that you can also look at these.

April Phillips: I gave you a few a minutes to quickly skim. Hopefully everybody had time to read every product on there. So, for Apple Health PDL, the penicillins are divided into four subclasses, the natural penicillins, the aminopenicillins, the penicillinase-resistant penicillins, and the penicillin

combinations. Our recommendation is that all products within each subclass are considered safe and efficacious within that subclass and are eligible for preferred status and grandfathering at the discretion of the HCA. All non-preferred products require a trial of two preferred products within that subclass with the same indication and different ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate or only one preferred product is available.

Lisa Chew: There are no stakeholders.

Dale Sanderson: I move that the Apple Health Medicaid Program implement the limitations for the Antibiotic Penicillins drug class listed on slide 39 as recommended.

Virginia Buccola: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Now onto macrolides.

Umang Patel: The next category will be macrolides/ketolides.

Just a little bit of a background, erythromycin, the first macrolide, was introduced in 1952. Activity against gram-positive cocci and atypical pathogens made erythromycin a good treatment option for upper and lower respiratory tract infections, along with soft tissue infections. However, erythromycin does have several limitations such as variable absorption, short elimination half-life, GI irritation, and lack of activity against hemophilus influenza. Both azithromycin, or Zithromax, and clarithromycin (Biaxin) demonstrate better tolerability with more convenient dosing regimens and improved activity against H. influenza. Macrolides have been shown to be useful agents in the treatment of upper respiratory bacterial infections, including CAP, or community-acquired pneumonia, acute sinusitis, and acute otitis media (AOM). Antibiotic resistance may limit the overall effectiveness of the agent in the class as multi-drug resistant bacteria become more and more

prevalent. Telithromycin, a ketolide, concentrates inside phagocytes and is effective against intracellular respiratory pathogens. It provides effective coverage against many respiratory pathogens in a once daily oral formulation for adults. Serious adverse effects, drug interactions and having only one indication limit the usefulness of Telithromycin.

You will see all the macrolides and ketolides listed along with their indications. Note that Zithromax, Biaxin and Biaxin XL, along with erythromycin, are available in generic form. The indications are broken down. The first AECB being acute exacerbation of chronic bronchitis, we have AOM, which is acute otitis media, CAP, community-acquired pneumonia, pharyngitis or tonsillitis, skin infection, sinusitis, and then we have other, and as you can see some have extensive other category than others.

Just to give a little bit of mechanism of action on this, macrolides and ketolides antibiotics bind to the 50S ribosomal subunit on the bacteria inhibiting RNA dependent protein synthesis. There may be bacterial static or bacteriocidal. So depending on the drug concentration, they are generally active against gram-positive cocci and bacilli and to a lesser extent, gram-negative cocci.

On the next slide here, we have all of the dosing and availability. Please note that along with the dosing, the duration has been bolded underneath each one as the duration can vary depending on the disease state.

In terms of special populations, for pediatrics safety and efficacy of Telithromycin in patients of lesser than 18 years of age has not been established. For clarithromycin, it is FDA approved for treatment for children six months and older for acute otitis media, CAP, pharyngitis, tonsillitis, skin and skin structure infections, and acute bacterial sinusitis. For the management of MAC, clarithromycin has been studied in children 20 months of age and older and clarithromycin ER is not indicated for children. Erythromycin has been approved for use in children six months of age and older for treatment of AOM, CAP, and sinusitis. Lastly, azithromycin and erythromycin are pregnancy category B, and

clarithromycin and clarithromycin ER, Telithromycin are pregnancy category C.

Here we have more dosing and availability. I felt it was necessary to put this in terms of HIV populations, patients with HIV, some of these are given for the prevention of certain opportunistic infections, such as MAC, so the dosing is listed there as well.

In terms of guidelines, community-acquired pneumonia guidelines by the American Thoracic Society and IDSA, recommend macrolides, very strong recommendation, or doxycycline for adult patients who are otherwise healthy, without risk factors for multi-drug resistance staph pneumonia. For adult outpatients with comorbidities including chronic heart, lung, renal hepatic disorders, diabetes, alcoholism, malignancies, asplenia, immunosuppression, use of any antibiotic within the last three months or other risk factors for MDSR, firstline therapy may include respiratory fluoroquinolone, such as moxifloxacin, gemifloxacin, or levofloxacin, or a beta-lactam plus a macrolide. For children defined as school age and adolescents, evaluated in outpatient setting, macrolide antibiotics should be prescribed when findings are compatible with CAP caused by an atypical pathogen. And antibiotics should be used judiciously with appropriate dosing in an effort to avoid resistance. For STD's, recommendations by the CDC in 2010 state that azithromycin is the recommended regimen for the treatment of chancroid, nongonococcal urethritis, cervicitis, and chlamydia infections. Uncomplicated gonorrhea, now recommends azithromycin one gram orally as a single dose or doxy twice daily for seven days along with ceftriaxone intramuscularly, as a recommended combo therapy due to increased resistance to the oral cephalosporin cefixime. Lastly, erythromycin base and estolate are considered alternative regimens for several infections. However, the GI adverse effects of erythromycin may reduce the effectiveness of the therapy if treatment is not completed.

For skin and skin structuring infections, including impetigo by the IDSA, azithromycin and clarithromycin are indicated for skin and skin structure infections. Some strains of staphylococcus aureus or streptococcus pyogenes may be resistant. For pertussis by the CDC, recommends erythromycin, azithromycin and clarithromycin for post-exposure

prophylaxis or treatment of pertussis. And lastly, for mycobacterium avium complex, or MAC, the CDC, the IDSA, and the NIH for the prevention and treatment of opportunistic infections in HIV infected adults and adolescents, they all recommend azithromycin or clarithromycin as a preferred prophylactic agent. Initial treatment of MAC should consist of two or more antimyobacterial drugs to prevent or delay the emergence of resistance, with clarithromycin being a preferred first agent. Clarithromycin has been studied more extensively than azithromycin in patients with AIDS and appears to have a more rapid clearance of MAC from the blood. And lastly, azithromycin maybe used in place of clarithromycin when drug interaction or drug intolerance are a concern. Any questions?

Lisa Chew: There are no stakeholders. Other antibiotics/penicillins, does that also include the macrolides? Okay.

April Phillips: Leta's going to go double check on those. I thought I grabbed them all.

Leta Evaskus: I didn't make one. Does anybody want to speak on, which one did I miss? The macrolides? No? Nobody is here to speak on that? Ok.

April Phillips: Our recommendation for the antibiotics, the macrolides, all products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of the HCA and all non-preferred require a trial of two preferred products with the same indication and different active ingredients before a non-preferred will be authorized unless contraindicated, not clinically appropriate or only one product is preferred.

Diane Schwilke: I move that the Apple Health Medicaid Program implement the limitations for the antibiotics/macrolides drug class listed on slide 48 as recommended.

Susan Flatebo: I second.

Lisa Chew: All of those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Do we want to do lunch now or keep going or? I say keep going but unless there are objections.

Dale Sanderson: Unless there are any stakeholders that are planning on coming back.

Umang Patel: The next one will be nitrofurantoin derivatives or urinary anti-infectives. Keep in mind this is going to be similar to the previous topic, where there is no clinical information. It is just a list.

These are the medications, the manufacturers in the brand name route that make up this class. Similar to the previous one, we'll give you a little bit of time just to review it over and then I'll let April.

Lisa Chew: There are no stakeholders.

April Phillips: For the urinary anti-infective class, our recommendation is that all products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA and all non-preferred products require a trial of two preferred products with the same indications and different active ingredients before a non-preferred drug will be authorized unless contraindicated or not clinically appropriate.

Amber Figueroa: I move that Apple Health Medicaid Program implement the limitations for the urinary anti-infective drug class listed on slide 52 as recommended.

Dale Sanderson: Second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Okay. The motion carries. Next, oral contraceptives.

Umang Patel: The next topic will be oral contraceptives. The order in this will be flipped a little bit. We will have background and then guidelines and then

we'll switch over to show you all of the medications that make up this class.

Just a quick overview, hormonal oral contraceptives, or OC's, are available in various dosage forms for prevention of pregnancy and are available as a combination of estrogen and progestin or progestin alone. Products differ in specific hormones they contain and how these hormones are dosed throughout the cycle hormone phase resulting in several product options. The various hormone combinations and phases in which they are dosed create products that produce different cycle lengths and physiological effects. Traditional OC's are administered for 21 days, followed by a hormone-free week in which menstruation occurs. Extended cycle products, for example a 91 day cycle, delay or completely eliminate the break in hormone use and may be desirable to women who wish to avoid menstruation all together.

The primary mechanism of this, and again sorry it's right before lunch, the primary mechanism of this, the progestin component prevents the luteinizing hormone surge required for the release of the ovum, secondarily progestin thickens cervical mucus and decreases tubal motility creating a more difficult passage for the sperm. The progestin also acts to thin the endometrium resulting in tissue that is less receptive to implantation. The estrogen stabilizes the endometrium providing for an acceptable cycle control and bleeding profile. Estrogen also contributes to efficacy in inhibiting the release of FSH or follicle stimulating hormone from the pituitary, which inhibits the development of a dominant follicle and thus potentiates inhibition of the LH surge.

To break down the components, the first being the estrogen component. The majority of OC's contain the synthetic estrogen ethinyl estradiol, and the dose varies across the products from 20 microgram per day to 50 micrograms per day. There are products that are still available that contain mestranol, the estrogen used in many of the original OC's. Mestranol is an inactive pro-drug of ethinyl estradiol which is metabolized in the liver to ethinyl estradiol. Progestin component, there are currently nine different progestins contained in OC's. Progestin varies in the progestational estrogenic, antiestrogenic, and androgenic activity. The progestin in an OC is the primary differentiator among

different OC's. They are commonly referred to as first through fourth generation progestins based on when they were introduced into the market. The older first generation agents include norethindrone, norethindrone acetate, and ethynodiol diacetate. Generally well tolerated but are associated with spotting and breakthrough bleeding. Second generation progestins include norgestrel and its active isomer, which is levonogestrel. More potent progestins with longer half-lives and they have more androgenic activity compared to the first generation drugs and may be associated with more androgenic side effects, such as hirsutism, acne, and dyslipidemia. The androgenic effect may also translate to improvements in libido. The third generation agents are norgestimate and desogestrel. They have less androgenic effects, have less adverse effects, such as acne, that occur less frequently. And lastly, the fourth generation agents are drospirenone and dienogest.

So those were the estrogen only, now we have the progestin only oral contraceptives. Contains 35 micrograms of norethindrone. They contain active drug in all tablets taken throughout the monthly cycle and there is no hormone free period. Primarily used during lactation and in women who need to avoid estrogen due to tolerance issues or contraindications. Progestin only OC's are associated with more break-through bleeding and possibly higher failure rates than combination. And for maximum effectiveness, it is essential that progestin only tablets be taken at the same time each day. For combination OC's, combinations are estrogen and progestin, and they are generally grouped based on the dosage regimen strategy used by a specific product. Most are a 28-day monthly cycle and are available as monophasic, biphasic, triphasic, or a 4-phasic product. There are also extended cycle products and a continuous-cycle products that are available. Monophasic products contain the same amount of estrogen and progestin in each tablet taken throughout the cycle and are most frequently dosed as daily active combined pills for 21 days followed by seven days of no pill or a placebo. Several monophasic pills vary the duration of active versus inactive pills, for example Minastrin 24 FE has 24 days of active combination followed by a four day placebo. Multiphasic, so that includes the biphasic, triphasic and 4-phasic that I mentioned earlier, contain different doses of one or both hormones in the active pills in an attempt to emulate the body's natural menstrual cycle and decrease dose-related adverse effects. Many

multiphasic products contain a lower dose of hormones over the course of a cycle.

In terms of guidelines, the CDC recommends combination oral contraceptives and progestin only oral contraceptives, as effective methods of contraception. Details on the appropriate selection of an effective contraceptive method, such as an IUD implant, injection or an OC are described in their published Medical Eligibility Criteria. The American College of Obstetricians and Gynecologists (ACOG) state that long acting reversible contraceptives are safe and have a higher rate of efficacy, continuation, and satisfaction compared with short acting contraceptives, therefore excellent contraceptive choices for adolescents. And please note that it is highly recommended that physicians and practitioners make sure that patients who are started on OC are not actively smoking in order to prevent clots.

This will go over to the appendix that are in the binders and I'll ask to be toggled over to.

April Phillips: I'm hoping everybody had a chance to look through those three or four products. So, the oral contraceptives for Apple Health PDL are divided into subclasses. We've got the progestin contraceptives-oral, the combination contraceptives-oral, the combination contraceptives-oral/biphasic, combination contraceptive-oral/triphasic, combination contraceptive-oral/extended cycle, and combination contraceptive-oral/continuous.

Our recommendation is that all products within each subclass are considered safe and efficacious within that subclass and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products within that subclass with the same indication and different active ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Lisa Chew: I actually don't know if there's stakeholders for this. Is there any?

Amber Figueroa: Oral continuous, meaning they never have the fourth week and when would that be indicated?

April Phillips: Do you happen to have that?

Virginia Buccola: I just want to add that I would use it in mood disorders when there's a high indication of PMDD or mood exacerbation premenstrually.

David Johnson: Do you actually mean the extended cycle ones?

Amber Figueroa: There's another subclass that says oral continuous, so that you would essentially never menstruate, is what I'm assuming that's what that means.

Petra Eichelsdoerfer: Don't know where this falls in terms of labeling but I know I have seen the continuous use used when you've got somebody that you need to prevent the bleeding for some reason, for example severe anemia, and difficulties with absorbing iron.

Susan Flatebo: I move that the Apple Health Medicaid Program implement the limitations for the contraceptives oral drug class listed on slide 61 as recommended.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? Then the motion carries. Ok, now prenatal vitamins.

Umang Patel: Prenatal vitamins are approved for nutritional supplementation for females of child bearing potential during preconception, pregnancy, or lactation. Prenatal vitamins provide supplementation for both the mother and fetus and while prenatal supplementation contains numerous vitamins and minerals, the folic acid, iron, and calcium content are particularly important. If you can go to not the next slide but the slide after, we'll just do guidelines and then I'll show them the….

In terms of guidelines, for folic acid, American College of Obstetricians and Gynecologists (ACOG) in 2017 recommended periconceptional folic acid supplementation, as it has shown to reduce the occurrence and reoccurrence of neural tube defects. All women of child bearing potential should take folic acid supplementation daily. For women at low risk of neural tube defects 400 mcg per day is recommended and supplementation should be initiated at least 1 month prior to pregnancy and continued through the first 12 weeks. For women at high-risk, defined as those who have had a prior neural tube defect pregnancy, who have a neural tube defect themselves, or who have a partner who have a neural tube defect or a child with a neural tube defect, 4 mg per day is recommended initiated at least three months prior to pregnancy and continued until 12 weeks of gestational age. Higher levels of folic acid supplementation, such as greater than 400 mcg per day, should be achieved by taking an additional folic acid supplement and not by taking excess multivitamins, since they may contain vitamin A, which is potentially teratogenic at high doses. The US Preventative Services Task Force in 2017 recommend that all women planning or capable of pregnancy take a daily supplement of 400-800 mcg of folic acid. It does not apply to women who have had a prior pregnancy affected by neural tube defects or women taking certain antiepileptic medicines. The task force found that most women in the US are not ingesting fortified foods at a level thought to provide optimal benefits.

The CDC and March of Dimes recommend that iron is recommended to prevent maternal anemia, preterm labor, low birth weight, and aid in maternal/fetal muscle development. For calcium and vitamin D, the Institute of Medicine states for pregnant and lactating women aged 14-18 years old, they recommend a daily allowance of 1,300 mg per day and 600 IU per day of calcium and vitamin D, respectively. For pregnant and lactating women aged 19-50, the RDA has changed to 1,000 mg and 600 IU daily of calcium and vitamin D, respectively. Lastly, the American Dietetic Association, the daily vitamin supplementation is not a substitute for a healthy diet. Prenatal vitamins should be used along with balanced meals to ensure adequate levels of vitamins and minerals and to ensure a healthy pregnancy outcome.

Lastly, whenever we talk about special populations there are no dose adjustments needed for hepatic and renal impairment and, I know this sounds silly but, patients who are pregnant as well because these are all category A.

We'll toggle over to the product list as well and give you all a few minutes to look it over.

April Phillips: For the Apple Health PDL, our recommendation is that all products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of the HCA. 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.

Lisa Chew: There are no stakeholders.

Amber Figueroa: Thinking about, in like the last 10 years, how they put the DHA supplement in some of them, I do see that listed as the prenatal vitamins. Do we cover the ones that have the DHA? I mean I know that's not something that we've decided yet or maybe, I mean I don't know, currently.

April Phillips: I don't believe we have successfully chosen our preferred, non-preferred products at this time. I believe there are some over-the-counter products that we would not cover but I'm trying to remember if there is a prescription version of it. I'm getting some confused looks.

David Johnson: I mean there certainly are prescription products that have DHA and things in there. I mean some of the new ones are $300 a month but there are other ones that are $50.

Amber Figueroa: There just wasn't any discussion of it in this review and so I'm not even totally up to date on…is that recommended by anyone to have DHA in it?

Umang Patel: These are the most up to date guidelines that there are. So, there isn't anything since this was last updated to indicate any changes, especially DHA.

Jordan Storhaug: I just think along those questions, the iron is also one of those ones that's commonly included, as well. In our formularies is it mostly only folic acid that's covered or iron-containing prenatals as well and DHA? I'm just kind of curious from the groups, if you guys have an idea of that.

Petra Eichelsdoerfer: The prenatal vitamin almost by definition is going to have more than just folic acid in it. It's just they tend to focus on the folic acid because of the concerns of the neural tube defects and also because there is a cutoff above which it is no longer over-the-counter versus it becomes a prescription item. Iron is almost always going to be at minimum at the RDA that is for a pregnant woman or a lactating woman. Now the form of iron, there's been an explosion in the different forms of iron available, especially in the prenatal products in the last 5-10 years, so there's a lot of variety out there. What I can recall in terms of the coverage from my retail days, which now are a couple of years ago, it was pretty limited within the Medicaid fee-for-service. So, I would look to the HCA for additional information as to if that's changed, but historically it's been pretty narrow.

Amber Figueroa: I think this is also a class where frequently when the women have a lot of nausea and vomiting that we recommend that they switch to a gummy, which historically hasn't been covered, or we've to had jump through a gazillion hoops and I'm just wondering if that's going to be addressed.

April Phillips: This is a particular class where we do cover some of the over-the-counter products for their prenatal vitamins, just because cost-wise they are occasionally cheaper than the prescriptions, but I don't believe we've included the gummies.

Petra Eichelsdoerfer: There are also other chewable products available besides the gummies. You know, if you were to think of the over-the-counter equivalent of like the Flintstones chewables or something to that effect and there are both prescription products, as well as OTC.

Lisa Chew: So I assume you can add a requirement for a chewable if you wanted to?

Amber Figueroa: I think that we should do that because when you, frequently the ones that can't keep their vitamin down are the teenagers that are eating Cheetos and drinking pop. They're the ones who really, really need it. So, if we could have some kind of a chewable one, they might be more likely.

April Phillips: Do you want specifically chewable or just any alternative to an oral tablet?

Amber Figueroa: Like what other alternatives?

April Phillips: Like you had discussed the gummies versus the chewables that aren't gummy and probably don't taste quite as nice as potential solutions. I'm not 100% sure what is out there, I'm just giving options, wording alternatives to oral tablets versus that specific form.

Diane Schwilke: I don't think that any of the gummies are available prescription strength, so they wouldn't have the full folic acid that's recommended.

Petra Eichelsdoerfer: They often times have a little bit less in the iron because what makes the chewables not taste so good and what makes the products hard on the stomach are the mineral contents, specifically the iron, and that's the thing that the women really, really need beyond the folic acid. As far as liquid goes, and I've spent a lot of time looking at these products, I have not seen very many liquid products. They are very few and far between. Even if the HCA should elect to cover them, they may be very difficult for pharmacies to obtain.

Ryan Pistoresi: Just looking at the list, the appendix, it seems like the most common outside of the tablet and caps were the soft gel, so is that..?

David Johnson: That's not a gummy.

Ryan Pistoresi: You're right, it's not the gummy, but is that something that you know, one that is easier to tolerate for the population that you are looking for?

Petra Eichelsdoerfer: Many of the soft gel products are going to be the ones that contain the DHA. Not all of them, but many of them are.

Ryan Pistoresi: Ok.

Amber Figueroa: I think that's fine. I'm just thinking about our midwives and how frequently that they will tell, you know when people say, ". . . we can't tolerate…it just makes me throw up." Okay. Well take it at night. "It still makes me throw up." So I think that's fine and then we just go with it and see how it works.

Virginia Buccola: I move that the Apple Health Medicaid Program implement the limitations for the prenatal vitamins drug class listed on slide 68 as recommended. A chewable product must be preferred.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. We are now two minutes to noon. Do you guys want to break for lunch and then come back and finish the rest? Okay. I see heads nodding. Okay. We'll reconvene at 1:00.

Alright good afternoon, I hope everybody had a good lunch. We're going to reconvene the DUR board, and we're going to continue with the diuretics.

Umang Patel: So for this topic, again, there is no background information or anything like that. I will refer you to the appendix, if I could ask you to toggle over. Take a quick minute to review, and I'll transition over to April.

April Phillips: Ok, so for the Apple Health PDL, the classes, the cardiovascular agents and then the diuretics, that class is divided into subclasses. The carbonic anhydrase inhibitors, the loop diuretics, the osmotic diuretics, the potassium sparing diuretics, the thiazide and thiazide-like diuretics, and the diuretic combinations.

Our recommendation is that all products within the each subclass are considered safe and efficacious within the subclass and are eligible for preferred status and grandfathering at the discretion of the HCA. All non-preferred products require a trial of two preferred products within that subclass with the same indication and different active ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate or only one product is preferred.

Lisa Chew: There are no stakeholders.

Diane Shwilke: I move that the Apple Health Medicaid Program implement the limitations for the cardiovascular agents diuretics listed on slide 73 as recommended.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries. Now on to dermatologics.

Umang Patel: The next and final one will be for dermatologics or emollients specifically.

Just a quick overview, atopic dermatitis, or atopic eczema or eczema, it's a common disease with worldwide prevalence. Clinically, eczematous patches and plaques are seen, which favor the face and extensor surfaces in young children and flexor surfaces, including the antecubital and popliteal fossae, the ankles and the neck, in older children. Management of almost every case of atopic dermatitis will include topical therapy. Patients with mild to moderate eczema, topical therapy may be entirely sufficient to control disease activity. Emollients should be considered as firstline therapy for mild disease. Patients with more severe disease may require more advanced therapy, including phototherapy or systemic therapy. Other topical therapeutic options for more advanced cases of atopic dermatitis include corticosteroids and calcineurin inhibitors. Xerosis or dry skin is caused by loss of water in the upper layer of the skin. Emollients work by forming an oily layer on the top of the skin that

traps water. These agents are designed to make the stratum corneum softer and more pliant by increasing its hydration. A large number of preparations are available, many of which are marketed as cosmetic and therapeutic moisturizers.

Here we'll pivot over to the appendix. I'm not quite sure if it may be in the binder. This appendix had about 22 pages worth of medications in there and….it is in there? Ok, it is in there.

April Phillips: I hope I gave you guys enough time to…so for the Apple Health PDL the dermatologic, emollient and kerolytic agents, all products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of the HCA. All non-preferred products require a trial of two preferred products before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate or only one product is preferred.

Lisa Chew: There are no stakeholders.

Dale Sanderson: I move that the Apple Health Medicaid Program implement the limitations for the emollients and kerolytic agents listed on slide 78 as recommended.

Susan Flatebo: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Ok now we move onto, unless people want another break? Let's move onto the Apple Health Policy Entresto.

April Phillips: So for Entresto the policy that we're proposing, so for the policy's inclusion criteria, a history of one of the following, either A, B, or C. A, the patient is currently taking therapy or it was initiated in the hospital. Patient B has all of the following: diagnosis of heart failure, ejection

fraction is less than or equal to 40%, heart failure is classified as one of the following: New York Heart Association class II, III, or IV.

And for C, the patient has one of the following: A history of trial, contraindicated, or intolerance due to adverse reactions to the following firstline agents; ACE inhibitor or ARB, diuretic, and beta-blocker or hospitalization for decompensated heart failure in previous 12 months, and prescribed by or in consultation with a specialist in cardiology.

For exclusion criteria, history of any of the following: History of angioedema, concomitant use of an ACE inhibitor, concomitant use of aliskiren in patients with diabetes, and our quantity limits are two tablets a day or 60 per 30 day supply.

Lisa Chew: Any questions for April?

Amber Figueroa: Can you give a second to read over this email?

Lisa Chew: April, what does it mean by, "...in consultation with cardiology?" Does the patient need to be seen by a cardiologist? Is it a verbal consultation?

April Phillips: It can be a verbal consultation with the prescriber and if they either have a history of, you know knowledge of what should be done or they're consulting with a specialist in cardiology. So it can verbal.

Amber Figueroa: What do you guys think about the cardiology part? I mean if somebody is getting it prescribed in-house, then usually they're having a cardiology consult, but the argument of this pharmacist is that primary care should be able to initiate it if they feel comfortable. April do you want to give the background of why you guys did that?

April Phillips: The reason why it was chosen was due to the nature of the client with the ejection fraction. I do not have the history on what a primary care provider, what they're able to do and background and what they're usually comfortable with, so I don't want to take that into, oh you know no primary care provider does that. So I don't want to assume that. It's just it was brought on so that mainly if a client does need this medication

chances are they should have at least been seen by a cardiologist and have been recommended that way.

Lisa Chew: But my earlier question, it sounded like a primary care provider could initiate it but it had to be in consultation with a cardiologist. The patient doesn't necessarily need to be seen in person, but just a verbal consultation with a specialist.

April Phillips: That's correct. That was the intention of the prescribed or in consultation.

Amber Figueroa: I'm thinking the only time when that might be difficult would be in a rural hospital where they don't have access to a cardiologist. I don't know, I don't live super rural, so I don't know. I would think you would still be able to call UW or somewhere and have someone give their blessing. So that's just my thoughts. I do think that the bulletpoints on B where it says, "A diagnosis of heart failure with or without hypertension." And then the third bullet is heart failure is classified as one of the following. I feel like those could be combined. Diagnosis of heart failure and New York Heart Association class II, III, or IV.

Lisa Chew: Makes a lot of sense to move that last bullet up and combine it with the first bullet.

Amber Figueroa: And I think you can take out with or without hypertension. I mean if it's either/or then it doesn't have to be there. It's not a requirement.

Leta Evaskus: Should I say classified by the New York Heart Association or as, does that make sense?

Amber Figueroa: I think as is fine.

Leta Evaskus: As is fine?

Amber Figueroa: Mmhmm.

Emily Transue: I don't know if this is helpful for the group but it seems as though there are sort of two questions that come up, or two ways that frame the

email, one is whether point C belongs as an and in combination with either you have to one of A and B and you have to have C or maybe you have to have A and you have to have both B and C, C are being used I think to indicate whether the patient is adequately medically managed. I agree with the writer of the email that C by itself doesn't really make sense. It doesn't even speak to [inaudible]. And then the question is whether you want to add current maximal medical management criteria for the use of this drug or whether you want to approve it even if maximal medically therapy hasn't been used.

Leta Evaskus: Lisa, did we have a stakeholder. Ok, maybe we should have that person speak before we finish the conversation.

Lisa Chew: We do have one stakeholder, Mary Kemhus. If you want to come up to the podium, introduce yourself and who you represent and you have three minutes.

Mary Kemhus: I'm Mary Kemhus, I represent Novartis Pharmaceuticals and I am a pharmacist, and I've spoken to all of you several times on this topic, but today I think just specifically talk to you about Entresto and the proposed PA criteria.

Just as a reminder, Entresto is the first drug in over a decade to demonstrate clinical and statistical superiority to an ACE inhibitor, which was previously the standard of care. And I'll also like to remind the committee that in the pivotal trial that Entresto was approved upon the majority of patients in that study, in fact 70% were stage 2 heart failure, and it is common for stage two heart failure patients not to be managed by cardiology. They are often managed by primary care. So with that in mind, I would ask that you would consider whether cardiology consult is really necessary in a patient population that it doesn't necessarily have to be managed by a cardiologist.

More recent Entresto analyses have demonstrated improvements in heart failure symptoms, like fatigue, shortness of breath, health-related quality of life. We've seen improved physical and social function in these patients. We've also seen data showing cost offsets, and these are analyses that have been done in other health plans independent of

Novartis funding, have shown that while, of course, Entresto costs more than a generic acerin/ARB, it does have cost offsets in decreasing medical costs on the other side of the budget.

So lastly, I would like to remind you of the guideline update. It was actually in 2017, it was the AHA, ACCE, HFSA guidelines. The highlighted, the clinical strategy of [inaudible] inhibition and that it can be achieved with either an ACE, an ARB, or an ARNI, which is another name for Entresto. The guidelines don't assign a specific order or restrict firstline use of these agents, and they do specifically highlight the need to replace an ACE or an ARB with Entresto in patients that are class II or II for failure reduced ejection fraction; so, that means the symptomatic patients, in order to further reduce morbidity and mortality.

So as you discuss Entresto today, just please remember that it's not guideline recommended therapy for patients with heart failure reduced ejection fraction. It demonstrates superiority to standard of care, and I would also ask you to consider whether a drug that has benefits in a population like this is worth restricting and delaying the time that a patient could get to therapy by unnecessary prior authorization steps. That's all I have for you. Thanks, I'm happy to take any questions.

Jordan Storhaug: So, clarification of the guidelines, cause I think that's the part that has changed, cause it looks like for class one, ACE's and ARB's are allowed for that but for class II and further on, Entresto is the preferred agent.

Mary Kemhus: Yeah, so it says that you can start patients with some sort of RAS inhibition, but then further more in those patients that are symptomatic they should be on an ARNI or Entresto to further reduce morbidity and mortality. It also allows room for the beta-blockers and all that other stuff, but it doesn't mandate the order that it should happen in. Did that makes sense? Does that answer your question?

Jordan Storhaug: Well I think the question that will be to this committee, is due to the increased cost of this. Is it reasonable for people to try other agents or whether the guidelines don't direct that, it may be appropriate for this body to do that, but if the guidelines are really saying go straight to Entresto in this class II, then it would be inappropriate to?

Mary Kemhus: Yeah, and I guess I should be careful in there because they aren't prescriptive of which RAS inhibition you should start with. They are very prescriptive about the patients that should be switched to Entresto but they are open in what kind of RAS inhibition you start with. Anything else? Thank you.

Susan Flatebo: On C, I agree with the email writer that maybe we should delete out the diuretic and beta-blocker, and also maybe we should delete out the bulletpoint about hospitalization? I mean, not all of these heart failure patients may have been hospitalized for their heart failure and maybe that should be removed?

April Phillips: It was just another option for our client to get this medication if they had been hospitalized for decompensated heart failure in the last 12 months. They don't necessarily have to have a trial and failure of everything else. It was one or the other, either the history of trial of the list of medications or the hospitalization. So, it was just another thing to kind of allow easier access.

Susan Flatebo: Oh okay, I guess I misunderstood it then.

April Phillips: Right, it's all squished onto one slide, so understandable.

Catherine Brown: I agree with removing the requirement about the cardiologist. It seems to me that it isn't adding anything by having it there, that the cardiologist isn't providing any additional insight into whether or not this is appropriate if we have these other criteria. These would all be things a primary care could determine. So, I'm not sure what value that adds.

Amber Figueroa: I agree with the pharmacist that did the email and switching it up and having it be either... can you go back to that previous slide? It be A or B, and then another bulletpoint way over. Like make this one, like they did in the email, and then make a second one that they... they should be on a beta-blocker at that point. I just think C is really confusing. So what that does is it moves it...

Female: You want it to be on its own. Is that correct? Not a choice?

Amber Figueroa: Yeah, like C would be gone. Which you don't have to do that yet, I may be the only one that thinks that.

Lisa Chew: And then what was C previously would be "this/that," right? Yeah.

Amber Figueroa: What do you guys think about instead of doing C, saying the patient must be on or contraindicated for beta-blocker use? Because I don't feel like the hospitalization for decompensated heart failure in the previous 12 months, if either A it was initiated during an in-patient or B they're symptomatic, you know, then most likely you're not going to be able to pick very many people up in your last statement there that you haven't already picked up in the top. Does that make sense?

Lisa Chew: I wanted to go back to Susan's question about whether diuretics should stay or be removed from that.

Jordan Storhaug: I think I'm definitely in the mood to decrease some of these requirements that we have. I'm just kind of imagining myself filling out this prior authorization of which I'm having to, I don't think in any quick way, be able to explain what I've done with their ACE's, with their diuretics, and their beta-blockers and then having to do all those are probably more than what I think anybody would want to read about this patient.

Amber Figueroa: I don't think that they should be required to be on a diuretic. Some people have heart failure that's mildly symptomatic and don't tolerate diuretics because of kidney disease or because of other reasons. So, I don't know that that should be a requirement.

Lisa Chew: So we got it down from two slides to one slide, what are folks thinking about this recommendation?

Jordan Storhaug: I guess the part that I still don't think is ideal is this kind of talks about titration of a beta-blocker. I think I would rather have it just that they have to be on a beta-blocker or intolerant to it.

Female: Then I propose a clean-up. So initially, we had one of the following in two bullets and now we only have one bullet. I would also propose

maybe an “and” after the 40% above to make it clear that they have to both of these bullets. Capitalize “and”.

Jordan Storhaug: I think we are just in the grammar part now, but I think we can remove the patient has the following and just move all of the bulletpoints back.

Amber Figueroa: I think the ACE or ARB, well in my opinion it needs to be taken off.

Ryan Pistoresi: I believe it said that in the clinical trial they had to be on an ACE or an ARB for four weeks prior to being enrolled in the clinical trial. Do you want to take that into consideration before they potentially start an Entresto without having history of an ACE or an ARB and then develop a side effect like angioedema?

Amber Figueroa: I think the benefit of this drug comes in the 30 days after, I mean 38% reduction in 30-day remission. So, if somebody has been admitted they’re significantly symptomatic, and if this proves that it’s superior then why would we make them take something that’s not if they’re sick enough to be in the hospital.

Female: But this doesn’t include hospitalized patients. This would include class II patient, right? There’s no requirement for hospitalization. So a class II patient...

Amber Figueroa: Sorry, I’m looking at the first bulletpoint in patient stay. Sorry, I was thinking about if it was being considered when they were in the hospital.

Female: I think the question is whether a patient with class II symptoms, so symptoms with normal activity, whose not been tried on other agents should be allowed to start with this.

Jordan Storhaug: That’s what I’m still seeing in practice is that newly diagnosed people are put on an ACE or an ARB, a cheap medication, frequently stabilized, and then they never get moved onto Entresto. A severe case, I would imagine, I want them to be able to go to that medication more quickly, but the majority of my patients have been able to get stabilized and become asymptomatic without the use of this drug.

Amber Figueroa: How much does it cost?

April Phillips: Do you happen to know that off the top of your head.

Male: I can give you a quick idea. Probably $475/month, roughly. High 400's. It appears to be priced the same regardless of dosage, so there isn't an increase cost for titration.

Susan Flatebo: I think we should leave the ACE or the ARB in there because I'm sure with prior authorizations, if you wanted to go directly to Entresto, you would just have to request it and meet certain criteria to get it allowed, I'm assuming.

Lisa Chew: I agree with that.

Amber Figueroa: When you say used in combination, are you saying that they need to have been on both of those at the same time?

April Phillips: Yes. That's the intention of the use in combination. What we could do, just as a suggestion, is used in combination and then behind that put "unless clinically inappropriate," that way, if it's appropriate for the patient.

Female: Do you not think that trial contraindication or intolerance captures clinically inappropriate?

Amber Figueroa: I'm just wondering if "used in combination" needs to be there. I mean, are you guys really going to go back and verify that they've been prescribed in the same 30 day period? I'm thinking about your end of the work, and I also think it's a little confusing, like the author of the email says, "If you have an adverse reaction to an ACE or an ARB then you shouldn't be on this medication." So that's a little caveat, which maybe everyone knows that.

Lisa Chew: Is the committee comfortable with how it's stated currently or any other concerns? And I'm always impressed with Leta's ability to work the PowerPoint.

Amber Figueroa: We still need to clarify, do they need to be in consultation with the cardiologist or not?

Lisa Chew: We took that out.

Amber Figueroa: Okay.

Lisa Chew: That was just the inclusion criteria we still have... there's exclusion criteria quantity limits.

Virginia Buccola: Is it necessary or would it be helpful for us to add as recommended by the author of the email, concomitant use of an ACE inhibitor with exception for a period of titration or some such language around that?

Amber Figueroa: Change the "with" to "of", Leta. The concern is that the patient will have an active prescription for enalapril and an active prescription for Entresto in the same month.

Ryan Pistoresi: So I'm thinking about a way that we could develop the PA criteria, just to have a check box saying that the patient will not be continuing once they start Entresto to make sure that even if there is those two active prescriptions within the same month, that the pharmacist that is reviewing this knows that the provider attests that the patient understands not to continue both. I think that could be a way to operationalize this policy in the PA criteria. So some way that it does not necessarily block a prescription going through when they are in the same month but that the provider knows and has informed the patient to discontinue the ACE inhibitor when they initiate the Entresto. Does that match what you were looking for with that? Okay, thank you.

Leta Evaskus: Do we need to write that in here then?

Ryan Pistoresi: Yes, can we write that in? I can help you with that. So for the concomitant use of ACE inhibitor, we can say as attested to by the prescriber, well, it's concomitant use so an exclusion.

Leta Evaskus: Did you want to keep that?

Ryan Pistoresi: I'm just trying to think of how to phrase this in an exclusion criteria rather than...

Lisa Chew: That's why I was thinking we put it under a new header.

Emily Transue: I would agree with that. The only real exclusion criteria would be the history of angioedema. The other two aren't something you would look at on a PA and exclude based on. There would be requirements for...

Ryan Pistoresi: So Leta, do you mind if we take the two sub-bullets that Emily pointed out and then kind of transfer them into an inclusion criteria?

Leta Evaskus: These two? The last two?

Ryan Pistoresi: Yes. Sorry, I think better that way.

Emily Transue: I would say avoid, so in front of concomitant for each of those, say avoid concomitant use, and then you can just simplify the exclusion criteria to just history of angioedema. I know it's worth nothing but it makes it a lot easier to implement.

Lisa Chew: Other thoughts or edits? Recommendations, modifications?

Amber Figueroa: I move that the Apple Health Medicaid Program implement the limitations for Entresto as listed on slides 2-3.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Okay, now we move onto Xiidra.

April Phillips: So the inclusion criteria, diagnosis of chronic dry eye, with documentation provided indicating abnormal result or response to one or more of the following dry eye disease diagnostic or assessment methods. Tear break up time, less than ten seconds, ocular surface dye

staining, Schirmer test, fluorescein clearance test/tear function index, tear osmolarity, and tear lactoferrin concentrations in the lacrimal gland are decreased. Also, a history of failure, contraindication, or intolerance to non-prescription ocular lubricant/artificial tear solution used at least four times a day and cyclosporine or Restasis. We have, since this was printed, we decided to remove the requirement of tried and fail of the non-prescription eyedrops, since there is no PA criteria that was removed for Restasis. It didn't make sense to have somebody who had tried Restasis to go back to an over-the-counter product. So that was removed, that requirement. The exclusion criteria is concomitant use with Restasis and a quantity limit of 60 single-use vials in a 30 day supply.

Lisa Chew: There are no stakeholders.

Amber Figueroa: I don't know how to do any of those tests. So you're wanting this to be something that only an ophthalmologist can prescribe, right? I don't even know what some of those are, so it's definitely not going to be primary care prescribing this, which maybe what we want. I'm just saying, don't expect a primary care to know how to do these things.

April Phillips: As you can tell, I have a hard time saying them, so yes. I'm guessing we would prefer to have a more specialized knowledge before prescribing this. Sorry, my words are not coming.

Emily Transue: I acknowledge that and agree. This would be ophthalmologist prescribing.

Amber Figueroa: So, I would refer someone to the ophthalmologist for a complaint of dry eyes? I don't know, it's not usually a common referral, to tell people to try artificial tears and then just tell them to suck it up. I mean I don't usually refer to ophthalmologists.

Leta Evaskus: Most patients would go to an ophthalmologist. I don't think you would go to your primary care for this problem.

Ryan Pistoresi: So I think in this situation, this is a patient that has failed alternatives to this. So, if they come in complaining about dry eyes and you recommend that they try artificial tears or other solutions and they continue to have

this issue, they may have k-sicca which then they would go to an ophthalmologist to determine, is this k-sicca or is this some other related disease of the eye, to which then they could direct them to therapy. So I think that's the way we are intending this policy to be, but I do take your point but not like everyone that comes in with dry eye to send to an ophthalmologist. Just the people that are not able to respond to OTC therapy.

Dale Sanderson: So just like an initial consult as opposed to ongoing prescribing this, right?

April Phillips: Yes, an initial consult, do we want to potentially add that to criteria? Prescribed by or in consultation...

Donna Sullivan: Once there's been an initial consult, you can go back to primary care.

Jordan Storhaug: I think its fine the way that it is. I mean I think this has worked with patients by panels, that they have seen me, we've tried over-the-counter things. I go, "Is there something... what horrible thing is going on?" They see the ophthalmologist. They get diagnosed and suggested to go on something like this, but then they're on it for longterm, in which case they don't go back to their ophthalmologist for the refills, but then I'm able to refill it, and at that point I'd have testing results, someone will be able to do a prior authorization if required based upon their previous test.

David Johnson: Just as a point of process, I mean probably 90% of all these that I see, even for the Restasis, come from optometrists not from ophthalmologists, and I've never seen any of these testing results included in any notes from anybody.

Amber Figueroa: I'm thinking the same thing. If somebody says they have dry eye, they say try this, and if that doesn't work, they say try this. I don't think that eye doctors take the time to do these tests, whatever they are. Maybe you want them to, I don't know. I'm not an eye doctor.

Leta Evaskus: They do. As someone with chronic dry eye, they do these tests.

Amber Figueroa: Okay.

Lisa Chew: How is the committee feeling about the inclusion and exclusion criteria for this, and quantity limit?

Diane Schwilke: Can you just remove the capitalization of cyclosporine.

Dale Sanderson: Are these the list of tests, like in the product insert of the drug? Where did it come from?

April Phillips: I have to be honest, I did not make them up myself. It's usual tests with diagnostic for dry eye.

Petra Eichelsdoerfer: Most, I'm not going to say that they're going to do every one of these tests in a routine work up for dry eye, but they are common tests that are used for the diagnosis of dry eye.

Dale Sanderson: And based on the results of these tests, you would then prescribe this? Is there a criteria that these tests produce?

Petra Eichelsdoerfer: Well yeah. There's criteria for interpreting the outcome. So for example, with the fluorescein clearance test, you put the fluorescein dye in the eye and then you see how long it takes to clear and that's going to give you an idea of how many tears are being produced, how fast they're being produced, and how fast they're draining. The Schirmer test is also looking at tear production. So, all of these things, you know they're going to do a certain number of them to arrive at A, is it dry eye, and B, get some idea of where the etiology might be coming from, and so that is the thinking behind including these. They're part of the diagnostic criteria for chronic dry eye when you are really looking into more than just the patient complaining of symptoms. So, if you're wanting to look at why they've got dry eye or if there might be something else going on.

Dale Sanderson: So are these tests something that basically an optometrist would do? Not only an ophthalmologist but an optometrist would do?

Petra Eichelsdoerfer: That one, I'm not so sure about. So, I don't feel comfortable saying whether they would or would not. I know they're fairly simple tests, but

I'm not sure if they would be within the daily scope of practice for an optometrist.

Lisa Chew: I move that the Apple Health Medicaid Program implement the limitations for Xiidra as listed on slides 5 and 6.

Amber Figueroa: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Okay. Now, on to the pulmonary fibrosis agents.

April Phillips: For the pulmonary fibrosis agents, our inclusion criteria would be a diagnosis of idiopathic pulmonary fibrosis confirmed by at least one of the following: The presence of usual interstitial pneumonia on a high resolution computed tomography or surgical lung biopsy and prescribed by or in consultation by a specialist in pulmonology. Exclusion criteria would be the combination use of nintedanib and pirfenidone.

Amber Figueroa: What are the agents?

April Phillips: I'm going to destroy how you say them, but Ofev and Esbriet.

Susan Flatebo: Did you say there are just two pulmonary fibrosis agents? Shouldn't their names be on that slide, or not?

April Phillips: We can count them out. The generic names are on there listed in the combination.

Susan Flatebo: Okay. Oh, I see.

Amber Figueroa: I don't have enough knowledge to know if that's the only two ways to diagnose pulmonary fibrosis. Does anybody else know? I mean I don't want to exclude someone from getting this if there's another way that it's diagnosed.

April Phillips: I don't know if there's another way.

Leta Evaskus: Do we have any stakeholders?

Lisa Chew: No, there are no stakeholders.

Emily Transue: There's certainly the standard ways of diagnosing it.

Amber Figueroa: Pulmonary function testing or anything like that with an X-ray or anything like that?

Lisa Chew: I'm not a pulmonologist, but I think it's either through high-res CT or an actual biopsy pathology diagnosis.

Amber Figueroa: I move that the Apple Health Medicaid Program implement the limitations for the pulmonary fibrosis agents, as listed on slide 8.

Jordan Storhaug: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Now we move onto Endari.

April Phillips: So the suggested policy for Endari, inclusion criteria would be the diagnosis of sickle cell disease, a history of greater than or equal to two painful sickle cell episodes in the last 12 months, greater than or equal to five years of age and a history of one of the following: Either stabilized on hydroxyurea for the last 3 months and it will be continued with Endari, or documentation of contraindication or intolerance to hydroxyurea. Prescribed by or in consultation with the hematologist or a specialist with an expertise in treatment of sickle cell disease.

Lisa Chew: We do have one stakeholder, Dr. Darrel Harrington. If you could state your name and who represent and you'll have three minutes.

Darrel Harrington: My name is Darrel Harrington, I'm the CMO of Emmaus Life Sciences, professor of medicine [inaudible] and board certified internist and critical care doctor, and I just want to talk a little bit about sickle cell quickly and then Endari and the rationale for its use. As many of you know, about 100,000 Americans are actually affected by sickle cell disease, many of which are individuals of color. It's designated as the "orphan's disease" not just because there are 200,000 or less than 200,000 people effected but I think also because very little has been done in the space for the last three or four decades. The life expectancy of people with sickle cell disease is reduced quite significantly, and it should be noted that half the people who die of this disease die so in acute syndrome, not with chronic organ failure, but just because they're coming in admitted with the sickle crisis or acute chest syndrome. This is important because we do know from even some of the early work with hydroxyurea, that if you can reduce the number of even painful sickle crisis syndromes, you can decrease the risk of death, and there's a really nice article from 2003 that actually demonstrated that a reduction to get the painful crisis less than three in a year, you can actually reduce mortality. So just reducing simple painful crisis is extremely important. Up until recently, only hydroxyurea was approved, as you all know, for use in sickle cell disease patients. There's over a decade of literature, which suggests strongly that compliance is an on-going problem with hydroxyurea for a number of reasons. Some of it actually includes perception and some real of its fear in use of toxicities, as well as ongoing monitoring. These perceptions are held both by physicians and patients. Sickle cell disease, as you know, is treated by a really specialized group of individuals who are passionate about the disease and because of FDA approval last year with Endari, clinicians and patients have been excited to get this prescribed as an efficacious therapeutic. Over four decades of data based in clinical science has fueled the rationale for [inaudible] use, and I think that we can all agree that as a pharmaceutical grade glutamine it represents a therapeutic, which delivers consistent and reproducible high quality results. The phase 3 trial that I think you're all familiar with, which was published last month, almost a year after the FDA approval, of about 230 patients with sickle cell disease from around the country had really striking and clinically relevant important results. I'll just read them very quickly. There was a 25% reduction in painful crisis placebo. This is important because, as I mentioned, reducing painful crisis has been

associated with actually not just improving quality of life but also, if you can get it under three has been associated in reduction of mortality and this is really important. The study was not powered for mortality, however. It's also important to note that about a third of reduction in hospitalization was known in those patients who were randomized to Endari compared to those who were on placebo, and that was substantiated by the observation that individuals who were in the Endari arm had a medium hospitalization, which was less than the placebo arm, 6.5 days compared to 11 days. So, again that actually supports the idea that this drug really works. A secondary analysis looking at acute chest syndrome also showed a 2/3 reduction in both patients with Endari compared to placebo. Again all of this, I think, supports the idea that this is a therapeutic agent that the FDA, as well the peer community, demonstrates efficacy. From a safety standpoint of view, there was no difference in severe adverse events compared to placebo, and the most common side effect with people taking Endari was mild GI discomfort. So our recommendation, my recommendation, as a clinician is that the sickle cell community, particularly those patients effected with sickle cell disease, have unrestricted access to this therapeutic, with or without the use of hydroxyurea. Thank for your time and any questions whatsoever?

Susan Flatebo: Did they understand the mechanism or how Endari works for sickle cell?

Darrel Harrington: So it's a really great question, an important question. So the research early on suggested that glutamine, which is what we call a ubiquitous conditional amino acid readily available is diminished in terms of its access for patients with sickle cell disease. The idea is that glutamine as a precursor to really potent antioxidants, namely NAD, glutathione etc., is important in actually sort of bolstering their levels, if you will. We know that sickle cell patients oxidant stress caused not only the sickling to occur but it's also an adhesion dysfunction that actually also occurs in sickle cell disease. And so glutamine has been shown to reduce what we call the redact potential. So, in other words it actually improves or reduces the oxidative stress or potential for oxidative stress, and in two small studies have actually also shown to reduce adhesion, which is actually something that is associated with improving flow. So those are two mechanisms that we do know and the current signs of thinking about sickle cell disease has been modified from just a bunch of sickling to

actually adhesion is extremely important and sort of flow, or velocity of flow through the small vessels. There are probably other things that glutamine does that probably also enhances its benefits in sickle cell disease, which is not necessarily completely characterized. Okay, thank you all so much.

Lisa Chew: Thank you, Dr. Harrington.

Amber Figueroa: I think it looks good.

Virginia Buccola: I just have a quick question, or I was just wondering about the 90 days on stabilized hydroxyurea. Is there a benefit to having that there, that time limit before you would, which I would assume then your adding on with Endari?

Female: I think the idea is to have enough time to determine whether hydroxyurea alone works and whether an additional agent is needed.

Virginia Buccola: Okay.

Lisa Chew: Any other modifications to the inclusion criteria?

Susan Flatebo: I move that the Apple Health Medicaid Program implement the limitation for Endari as listed on slide 10.

Amber Figueroa: I second.

Lisa Chew: All those in favor say aye.

Group: Aye.

Lisa Chew: Any opposed? And the motion carries. Now we'll move onto the Apple Health preferred drug list, April.

April Phillips: So, the drugs that have been provided, the drug classes, these are the ones that will be implemented in October and so we are providing what drugs will be preferred or non-preferred for these subclasses. Just to save time, I'm assuming you guys don't want me to read everything to

you, I'm just going to go over the drug class and then if there's any edits, because I noticed there's a few little things that needed to be changed on here after they were printed, I will point those out as we go along. Unless you want to have a good laugh and listen to me try to pronounce some of these names. Just making sure.

So our first one is for the allergenic extracts and biologic miscellaneous, and the next one for allergy is the nasal histamines. We only have one product that's going to be preferred on this. For the next slide, the analgesic/anti-inflammatory antirheumatic/antimetabolites there are going to be four preferred products. The generic methotrexate and then two others, the trexall (the oral tablet) and the other two are a liquid and an autoinjector.

Analgesics/anti-inflammatory other, you've got two preferred and one non. For the analgesic/opioids the long-acting partial agonists, the buprenorphine patch is the only preferred.

The analgesic/opioid the short acting- agonist, for the preferred product you can see there's quite a few listed on there.

Then the next slide is the non-preferred products and then the next slide after that is the same thing and the non-preferred products continued. The next slide the analgesics/opioid short acting.

Diana Shwilke: Excuse me, you have morphine sulfate in preferred and non-preferred. On this handout, it's in both.

April Phillips: It was not.

David Johnson: I noticed it on several things, and I think what it is, is like a cap and a tab, works in different forms that aren't reflected on the slides. Cause there's hydromorphone is on the same thing, but its different forms. April can confirm that but I think that's what it is.

April Phillips: Yes, that's usually the most of them, and I tried to catch most of them through here and I will point those out. I did miss this one and usually

yeah, that's the difference, tablets, capsules. Sometimes it's injectable versus orals.

Female: Is there another list some place that lists that out, so the prescribers can figure it out. So pharmacists can figure it out.

April Phillips: It will be updated on, when we post our preferred drug list online, it will be made more clear rather than just staying the generic morphine sulfate. It'll either say morphine-sulfate capsules or morphine-sulfate tablets extended release versus immediate release more specific to that, and I've got my team here that will take note of that and make sure that it's very clear. So for the analgesics/opioids the short acting partial agonists the Belbuca film is the preferred and there are no non-preferred in this class. So the analgesic migraine agents, the miscellaneous, they are listed below. This is the class I really didn't want to have say out loud, and there are no non-preferred products in this class. So, the antianxiety agents, the benzodiazepines, we've got four preferred and then the non-preferreds are listed there. The antianxiety agents, the miscellaneous.

The antibiotics-aminopenicillins, and we have two preferred and no non-preferred agents.

The antibiotics-natural penicillins, we only have one non-preferred in that class.

Antibiotics-penicillin combinations, on this particular slide I will point out there is Zosyn listed both on preferred and non-preferred, it should be on the non-preferred side and not the preferred side.

Amber Figueroa: That doesn't include in-hospital? This is just outpatient? Okay.

April Phillips: So the antibiotics-sulfonamides, and then our next class is the antibiotics tetracyclines. On this slide, you will see the Morgidox listed on both preferred and non-preferred. The non-preferred is the Morgidox kit, which includes a cleaner in it, and the preferred is just a capsule.

The next slide is the antibiotics-vaginal. The next slide is the antidiabetics alpha-glucosidase inhibitors. We only have one preferred, the Arcabose.

Next slide, antidiabetics biguanides, and the only preferred is the Metformin and the Metformin ER. The osmotic and the modified releasing Metformin are both nonpreferred.

Antidiabetics dopamine receptor agonists, no preferred agents, and the nonpreferred is the Cycloset.

Next slide, antidiabetics meglitinide analogues. The next slide is the antidiabetics SGLT2 inhibitors, and this one I wanted to point out that when this class was reviewed with the board, they did recommend that we provided at least one product with cardiovascular benefit. So, that's why the Jardiance is in the preferred.

Next slide, antidiabetic sulfonylureas, generics are preferred. Antidiabetics thiazolidinediones, only one preferred product in this class, the pioglitazone.

Next slide, antiemetics, antivertigo, substance P/neurokinin receptor antagonist combinations. The Akynzeo is nonpreferred, and it's the only product in this class. So, it will require prior authorization.

Next slide, the antineoplastic adjunctive therapies, progestin antineoplastics oral. The megestrol is the preferred product, and the brand is the not, the Megace.

Next slide, antiparkinson's agents, the anticholinergics. Both products are preferred in this. There is no nonpreferred.

Next slide, antiparkinson's agents COMT Inhibitors. Generics are preferred. Brand is nonpreferred.

Next slide, antiparkinson dopaminergics. So, on this one, I wanted to point out that amantadine capsules are preferred, but the amantadine tablets are nonpreferred.

Next slide, antiparkinson's agents, the monoamine oxidase inhibitors, selegiline, the only preferred product.

Next slide, the asthma/COPD agents, the long-acting muscarinic agents, on this particular one, the Spiriva Handihaler is the only preferred product. The Spiriva Respimat is nonpreferred.

The cardiovascular agents, hyperlipidemics, the generic Zetia, ezetimibe, is the only preferred product in this class.

Next slide, cardiovascular agents, antihyperlipidemic, bile acid sequestrants.

Next slide, cardiovascular agents, the fibrinic acid derivatives, fenofibrate and gemfibrozil are the preferred products.

Next slide, cardiovascular agents, hyperlipidemics, HMG CoA reductase inhibitors and combinations, the usual lovastatin, pravastatin, rosuvastatin, and simvastatin are preferred.

Next slide, cardiovascular agents antihyperlipidemics, microsomal triglyceride transferase protein inhibitors. The only product in this class is Juxtapid, and it is preferred requiring PA.

For the cardiovascular antihyperlipidemics nicotinic acid derivatives, niacin ER and niacor are the preferred products.

Next slide, the antiadrenergic combinations, we have no preferred products in this class, and the two nonpreferred products require prior authorization.

Next slide, cardiovascular agents, antihypertensive, antiadrenergics, so this class the preferreds are generics.

Next slide, the cardiovascular antihypertensive beta-adrenergic combinations.

Next slide, the cardiovascular antihypertensive beta adrenergic, so you'll notice with this slide and the following slide, they both have beta block

on them, the beta block should be non preferred. It should be removed from the preferred side.

Next slide, and this is the list of nonpreferreds.

Amber Figueroa: Is there... never mind. I was looking at the wrong column. Never mind.

April Phillips: So, the calcium channel blocker combinations, there are two products, and they are both nonpreferred and require PA.

So, the calcium channel blockers, all the preferreds listed there. The nicardipine is the nicardipine IV. The nicardipine IV is the preferred product on the next slide, it lists the nonpreferred, and that is the nicardipine capsule is the nonpreferred agent.

Next slide, so the antihypertensive others are listed there.

Next slide, the cardiovascular cardiotonic cardiac glycosides. We've got Digitek, Digox, digoxin, and nitroglycerine, and dextrose IV. The only nonpreferred is the Lanoxin.

For the phosphodiesterase inhibitors, Milrinone is the only product in this class, and it's preferred with PA.

Cardiovascular agents diuretics, the carbonic anhydrase inhibitors.

Next slide is the diuretic combinations, and the generics are preferred, and brands are nonpreferred.

Next slide, the loop diuretics.

Next slide, the potassium sparing diuretics.

Next slide, thiazide and thiazide like diuretics.

Next slide, cardiovascular agents – miscellaneous. The antianginal agents-nitrates.

Next slide, the antianginal agents – other. Ranexa is the only product in this class, and it is a preferred.

Next slide, the cardiovascular agents – miscellaneous. The antiarrhythmics, the lidocaine IV is preferred. Sorry, ignore that. So, the preferred, and then the next slide is the nonpreferred.

Next slide, for the sinus node inhibitors, there is only one product in this class, Corlanor, and it requires PA.

Next slide, for the hematopoietic agents, the erythropoiesis stimulating agents, Aranesp and Epogen are preferred.

Next slide, granulocyte colony-stimulating factors, Granix and Neupogen are preferred.

Next slide, the cycloplegic mydriatics, and then the next slide, the ophthalmic immunomodulators. Restasis is preferred and Xiidra is nonpreferred. The Xiidra requires PA. Obviously, that's the policy that we reviewed today.

Next slide, ophthalmic local anesthetics.

Next slide, ophthalmic cystinosis agents, one product in this class, and it's preferred and requires PA.

Next slide, otic agents, otic analgesic combinations. There are two products in this class, and they are both preferred.

Next slide, otic agents, the otic steroids.

Next slide, respiratory agents, alpha-proteinase inhibitors. There are four products in this class, and they are all preferred.

Next slide, respiratory agents, pulmonary fibrosing agents, and this is the Esbriet and Ofev, the policy that we discussed earlier today. They are both preferred and require PA.

Amber Figueroa: That should be pulmonary fibrosis agents, not fibrosing agents? We don't want to further fibrose them.

April Phillips: Sometimes, we like to cause diseases. Okay. Substance use disorder, alcohol deterrents. We've got two preferred and the one nonpreferred.

Final slide, the vasopressors. It looks like all the products are preferred with no nonpreferred.

I know I went through that really quickly, but are there any questions?

Leta Evaskus: Were there any stakeholders?

Lisa Chew: There are no stakeholders. Do we need to make a motion or how does that work for this?

April Phillips: No, that's what we were just discussing. We might as well do it. I don't know that it would hurt anything.

Leta Evaskus: Probably just say that the DUR board approves of the proposed preferred drugs for the Apple Health PDL.

Lisa Chew: Whatever she said just now.

Leta Evaskus: The DUR board...

Female: The DUR board approves the Apple Health preferred drug list, as proposed. Can I get a second?

Virginia Buccola: I second that.

Lisa Chew: All those in favor, say aye.

Group: Aye.

Lisa Chew: Any opposed? The motion carries, and we are now adjourned.