Ginny Buccola: Good morning, everybody. This is Virginia Buccola, committee chair and welcome. We're going to convene the DUR portion of our meeting for October 20. I'm going to read off the names of all the attendees. And if you could just unmute and say "here" when I call your name. And my apologies in advance if I'm mispronouncing. Feel free to correct me. I really hate saying names wrong. So for our P&T committee members, there is Alex Park.

Alex Park: Here.

Ginny Buccola: And Diane Schwilke.

Diane Schwilke: I'm here.

Ginny Buccola: And Jordan Storhaug.

Jordan Storhaug: Here.

Ginny Buccola: Nancy Lee.

Nancy Lee: Here.

Ginny Buccola: Leah Marcotte.

Lean Marcotte: Here.

Ginny Buccola: Susan Flatebo.

Susan Flatebo: Here.

Ginny Buccola: Catherine Brown.

Catherine Brown: Here.

Ginny Buccola: Kavita Chawla.

Kavita Chawla: Here.

Ginny Buccola: And Michael Corsilles.

Michael Corsilles: Here.

Ginny Buccola: And our Health Care Authority members this month are Leta Evaskus.

Leta Evaskus: Here.

Ginny Buccola: Ryan Pistoresi.

Ryan Pistoresi: Here.

Ginny Buccola: Luke Dearden.

Luke Dearden: Here.

Ginny Buccola: Ryan Taketomo.

Ryan Taketomo: Here.

Ginny Buccola: Joey Zarate.

Joey Zarate: Here.

Ginny Buccola: And our presenters today are Heather Whitley. I saw her hand up just for the record. And Beth Shaw.

Beth Shaw: Good morning.

Ginny Buccola: Good morning. Thank you. Our Magellan Medicaid administration presenter is Umang Patel.

Umang Patel: Here.

Ginny Buccola: And our managed care organization representatives are Greg Simas with Molina. Going Heidi Goodrich with Molina. Petra Eichelsdoerfer with United, who I see logged in. And Omar Dauod with Community Health Plan. And Geoffrey Natividad of Community Health Plan of Washington. I'll turn it back over to Leta for logistics.

Leta Evaskus: Thank you, Ginny. So panelists, you can mute and unmute yourself. Please mute yourself when you're not speaking to limit the background noise. Presenters, please share your web camera when you're presenting and the

committee, please share your cameras when you're deliberating. The meeting is being recorded so please state your name every time you speak. For stakeholder participation, the chair will first call the names of the people who pre-registered to speak. And then you can use the raise hand function and I will call on you and unmute you. You will each have three minutes to speak. And that's it. So I'm going to turn it over to Heather and I'm going to share my screen.

Heather Whitely: Well, thank you very much for inviting me today. It's lovely being here with you. Good morning. I'm a clinical professor with Auburn University, which is in Alabama, and a Clinical Pharmacy Specialist at Baptist Health System, which is a three hospital wide system. And I am placed in a large family medicine residency program specializing exclusively in the care of patients with diabetes, both type one and type two, adults and adolescents. Not many young children for me in a family medicine realm. But many of my patients use these long acting insulins. So it's a pleasure to share with you the project that we conducted through DERP earlier this spring. The next slide goes over just the overview of the process. And I'll walk through each of these components with you over the subsequent slides. But in short, our goal was to identify randomized and non-randomized controlled trials assessing the efficacy and safety of these long acting insulins in patients with either type one or type two diabetes. And then the second component was to articulate the number and the nature of eligible upcoming studies. Now on the next slide we look at the background. I just wanted to provide context because I know not everybody practices in the realm of diabetes. But as a reminder, it is a metabolic disease process characterized by hyperglycemia that results from either inappropriate insulin secretion, insulin action, or a combination of the two. Type One Diabetes is an autoimmune process where the beta cells completely can no longer make their own endogenous insulin and therefore exogamous insulin is required for administration to sustain life. That is typically either given through a continuous insulin infusion pump using predominantly rapid acting or bolus insulin, or through injected insulin commonly in the combination of a basal insulin that we're looking at today as long acting insulins with a bolus insulin. In that context, the basal insulin is used to control the fasting blood sugars and the overnight blood sugars whereas the bolus insulin is to prevent glycemic excursions caused commonly by ingestion of carbohydrate foods or illness or stress and so on. Type Two Diabetes is much more complex, where we have a lot of other pathophysiologic factors going on that allow for different therapeutics to be used commonly starting with Metformin after behavioral modifications and

then augmenting up with a handful of other agents before finally getting to the addition of a long acting insulin when we're not talking about a catabolic extreme hyperglycemic crisis situation. And that long acting insulin is typically added on as a fourth line, third line product. Nonetheless, many, many patients with type two diabetes are reusing long acting insulins. As I mentioned, I have patients using all of these different products that we'll be talking about today. Nancy, since you and I graduated from residency, you know that's when Lantos came out when we started school. And then since then, we've had some more advances in the realm of these long acting insulins, three that I have listed here for you today. And I'm going to talk from the bottom up. The first one of the more recent ones is the addition of biosimilars, which are also called follow-ons. Now, if you remember, insulin itself is a very large, bulky molecule. And so not only does it have this primary amino acid sequence, which can be replicated by other manufacturers perfectly, but it also has secondary, tertiary, and quaternary complexes, which cannot be replicated, meaning the secondary like the beta pleated sheet, the alpha helixes, the tertiary being how that molecule folds on top of each other and coronary binding with other products like albumin. That's what is harder to formulate exactly. Nonetheless, these biosimilars or follow-ons studies are conducted to verify similar extent in rate of absorption and then pharmacodynamic impact as well. And so that's been a big change in recent years because the additions of the follow-ons, which are the exact same chemical of the parent compounds, help to drive down price and improve costs. And we have two available on the market for the parent compound [indistinct]. We also have concentrated insulins now. It's all about a difference in volume. The standard concentration of insulin is U100, being 100 units per milliliter. And now we have concentrated long acting insulins. And these are some of our second generations long acting insulins, where it is two times or three times the concentration, meaning that you can give the same number of units in half or a third of the volume. When you do that, you're improving the surface area ratio to the number of units and theoretically improving the absorption. And what we do see is it flattens out the curve, extends the duration of action of at least one of the products and lowers some risk of nocturnal hypoglycemia. And then lastly, we have these longer acting insulins that have increased duration of actions. So on the next slide I have a pharmacokinetic profile for you where we have on the x axis time over a 24 hour period and the y axis shows plasma insulin levels. The first few peaks that you see in black and in red represent those bolus insulins that are commonly used to prevent glycemic excursions from carbohydrate absorption or consumption. And blue, we have NPH. This is an intermediate

acting insulin sometimes used as a basal insulin dosed once or twice a day, because as you can see, it only lasts about half a day. You also notice there's a peak. At about five hours we have a peak in the pharmacokinetic profile that intermediate acting insulin showing that there is an increased risk at that time point for hypoglycemia. As we move into the first generation, long acting insulins, which is glargine U100 and then detemir. And then over to the second generation long acting insulins, which is the concentrated Glargine and Degludec. We are extending the interval and flattening the curve, so becoming more [indistinct] as time goes on. So Glargine you see there is our first long acting U100 insulin lasting about 24 hours and Detemir just short of that. But interestingly, when we concentrate Glargine going from that U100 first generation to a U300 second generation, we are extending the duration of action from almost 24 hours to a full 24 hours, 25 an hour duration. And then with Degludec, which is in the yellow, that one is an ultra-long acting insulin lasting about 42 hours. So way into the next day, which actually seems to provide a much more firm foundation of basal insulin control and allows for some flexible dosing as well. Okay, so moving on with the project after a bit of that background information, this topic brief that we conducted was on the backbone of a systematic review that was presented several years ago in 2018, and then a surveillance report in August 2020. And collectively, those previous investigations identified 71 studies for the interventions that I'll be sharing with you on the next slide, which is looking at the patient populations of adults or children with type one or type two diabetes on slide five, and then the interventions we evaluated was the use of any first generation or second generation insulin. So on slide five in the table, you'll see that we have listed those insulins for you. The first generation insulins of the U100 insulin glargine and then also their follow-on brand name, Semglee, which was new to the market just last summer, 2020 and then Basaglar. And then the other first generation insulin Detemir further down, the second generation long acting insulins, which is a concentrated formulation of insulin glargine, which is a U300, so three times the concentration. That brand name is Toujeo. And then the second generation insulin which is an ultra-long acting insulin of Degludec insulin Tresiba. And then lastly, on the third row, you see this 70/30 pre-mixed insulin of Ryzodeg. And that's a fixed dosing of 70% Degludec 30%, aspart. So these were our interventions that we investigated. Onto slide six, you see some of the comparators. We're looking for head to head studies evaluating one of these long acting insulins compared to another. Now at times, this would be compared to a follow-on. So it might be glargine versus glargine, meaning their original compound to a follow-on or called a biosimilar. Or to U100 first

generation to a U300 second generation or a difference in the administration methods, so meaning insulin syringe versus insulin pen. And then on the third bullet point, evaluating these individual components to that pre-mixed insulin that we now have available with the second generation insulin as well. The next slide shows the outcomes of interest. We searched studies to have, they're either glycemic in nature of improving blood sugar as you would expect, or microvascular benefit, or macrovascular benefit. As a review, the macrovascular outcomes are those that are affecting our heart or brain or also amputations of extremities by peripheral vascular disease, or then macrovascular disease with neuropathy, nephropathy, retinopathy. And then we also had outcomes of harm on slide eight, which could be all cause mortality or glycemic in nature focusing on hypoglycemia, whether that was nocturnal hypoglycemia or severe hyperglycemia. Then adverse events that lead to withdraws or malignancies. All right, onward to slide nine, we had study designs of either randomized control trials lasting at least eight weeks in duration, or observational studies that enrolled at least 1000 participants. The key questions that we thought to answer were either in slide ten, comparative efficacy or harm by vial and syringe versus insulin pin, or a difference of that original compound compared to a biosimilar by subgroups. And then lastly, characteristics of ongoing studies that have not been published. The next slide simply depicts these two processes for you. The methods that we searched for randomized control trials or observational studies that have been published, and then the second of our method of evaluating unpublished studies that were ongoing using clinical trials.gov or Cochrane Library through the search dates listed below. So advancing forward two slides, I have for you our findings. This was where we identified 22 eligible trials in 30 publications. The majority were either one of these two first bullet points, either looking at the comparison of insulin glargine versus insulin degludec, most commonly looking at the concentrated formulation of glargine. So a second generation acting insulin compared to the other second generation long acting insulin, seven studies there. And then the next bullet point, eight studies comparing glargine versus glargine. And as you'll see in the coming slide, this was oftentimes looking at the U100 original insulin glargine compared to the U300 or looking at biosimilar comparisons. So I'll start on this slide here. But over the next three slides, I'm breaking down those components that you see on that previous slide into the different subgroups. And I'm just going to talk through these in detail to give you a little bit greater grasp, richer information about the data that we found. So on the first row, here, we see that we have these seven randomized control trials evaluated in patients with type two diabetes. The majority were

looking at the concentrated formulation, second generation insulin glargine compared to U100 degludec. So second generation versus second generation long acting insulin. But I'll point out that Degludec comes as a U100 and a concentrated U200. So the majority of these, meaning six of them, we're comparing the concentrated glargine to the unconcentrated, the regular concentration of Degludec. There's one study that was evaluating concentrated glargine versus concentrated degludec, which I think would be noteworthy and worth evaluating further. Next, we had insulin glargine versus glargine. Six of these eight trials, we're looking at the concentrated formulation, the second generation glargine versus the original U100 glargine. And then the remaining two, we're looking at the original U100 glargine versus a biosimilar. So a good mix there. And then lastly, we have two studies, one randomized controlled trial when observational trial, both in patients with type two diabetes that had a three treatment arm. One was U300 second generation glargine and then U100 Detemir, another first generation long acting insulin, and then the third arm with a biosimilar. So two studies evaluating these three competitors here. The next slide evaluates studies that we found where we're looking at a basal bolus comparison of insulin use. So the first one is insulin degludec versus insulin detemir. But both of these were in patients with type one diabetes, and that was added on top of a bolus insulin aspart, so a true basal bolus regimen for the study population. The next two studies is evaluating that pre-mixed insulin, the insulin degludec aspart in the 70/30 ratio, both compared to a first generation insulin. So the first one compared to insulin detemir, the second one compared to insulin glargine with aspart added on top of those as bolus. Then the next slide shows two observational studies that we found and truly I believe the outcome of these will be informative at the point of the patient bedside to truly inform application of utilization of these products. So assuming that the previous studies I just presented to you show safety benefit or efficacy benefit, particularly when comparing a second generation insulin to a first generation insulin, then in clinical practice, it would make sense to be using a second generation insulin when possible in patients. So this first study, looking at insulin that degludec is evaluating. Well, then if that's true, if it's more beneficial by safety or efficacy, how do we safely switch or interchange a first generation insulin over to this ultra-long acting insulin degludec? And then the next line with insulin glargine is comparing this new 300. So the second generation long acting insulin in insulin naive versus insulin experienced patients. So typically, concentrated insulins are reserved for patients requiring larger amounts of insulin. So we concentrate that dose, decrease the volume, improve the absorption theoretically, so

reserved for patients requiring longer acting insulin. But as we see when we concentrate glargine, we extend the interval and flatten the curve. And so if it does show that it's more beneficial in patients then it would make sense to us that earlier on. So this study is comparing that concentrated insulin in patients that are insulin experienced versus insulin naive. And I think it will help to inform us as to whether using that concentrated second generation insulin is safe in insulin naive patients. So that concludes the 22 studies that we found through this first portion of the project that were all published. The next slide, thank you, shows these ongoing trials that we found. And there were 15 that were eligible based on the scope of the project. The majority were randomized control trials, most of which were evaluating insulin glargine to degludec. And then we also found five observational studies as well, as you see articulated here. And so that concludes the presentation that I have for you today. Leta, you can weigh in if they've been provided the detailed information that outlines each one of these studies, and a table formulation. But thank you for allowing me to share this information with you today.

Ginny Buccola: Thanks, Heather. Any questions from the committee for Heather?

Nancy Lee: Hi, Heather. It's Nancy. You mentioned when you were talking about the concentrated glargine, I think the degludec 200, something that you thought would be interesting to look at. Did you delve into that a little bit further to see if there was a significant clinical difference?

Heather Whitley: Yes, great question. So that was in that first line of the very first table where we saw seven randomized control trials, looking at the second generation U300 glargine versus the second generation Degludec. And only one of those studies was bold enough to compare the difference of the concentrated glargine to the U200 concentrate of degludec. And I did. I pulled that study and looked at it, but now I can't remember what it said. So there's that. Because I was interested in what that was. And see I'm turning a little bit red in the face because I can't remember now. But it's true, I was interested. So I'm sitting here like, well, maybe it wasn't a clinically significant difference. And that's why it didn't stick in my brain.

Nancy Lee: Thank you.

Ginny Buccola: Any other questions? And thank you, Heather. That was a really comprehensive overview. It looks like we have one stakeholder for this topic.

I see Sarah Villareal is listed, with Novonordisk. Sarah, if you can just go ahead and introduce yourself and any affiliation with pharmaceutical company and then you'll have three minutes to present.

Sarah Villarreal: Good morning, everyone. My name is Sarah Villarreal. I am a clinical pharmacist and I function as a medical accounts director with Novonordisk and I would like to provide highlights on the insulin degludec, which was branded as Tresiba. Tresiba is the only long acting basal insulin analogue indicated to improve glycemic control in both adults and children as young as one year of age with diabetes, both type one and type two. Tresiba has a half-life of approximately 25 hours and a duration of action of at least 42 hours. This is the longest half-life in duration of action among the basil insulins. It is administered once daily and unlike other once daily basil insulins, which by label must be administered at the same time each day. In adults Tresiba may be administered at any time of day. The recommended starting dose of Tresiba in insulin naive patients is outlined in the package insert. For adult patients on insulin, it is recommended start Tresiba at a one to one basal conversion. In the pediatric patient population already on insulin, it is recommended to start Tresiba at 80% of the total daily long or intermediate acting insulin dose to minimize the risk of hypoglycemia. As the U100 and 200 formulations are bioequivalent, there is no requirement to perform a dose conversion when using the two pens, as the pen dose window shows the number of insulin units to be delivered. After being open, the Tresiba flex touchpad may be used for up to 56 days. The Tresiba label was updated to include the devote trial, a randomized head to head cardiovascular outcomes trial comparing Tresiba and glargine 100 in more than 7600 adult patients with type two diabetes. The primary objective was to evaluate cardiovascular safety and was achieved. Secondary endpoints also included the incidence and prevalence of severe hypoglycemia, a significant reduction in both incidence and rate of severe hypoglycemia as compared to glargine U100. Specifically Tresiba demonstrated a 27% relative reduction in the incidence of severe hypoglycemia. In regards to efficacy, I would also refer you to the PI, which includes the results of 11 head to head clinical trials, evaluating Tresiba against a variety of competitors, ten of which were other basal insulin analogues. Tresiba met the primary objective of non-inferiority in regards to A1C reduction. In addition, a statistically similar percentage of adult patients on Tresiba versus comparators achieved an A1C value of less than 7%. With the data presented, including several characteristics that set Tresiba apart within the basal insulin class, I would respectfully request

consideration that you add Tresiba as a basal insulin option to the PDL. Thank you.

Ginny Buccola: Thank you, Sarah. Are there any questions from the committee for Sarah? Okay, looks like we're ready to go to the motion.

Leta Evaskus: Hi, Ginny. This is Leta. I just want to give stakeholders a chance, if you would like to speak, just raise your hand. I don't see any other hands raised.

Ginny Buccola: Thanks Leta.

Diane Schwilke: This is Diane Schwilke. I move that after considering the evidence of safety, efficacy, and special populations for the treatment of type 1 and type 2 diabetes, I move that insulin detemir, insulin glargine, insulin degludec, and insulin degludec/insulin aspart combination are safe and efficacious for the treatment of their approved indications. Single agent long acting insulins can be subject to therapeutic interchange in the Washington preferred drug list.

Jordan Storhaug: This is Jordan Storhaug. I second.

Ginny Buccola: This is Virginia Buccola, committee chair. All those in favor, please say aye.

All: Aye.

Ginny Buccola: Are there any opposed? And the motion carries. And then I see on our agenda that we have an archive motion.

Ryan Pistoresi: Good morning. This is Ryan Pistoresi. I just want to provide a little bit of context why we're looking at having this be archived. As you can see from the previous slide, the last time we reviewed the long acting insulins was back in August of 2018. And as we do get our evidence reports from the drug effectiveness review project. Given that there hasn't been as many new to market innovative drugs in the long acting insulin space and a lot of our state's focus has been towards some of these other newer novel drugs where a lot of our new reports are being commissioned, we thought it would be an appropriate time to archive this just given that we aren't expecting any new updates to this report in the near future.

Nancy Lee: This is Nancy. Ryan, I had a question and it's just more of a reminder for myself. So when we archive, are we also going to continue to do this scans

just to keep up with if there are any changes or new additions that maybe -- I'm guessing yes, but I just wanted to confirm that may be changing practice.

Ryan Pistoresi: This is Ryan and yes, we can continue to do scans. It's just that we may have to commission them individually as a state outside of the normal evidence review process now for the DERP collaboration. So we can and especially if there is going to be a new product coming out I think there would be definitely some momentum to initiate a scan again. But for the foreseeable future, we don't see this really being scanned. And the purpose of archiving allows us to continue to do cost analyses so as these drug prices change, as different rebate options become available, we as a program can continue to do these cost analyses without having to wait for another scan and then to bring it to the P&T to consider. So this allows us to continue to do our cost analyses processes and still allow for an evidence review if it is warranted.

Nancy Lee: Great, thank you. Thanks for clarifying.

Kavita Chawla: Hi, Kavita here. As I'm reading through this motion that's on the screen right now, I'm asking for what might seem really obvious question. It says that with updated cost analyses, approvals might change. My question is, is that to say that even with cost analysis, at least one of these four long acting insulins will remain preferred and fully covered by HCA for all members?

Ryan Pistoresi: So this is Ryan. So yes, when we do our cost analyses, we always look to have a preferred in a class. And it would be for the programs that it applies to. So for this class, specifically, it applies primarily to UMP. Other classes, there's therapeutic interchange with Medicaid. There's Labor and Industries that also participate on the Washington PDL. So there are programs that are impacted. And specifically for this one, we can think really that the decisions that we're making are going to be for the UMP population. Did that answer that question?

Kavita Chawla: Yeah, so I guess just to call it out, at least one of the fours of the detemir, the degludec, the degludec aspart combo, or the glargine, at least one of them will be preferred. And a corollary question is, it's not that NPH or one of the older insulins will end up being a preferred long acting insulin.

Ryan Pistoresi: So this is Ryan and yes, we'll have a preferred in the long acting insulins for UMP. Yeah, so when we do our cost analysis, we'll be looking at what

combination preferred long acting insulins makes the most sense for our plan.

Kavita Chawla: Thank you.

Nancy Lee: This is Nancy. I propose that the drug class diabetes long acting insulins, after considering the topic brief presented today, I move to archive the following drug class from further regular review by the P&T committee: diabetes long acting insulins 10/20/2021. The drug class will remain on the PDL and the committees last motion will remain in effect until changed by the committee. The agencies may conduct updated cost analyses of this drug class without additional committee approval so long as any resulting change in the preferred status of a drug remains consistent with the committee's last motion for the drug class. The committee may review the archive status of a drug class upon its own initiative or by request of the participating agencies at any time.

Catherine Brown: Catherine Brown. I second.

Ginny Buccola: This is Virginia Buccola, committee chair. All those in favor please say aye.

All: Aye.

Ginny Buccola: Are there any opposed? And this motion to archive the drug class carries. Our next topic is multiple sclerosis and Beth Shaw with DERP is going to be our presenter.

Beth Shaw: Thank you very much. So my name is Beth Shaw. I'm a senior systematic reviewer at the Center for Evidence Based Policy. And I will present to you the surveillance report on disease modifying drugs for multiple sclerosis. So the aim of surveillance is obviously to identify any studies that have been published since the publication of the most recent systematic review to inform your decision making. On the next slide, you can see the order of the presentation. So I'll take you through some of topic history. We'll go through a background about multiple sclerosis. We'll work through the PICOS and the key questions and the methods. And then of course, I'll take you through the findings, and then we'll move through into the summary. So on the next slide, you can see the history of this topic. So on the left hand side, you can see the document type, moving through to the right hand side where you can see the search dates for those reports. At the bottom, you can see that this drug class

review was originally published in July 2007. And then it's been updated a number of times with the most recent update 4 that was published in May 2020. So on the next slide, you can see a bit of background about multiple sclerosis. Multiple sclerosis or MS is the most common immune mediated inflammatory demyelinating disease of the central nervous system. And in a study conducted by the National MS Society, nearly 1 million adults were estimated to be living with MS in the United States. Evidence also suggests that the prevalence of MS has been increasing over the past five decades, and that the occurrence of this disease tends to be higher in women than in men. And MS occurs when the body's immune system attacks the fatty tissue myelin, which surrounds and insulates neurons, and allows for efficient transmission of nerve impulses. In MS, this abnormal immune response causes the degradation of myelin leading to neurologic dysfunction. And symptoms of MS include sensory issues such as numbness, muscle weakness, or spasms. And we also see things like vision problems, dizziness, and trouble walking or speaking. And MS typically presents in early adulthood, with patients experiencing one or more clinically distinct episodes of neurological dysfunction that partially resolve in many cases. So on the next slide, you can see what happens in MS over time. So approximately 85 to 90% of MS cases are with the relapsing remitting type, or RMS, and that's at onset. So you can see the pattern in the top left hand corner where people relapse and then they return to either the previous level of disability or perhaps slightly higher levels of disability and that progresses over time. The majority of those cases eventually move into a secondary progressive type of MS or SPMS. And that's often over the course of decades. And again, you can see that pattern of the disease progression in the top right hand corner. Around 10% of patients have what's called steadily progressing neurological disability. And that's independent of relapses, which is considered to be primary progressive MS or PPMS. And again, the pattern for that is in the bottom left. But we also have a group of people diagnosed with clinically isolated syndrome, which is also known as the first demyelinating event. And that's the first clinical attack that's suggested of MS. So moving on to the next slide, the disease modifying drugs for MS largely consists of treatments targeted to patients with the relapsing forms of the disease. And the aim of these disease modifying therapies is to reduce the number of relapses to delay that progression of disability and to limit new MS disease activity as seen on MRI. These drugs can also be used for clinically isolated syndrome, so that first suggestive attack of MS, and they’re used to delay that second attack. So let's move into the details of this report. So in terms of our PICO, we're looking at that population of adults with MS, including all those

different types of MS that we've just talked about. So that's relapsing remitting MS, secondary progressive, primary progressive, and that progressive relapsing MS. That tends to be an older term, but obviously that's still reflected in the literature. And we also looked at those group of patients with that first attack, so with that clinically isolated syndrome. On the next slide, you can see the list of interventions that we're looking at. So there's a range of drugs, I think there's around 13 to 14. On the left hand side, you can see the generic name. In the middle column, you can see the brand name, and then on the right hand side you can see the FDA approval date. And in this table, the drugs are ordered by FDA approval date from the most recent down to the bottom of the table. On the next slide, in terms of the comparators that we're looking for, we were looking for head to head comparisons, so those direct comparisons of the disease modifying therapies. We were also looking for placebo as a comparator for interventions that lacked those head to head comparisons, and for pipeline drugs, so those new drugs, things like [indistinct], where we wouldn't yet anticipate any head to head comparisons. In terms of outcomes, we were looking for health outcomes, so things like disability, the ability of the patient to function, so things like time lost from work, the ability to attend school. We were also looking at clinical exacerbations or relapse, as well as quality of life. And importantly, for these drugs, we were looking at persistent rates, the ability of the patient to continue on these disease modifying therapies. For the group of people with cis, we were also looking at progression to MS diagnosis. And of course, we were interested in adverse events and withdrawals due to adverse events. So on the next slide, we were also looking for specific study designs. So we were looking for randomized controlled trials that lasted 12 weeks or longer. For those pipeline therapies or interventions that lacked head to head studies, we were looking for placebo controlled trials, again at 12 weeks or more duration. And then we were also looking for retrospective and prospective cohort studies that we're looking at the direct comparison of disease modifying therapy specifically for harms Again, they've had for the last 12 weeks or longer, and we were looking for large studies of those harms, so a minimal total sample size of 1000 participants. And in terms of the questions, we had five questions in the systematic review. We were looking obviously for effectiveness for MS. The second question was around the effectiveness of these therapists for clinically isolated syndrome. The third question was around harms for both of those indications and whether they varied by indication. Fourthly, we were looking for any variation by subgroups. We're thinking of patient characteristics there such as age, perhaps subtype of MS, presence of

comorbidities, et cetera. And we were also looking for ongoing studies. On the next slide, you can see the methods that we used for this surveillance report. So just a reminder, that's to identify any published trials or important FDA actions that have been published since that systematic review. So we searched for registered trials using online trial registries, such as clinicaltrials.gov and the International Registry. So we use drug names and keywords to identify those clinical trials. And then we use those trial numbers or trial identifiers through Ovid Medline and Google Scholar to see if those trials have been published. So again, reminder we're looking for RCTs in cohort studies, the harms. And then of course, we looked on websites for important FDA actions such as newly approved drugs or changes in formulations or indications. Moving on to the findings. You can see on the next slide that we identified three randomized controlled trials, two in relapsing MS and one in acute optic neuritis. And we didn't identify any newly published cohorts since that most recent systematic review in May 2020. So in the next slide, you can see the details of those three published randomized control trials. So on the left hand side, you can see the details of the trial. So that's the citation, the trial registry number, and the study name. Then we have details of the population and the sample size. Then we have the intervention comparator and the outcomes of interest on the right hand side. So we identified three new randomized control trials published in searches in the most recent systematic review. The assessed trial in the first row compared two doses of all fingolimod with subcutaneous glatiramer acetate over a period of 12 months. However, the trial was stopped prematurely because of slow recruitment. The second trial is the relief trial. And this compares the use of subcutaneous interferon beta 1A administered in the morning with a subcutaneous interferon beta 1A administered in the evening over a period of 12 weeks. And then the third trial is a moving trial. And this compares the use of all fingolimod and subcutaneous interferon beta 1B for the treatment of acute optic neuritis over six months. Again, the trial was stopped prematurely because of slow recruitment. And the only publication we found reported preliminary results for 13. So that's 1-3 patients. So a very small sample size there from that prematurely stop trial. Moving on to the ongoing studies, we identified six ongoing studies. And that's two randomized control trials and four cohort studies that were completed in the last three years. The two randomized control trials are head to head comparisons. They're in adults with that relapsing remitting form of MS. And they compared peginterferon on beta 1a with interferon beta 1a or 1b. And on the next slide, you can see the details of those four cohort studies. So these all we're really focusing on homes And these, again, are large cohort

studies. And the sample sizes range from just over 2000 to 200,000 patients with MS. So we have the passage study that was really focusing on the safety fingolimod versus other disease modifying therapies. We have the EPID MS pregnancy study that's looking at the impact of interferon beta 1a, beta 1b, and the peginterferon against other disease modifying therapies in people who are pregnant. And then we have the PVSEPK study that's looking at MS treatment. I couldn't find any details of what that treatment was versus no treatment. And they're really looking at the impact of those therapies on cancer outcomes. And then we have DRUMS, which is looking at the harms of these therapies, specifically related to hospitalization, mortality, and adverse events. Moving now on to kind of FDA actions. In terms of new drugs and formulations, we identified three new drugs that have been approved by the USFDA since the publication of the report. Worthwhile noting that Ozanimod was included in a systematic review but we included it as one of those pipeline therapies. So one of the therapies that we knew was likely to be coming through, and it was actually approved during the writing of that report. So Ozanimod, brand name Zeposia was FDA approved in March 2020. And the approval was based on two randomized control trials comparing Ozanimod with interferon beta 1a. The trials were called [indistinct]. And both of those were included in that most recent systematic review, as I said, because we included that drug as a pipeline therapy. We have Ofatumumab or Kesimpta and that was FDA approved in August 2020. Again, the approval was based on two randomized controlled trials. And these compared Ofatumumab with teriflunomide. And also the Asclepios trials Asclepios one and Asclepios two. The third drug that has been approved since the publication of the most recent systematic review is Ponesimod, the brand name Ponvory and that was FDA approved in March of 2021. And the approval there was based on one randomized control trial, comparing Ponesimod with teriflunomide. And that's the optimum trial. And each of the three new drugs were approved for use in the treatment of the relapsing forms of MS. So that includes the clinically isolated syndrome, the relapsing remitting MS, an active secondary progressive MS in adults. So in terms of new drugs and formulations, on this next slide, you can see that in December 2020, the FDA approved a reduced infusion time for ocrelizumab, from three and a half hours every six months to two hours every six months. And in January of this year, the FDA approved the use of peginterferon beta one a via intramuscular injection, as well as the already existing approval of subcutaneous use. Moving on to new indications and harms. In October of 2020, the indications for alemtuzumab were revised to reflect more concerns about safety. So they limited the use to patients who already have had an

inadequate response to two or more drugs. And the reason that they've limited this use was because of concerns around its safety profile. And along with those concerns, they also recommended that alemtuzumab should not be used for people with that first attack, that clinically isolated syndrome, again because of those safety concerns. On the next slide, you can also see that the FDA also added a series of additional safety warnings to many other drugs in this disease modifying therapy group for MS, from alemtuzumab to teriflunomide. And details of those can be seen in this surveillance report. On the next slide I just wanted to highlight there were two new updated box warnings for alemtuzumab and for teriflunomide. Both of these occurred in 2020. And for alemtuzumab, they updated the box warning to reflect these fatal autoimmune conditions. And they recommended the need to monitor complete blood counts for people on alemtuzumab. And for teriflunomide there was a note about the risk for significant liver injury, including acute liver failure. Again, these were based on reports in the post marketing setting. So those were two new boxed warnings that were updated. And on the next slide, you can see again, some of those details of those serious harms from serious and life threatening infusion reactions with alemtuzumab. We have that hepatic injury with glatiramer acetate, and again, a series of warnings for the newly approved ocrelizumab, including again the risk of infection and liver injury. So in summary, moving on to the next slide, thank you, since the completion of the most recent DERP systematic review, we identified three new randomized control trials. So that's the assess trial comparing fingolimod and glatiramer acetate. We have the relief trial comparing that morning and evening administration of interferon beta 1a, and then the moving trial looking at fingolimod and interferon beta 1b for acute optic neuritis, and then those six ongoing studies, two head to head randomized controlled trials comparing peginterferon beta 1a with the interferon betas. And then four cohort studies comparing the harms of those different disease modifying therapies. And on the next slide, you can see that since the completion of the most recent systematic review, we have that one new indication so the restriction of the use of alemtuzumab, those new series of warnings and serious harms for the listed drugs. And then on the final slide, you can see the newly approved three drugs. So that's Ozanimod, Ofatumumab, and Ponesimod, as well as the addition of the intramuscular use of peginterferon beta 1a. Thank you.

Ginny Buccola: Thanks, Beth. Are there any questions for Beth from the committee?

Kavita Chawla: Kavita, here. I have a question. And this is more maybe about the protocol. So the RCTs that Beth shared, two of which actually had competitors. So like one had a head to head, the fingolimod versus the glatiramer. I see which metrics were measured and the outcomes but what were the outcomes? Do we review that during these DERP reviews?

Beth Shaw: The aim of the surveillance is really just to identify that the trial has been published. We don't go into the details. So we don't look at the results for this. So I've not looked at the results of the trials.

Ryan Pistoresi: This is Ryan. I can explain a little bit further. So, we do get different types of evidence reports from the drug effectiveness review project. And this one here is a surveillance document. These documents primarily serve the DERP states to help us understand whether a drug class is ready for a full update or not. And this was one that we decided that we wanted to bring the surveillance document to you because we wouldn't be getting a report for a while. And that way, we could continue to have some type of review for this class going forward, especially since we need to do these for the cost analyses. We are in the middle of our next report development period. So we are going to start getting some more reports through this upcoming year. And so we'll actually be bringing those types of reports which actually do go into the details of the randomized control trials and go into the primary and secondary outcomes and go into those measures. So for today's P&T meeting, unfortunately, the two documents that we have are both surveillance documents. And I think going forward, we'll start bringing some of the updated reports for other drug classes. That's the way it worked out for this meeting.

Kavita Chawla: So what are those other reports called, just for my reference and education, where they actually delve into the outcomes?

Ryan Pistoresi: I think evidence reports are the name and then we get updated reports once a class gets a re-review. And so they take the original report and then build off of that. Today was a surveillance document and actually scanned documents that some of our other P&T team members may be familiar with that term, that actually is being retired. And so these surveillance documents are what we'll have as scan-like documents wide forward. They are a little bit more robust and detailed than the scans were previously. You remember that those are just a couple of slides and that they just said, there are studies. Here, we're actually talking a little bit more about what's going on in the drug

class, which we, as states found more informative to help us understand what's out there and what should be reviewed. And hopefully, for you, as our P&T committee, to kind of understand what we're seeing and kind of what the landscape is for some of these drug classes.

Kavita Chawla: I see. So, the main purpose right now is just to see whether there are enough new published studies, not necessarily what the outcomes are, but if there are enough new published studies to review whether the drug class needs any changes on the formulary?

Ryan Pistoresi: This is Ryan. So these types of surveillance documents are actually created for the states in the spring for when we vote for which drug classes are to be updated, and to be commissioned into full reports. So I believe that these two were brought here today because they weren't voted to go forward. Or if they are voted to go forward, they're not going to be completed as a full report until maybe spring of 2022. So we wanted to make sure that we had some sort of information be presented between now and then. And different states use these reports for different purposes. And so for us, we bring these surveillance documents so that way we can have it be reviewed by you to see if there's any changes in how the class may be managed. And then we do the cost analyses following this, so that it may change, what is the preferred and non-preferred status of the drugs in these classes.

Leta Evaskus: And this is Leta. So today, we're actually going to have Umang next present MS in his review, so we're not going to do the motions until after you see his report as well. So you might get more information in that. And so we're going to have Umang present MS. And then we'll do the stakeholders. And then we'll come back to the P&T motion and then we'll do the DUR motion. So when we do have both reviews for P&T, as well as, DUR. So for uniform medical plan, Labor and Industry, and then for Medicaid, Apple Health, we try to do them back to back so you get as much information as you can before making the motions.

Kavita Chawla: Thank you.

Alex Park: Ryan, it's Alex Park here. Can I ask a follow up question to Kavita’s question?

Ryan Pistoresi: This is Ryan, you may.

Alex Park: Thank you. So are you saying that we are not doing literature scans anymore and we're switching to these surveillance reports?

Ryan Pistoresi: So this is right. And yes, so the scan documents really are being retired and these surveillance documents are taking their place. So we aren't necessarily scanning every single DERP drug class anymore. So we're not looking at like the macrolides or the beta blockers or the calcium channel blockers or some of those really, really old classes that we used to still get some scans for. Really, the way that DERP has kind of evolved is to instead of do a scan for every single drug class once a year, is to really focus in on the surveillance reports that have more meat to them and can really tell us as a state, is this really worth a full report now or should we hold off on a year. It generates more discussion between states. And so these types of surveillance documents are going to be kind of the replacement for the scan where we are able to see what's going on in that drug class. But there's not enough information in order for us to really consider whether new drugs should be added to the class, though you are welcome to change the motion so that way if there is something that you see as kind of a signal that you are free to do so. This is really when we get the evidence reports that have the actual outcomes and these comparative effectiveness studies. That is where we do see a lot of the motions be changed or updated to reflect the current body of evidence.

Alex Park: Thank you, Ryan. So my question is, with the scans, I think what we used to do is we used to, as a P&T committee, approve the scan is adequate. Or if it wasn't then we would go ahead and request a full updated class review. So is the motion today looking at the surveillance report to do the same thing as what we used to do with the scan? Or are you guys going to consider the surveillance report adequate to move toward a more traditional P&T committee motion in terms of safety and efficacy for therapy, interchange, and et cetera.

Ryan Pistoresi: So this is Ryan. I think these are not detailed enough that it would really warrant adding a new drug to a drug class. So when we have a new to market drug, we aren't diving into the outcomes and really doing that full clinical and safety review. And so we made the decision that when we do review these surveillance documents at a P and T meeting, it's going to be like the same role as a scan where it does count as a rereview of a class, but it doesn't necessarily allow for a new to market drug to be considered eligible to be preferred. And you certainly have the ability to make a recommendation to

us that you think that this is a drug class that warrants a full rereview and an updated report. And then we can take that back to the Center for evidence based policy and let them know, here is what our P&T recommended and here's what we would like to do. And we have done that in the past, I believe with the sedative hypnotics. There wasn't enough evidence in children. And the P&T committee actually said that the scan was not adequate for them at that time, and they directed us to commission a report on hypnotics for children. And I believe that we did come back. It was a slightly different report. But we were able to do something like that. I believe that was in 2017. I think we'd have to look and kind of confirm the exact history of how that process happened. But I do know that has happened in the past.

Alex Park: I see. So then the motion today, if I'm understanding you right, you're saying that were not so much voting on the scan being adequate -- well, we could. But it sounds like the intent from your end is that we vote on the drugs minus the new agents that Beth identified and that those would somehow be folded into a future report at a defined cadence?

Ryan Pistoresi: This is Ryan and yes, I think there are plans on updating the MS class. But I think that we're not going to get an updated report until spring of 2022. And so this is kind of a halfway point. And we may be bringing it in either June or August, so almost a year from now, just a little less than a year. And we would have that updated safety and efficacy information. I'd have to double check the actual report timeline to see what are all the reports that we're getting in the new DERP year that just started this this last July. But yeah, so today is really thinking, is the surveillance document adequate? If it isn't and you do have concerns that we really need to focus in on a separate area, like a sub population, or looking at any of these new drugs, if they're like really blockbusters that are going to be changing the standard of care for MS. Then we can take that back as the recommendation from our P&T committee.

Alex Park: Okay. And then just two last questions then I'll stop hassling you, I promise. Number one is, if we accept the surveillance report as adequate and do not request the next step review, will that report that you estimated for summer 2022, will that just come out on a natural cadence without us needing to request that? And then number 2, am I correct in understanding that I don't think this class is subject to therapeutic interchange, at least how we did the motion last time.

Ryan Pistoresi: Yeah, this was Ryan. Leta, can we pull up the motion just to double check that? I don't think we do have therapeutic interchange. Yeah, so the MS drugs cannot be subject to therapeutic interchange for the treatment of MS.

Alex Park: Okay. And is that other report that you mentioned going to come out in 2022 regardless of whether the committee today identifies the scan as adequate or not.

Ryan Pistoresi: Actually, I am kind of curious. So I'm going to try to log into the DERP clearing house and see if I can get the most recent report timeline and actually confirm that. Because I'm trying to remember why we decided that MS would be brought today and whether we were going to be getting it later on or if it actually was not voted to go forward. Hey, Ryan.

Curtis Harrod: Good morning, Ryan. This is Curtis Harrod. I'm with the Center for evidence based policy. I'm the research director on the DERP project. So what's going on right now for the group is that DERP is going to prioritize their topics in the next month or so for the next surveillance cycle. I envision MS, which is an active and interesting topic area will likely be prioritized But we don't know that as of today. So we would be able to inform through Ryan, you all, what gets prioritized and when MS would be rolled out. Probably in the next one to two months. A good guess would be probably summer to fall of next year that MS would be presented to DERP and then subsequently probably brought back to this committee.

Ryan Pistoresi: Great. Thank you, Curtis.

Nancy Lee: This is Nancy, I just have a quick question for Curtis and for Beth as well. Just looking at the surveillance of this information and you presented a lot of really good information about some of the long term safety things that are being pending or in the pipeline, based on your review and surveillance of the realm of the literature for MS, do you feel like you'll have enough information to present for that timeline that you perceive? We're kind of looking at a crystal ball to kind of guesstimate that some of these studies will be published by the time that you anticipate getting it done. So I guess I just wanted to see what your thoughts were, since you guys actually did the surveillance and kind of see what's in the pipeline on clinical trials.gov and all that.

Curtis Harrod: Beth, do you mind if I take this question?

Beth Shaw: No, that's fine.

Curtis Harrod: Okay, so I do want to clarify. So we've been doing surveillance for a few years now, switching from the scan method. And it's important because you're not missing anything versus the documents. So the surveillance document actually provides you more data and information than a scan would. So what I mean by that is you're not just getting the lay of the land or body count of the studies, you're also getting a list of ongoing studies. So you used to get just published with a scan, and now you get published and ongoing studies. And Nancy, that's to your question of what's in the future, what's that crystal ball look like? So pending additional COVID related peaks and valleys as we approach that and which can be leading to delays in study publication and process, we do envision that we'll have six ongoing studies that could be published in the next a year or two here. And so we have two RCTs and four cohort studies that we believe will be published in the next year is what we identified in this document. So that would be a good chunk of new evidence that would come and add on to the three comparative trials that we talked about today, one of which we think is pretty meaningful as far as a head to head that we didn't necessarily have a lot of information in the previous report. So, Nancy, just to summarize, because I went a little long winded there, but we think six more studies in the next 12 months would likely be published pending, obviously decisions made by the investigators.

Nancy Lee: Great, thank you that was exactly what I was looking for.

Beth Shaw: If you included those new drugs, there were another three randomized control trials that the approval was based on. So the new drugs added in, potentially those would be -- [audio dropout].

Nancy Lee: Great, thank you so much. Appreciate it.

Ginny Buccola: This is Ginny chiming in just to make sure there are no more questions. Okay, so we're doing a little pivot where we will adjourn the P&T committee meeting, but we will convene the DUR meeting and move to Umang to talk about the Multiple Sclerosis agents. And then as Leta lined out, we'll go to stakeholders and then do both the P&T motion and the DUR motion.

Umang Patel: Alright, so this is Umang with Magellan, is it okay for me to go ahead and start?

Ginny Buccola: Yes, please go ahead.

Umang Patel: Perfect. Thank you. And so just to remind the committee, normally for my clinical updates and presentations I tend to provide recent clinical updates and recent is defined as within the last roughly one year. So anything prior to that, such as older guidelines usually found in the appendix and/or in the TCRs that are in the SharePoint site that all the committee members have access to here. So we'll go ahead and get started. First slide, the first topic we'll be talking about is multiple sclerosis. And again, just to give a little bit of background information here again, MS is a complex human autoimmune type of inflammatory disease of the central nervous system. More than 2.3 million people worldwide have MS, one million being in the US. It occurs most commonly in Caucasians with rare cases in African American and Asian Americans. Although the etiology is predominantly unknown, it's characterized pathologically by demyelination and subsequent axonal degeneration. And so the nerve degeneration associated with MS can result in a wide variety of symptoms, which includes sensory disturbances like numbness, paraesthesia, burning pain in the limbs, optic nerve dysfunction, ataxia, fatigue, bladder, bowel, and sexual dysfunction. It may result in partial or complete paralysis. And while cognitive impairment occurs in approximately 50% of people with MS, only 10% experience serious intellectual deterioration. And MS can be categorized as either relapsing remitting, which is observed in the majority, about 85 to 90% of patients, or primary progressive, which is in about 10%. Relapses or attacks typically present sub-acutely with symptoms developing over hours to several days, persisting for several days to weeks, and then gradually disappearing. On the next slide here, the clinical course of MS falls into one of the following categories, with the potential to progress from less severe to more serious types. First being a clinical isolated syndrome. And the first episode of the neurological symptom due to inflammation or demyelination, lasting at least 24 hours. Patients with MRI detected brain lesions consistent with MS are at a high risk of developing MS. Next, we have relapse remitting. This is clearly defined self-limited attacks of neurological dysfunction, followed by periods of remission without disease progression. Most patients experience a recovery of function that is often but not always complete. And we have primary progressive, nearly continuous worsening of the disease not interrupted by distinct relapses. And some of these individuals have occasional plateaus and temporary minor improvements. And lastly, secondary progressive, and this is where relapsing remitting disease course

at onset, followed by progression with or without occasional relapses, minor remissions and plateaus, and most patients eventually convert to progressive. On the next slide here, you have updates in terms of medications updates, first being in September 2020. The FDA approved Kesimpta for a new indication and a new brand name to correspond with the new use. It's indicated for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing remitting disease and active secondary progressive disease in adults. In terms of limitations, first being infections, it's recommended to delay this medication in patients with active infections until the infection is resolved. Vaccination with live attenuated or live vaccines is not recommended. There's a fetal risk as well and may cause fetal harm based on animal data. It is recommended to advise females of potential risk to a fetus and the use of effective method of contraception during the treatment and for six months after treatment, discontinuation, or completion. The dosing here as you can see is 20 milligrams at week zero, one, and two with subsequent dosing monthly after that. And it's available in a single dose prefilled pen and syringe for injection. And no studies have been conducted in patients with hepatic or renal impairment yet. Next, we have Pegridy, where in February 2021, FDA approved an IM intramuscular route of administration in the corresponding prefilled syringe. Dosage is the same as the subcutaneous form. Again, just to remind the committee, when there are medications that have an update, I tend to bold the relevant, pertinent information here. No changes to the indication limitation as you can see where dosage. As I mentioned earlier, it was available in subcutaneous and still is and now there is an additional intramuscular administration available as well. On the next slide here in March 2021, FDA approved Ponvory, which is indicated for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease in adults. In terms of limitations, similar to previous medications, infections and liver injury. It is recommended to discontinue Ponvory if significant liver injury is confirmed and that's obtained by LFTs before initiating treatment. In terms of dosage, as you can see here, recommended dosage is, it's an oral tablet taken once daily. And the availability is in varying strength tablet forms here. In terms of pregnancy for this medication, it may cause fetal harm based on animal studies. Because it takes approximately one week to eliminate from the body, women of childbearing potential should use effective contraception to avoid pregnancy during and up to one week after stopping treatment. There is no dose adjustment necessary for patients with severe renal impairment. And as I mentioned earlier, there is hepatic impairment limitation corresponding

with the liver injury. I'll pause right there. That's the end of the clinical updates for MS and see if anyone has any questions.

Ginny Buccola: Thanks, Umang. This is Ginny. Just making sure that we've got time for more questions if needed. So if not, we'll move to stakeholders. I see two stakeholders listed. Linda Finch with Biogen and Kyle Downy with Genentech. If there are any other stakeholders that I didn't list, please go ahead and raise your hand so I know that you're there. And whenever you're unmuted, Linda, you'll have three minutes to present.

Linda Finch: Good morning. My name is Linda Finch. I'm a medical account director with Biogen and today I'm going to speak with you about Vumerity or diroximel fumarate. Vumerity was approved in October 2019 for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing remitting MS, and active secondary progressive MS in adults. Vumerity has a distinct chemical structure from that of Tecfidera or dimethyl fumarate, but it's converted to the same active metabolite monomethyl Fumarate. And because of this bioequivalence, we expect to see the same efficacy and safety as Tecfidera, which has now been prescribed in over 425,000 patients representing 810,000 patient years. There's 10 year data available from the long term study of Tecfidera that was recently reported with 73% of patients having zero or one relapse, and over 50% of patients had no relapses in 10 years. 64% of patients had no progression in disability in that 10 year time period. Vumerity has been studied for improved patient reported GI tolerability versus Tecfidera. There's two distinct Vumerity studies. They're called evolve MS one and evolve MS two. Evolve MS one is an ongoing 96 week open label, single arm phase three study assessing long term safety and tolerability as well as exploratory efficacy, familiarity in patients with relapsing MS. In a prespecified interim analysis, 30% of patients had a GI adverse event, but most were mild to moderate in intensity and less than 1% of patients discontinued due to GI adverse events. The evolve MS two study is a phase three randomized, active controlled head to head study that evaluated patient reported GI tolerability for humanity versus Tecfidera in relapsing MS patients. Patients treated with Vumerity experience a statistically significant improvement in a patient reported outcome measuring GI adverse event symptom intensity. Adverse events leading to study discontinuation were reported in 1.6% of Vumerity patients versus 6% in Tecfidera patients. The GI discontinuation rates were .8% for Vumerity versus 4.8% for Tecfidera. And recently published real world data has reinforced that patients are highly adherent to Vumerity consistent with

expectations based on clinical trials. The most common adverse reactions for dimethyl Fumarate, which has the same active metabolite as Vumerity is flushing, abdominal pain, diarrhea, and nausea. And Vumerity's warning cautions are the same as for dimethyl Fumarate. So I refer you to the full PI for this information. As you know, MS is a very heterogeneous disease. Patients with a progressive illness like this need to have access to appropriate medication as early in the disease as possible to prevent relapse and disability progression. And the oral DMTs are very different medications, different MOAs, different tolerability profiles, monitoring requirements, drug interactions, and contraindications. And all of these factors into appropriate drug selection. So in conclusion, I respectfully ask that you consider adding Vumerity to your PDL today and thank you for your time. I'm happy to answer any questions that you have on Vumerity.

Ginny Buccola: Thank you, Linda. This is Ginny. Any questions for Linda from the committee? We'll go next to Kyle Downey with Genentech.

Kyle Downy: Good morning, Washington State P&T committee. My name is Kyle Downey. I'm our medical affairs Executive Director for Genentech here in the state of Washington and here to talk to you about Ocrevus. Again, I refer the committee to our safety and efficacy information to our USPI and really going to point out some salient points around the use of Ocrevus. Ocrevus is indicated for the treatment of adults in both relapsing forms of multiple sclerosis, including clinically isolated syndrome, RMS as well as active secondary degrees, as well as primary progressive forms of multiple sclerosis. PPMS for the treatment, Ocrevus was the first and only disease modifying agents to be approved by the FDA, as well as Ocrevus is indicated for RMS treatment options in both treatment naive as well as treatment experienced patients with the vast majority of patients about 70% in our clinical trials being treatment naive entering into our opera one and two studies. In an open label extension trial of those one and two studies, patients actually received Ocrevus in an open label extension or continued treatment. And what we saw was from the transition from subcutaneous interferon beta 1a that we saw reduction in annualized relapse rates as well as continuation for those patients that stayed on Ocrevus out to the treatment of 6.5 years. Next, we actually have some real world data on persistence and adherence, where a US claims analysis was done ending in 2019, where we saw persistence was higher for the Ocrevus treatment groups compared to other heavy agents, oral agents, as well as injectable agents as well as adherence was higher in the Ocrevus group at 80% compared to other IV agents at 54%,

oral agents at 55%, as well as injectable agents at 35%. In addition, those DMT agents were associated with lower overall total cost of care and non-adherence reduce the cost of treatment in patient populations by roughly $19,000 overall in total healthcare costs. Again, four warnings and precautions as well as contraindications, I will refer the committee to our SPI. And with the information I presented today, I would respectfully ask for the Washington State P&T to continue to have Ocrevus on the Washington State PDL and remove any first line restrictions that would be encompassing patients' treatment for both PPMS and RMS patient population. Thank you, and I'll open it up to the committee for any questions.

Ginny Buccola: This is Ginny. Thank you very much. Any questions from the committee? And are there any stakeholders that were missed?

Leta Evaskus: Yes, we have Sara Hovland.

Ginny Buccola: Thank you.

Sara Hovland: Good morning. My name is Sara Hovland and I'm a pharmacist and health economist currently in the health economics and outcomes research department at Bristol Myers Squibb. Today I will be presenting Zeposia or ozanimod, which is a once daily oral sphingosine one phosphate receptor modulator that was recently approved in the US in March 2020 for the treatment of relapsing forms of MS, including clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease in adults. Zeposia was studied and two active controlled registrational phase three trials that Beth Shaw mentioned earlier that demonstrated its efficacy and safety against avionics. And recently data from an open label extension of four parent studies which included a phase one study, phase two and three radiant studies, and the sunbeam studies was published. It evaluated the long term safety and tolerability of Zeposia and safety findings were generally consistent with the phase three parent studies. And the efficacy results in the open label extension with respect to ARR T2 lesions, gadolinium enhancing lesions were consistent with the results from the parent studies. Two additional matching adjusted indirect comparison analyses were conducted comparing Zeposia versus Abajo and Zeposia versus Tecfidera. This study compared key one year safety and efficacy outcomes between Zeposia versus Abajo and Zeposia versus Tecfidera. It adjusted for cross trial differences in patient data from their pivotal clinical trials. For key safety outcomes, Zeposia had statistically significant lower rates for overall AEs and

discontinuations due to AEs versus both Abajo and Tecfidera. For key efficacy outcomes, Zeposia had statistically significant lower rates for annualized relapses, and proportion of patients relapse versus both Abajo and Tecfidera. Additional endpoints and safety information are reported in the corresponding peer reviewed publications and also in the USPI. So based on the clinical evidence I just described, we appreciate that Zeposia has been on the PDL, and respectfully request that Zeposia remain on the PDL in accordance with the FDA approved label. I appreciate your time and thank you for the opportunity to speak today. I can take any questions.

Ginny Buccola: Thank you, Sara. Any questions? And Leta, do we have any other stakeholders?

Leta Evaskus: I do not see any other hands raised.

Ginny Buccola: Okay. So it looks like we're going to see the P&T motion first.

Leah Marcotte: I did have one question.

Ginny Buccola: Go ahead, Leah.

Leah Marcotte: Leta had sent out a stakeholder notice from the National Multiple Sclerosis Society. And they had brought forth a few recommendations. And I just wanted to understand particularly the recommendation for talks about the need for switching MS medications due to the COVID-19 vaccine. And I don't know how that's being -- I would like to understand a little bit about how that might be playing out in practice based on the current guidelines. This may be out of scope of our current motion, which is okay and we can table it. But I just thought that was an interesting recommendation. Just wanted to check in.

Ryan Pistoresi: So good morning, this is Ryan. So I would say that that sounds more like a clinical policy. Not so much like on the preferred status of drugs, like what the scope of this motion is. I think that that may be handled more kind of on an individual patient basis on how these clinical policies are developed. And I don't have any examples that I can provide off the off the top of my head right now, but I would say that that's likely outside the scope of what this motion is.

Leah Marcotte: Thanks, Ryan. Is that being reviewed at all at HCA in terms of the need for switching our medications like this for in the setting of the pandemic?

Ryan Pistoresi: So this is Ryan again and I have not heard anything from our third party administer for UMP, that's MODA Health on any issues with this. So to my knowledge, no, I haven't seen anything come up.

Leah Marcotte: Okay, thank you.

Ginny Buccola: This is Ginny. Leta, I can see maybe you're just scrolling down the motion for us.

Leta Evaskus: Oh, yeah. I'm sorry. I was letting you read the previous one. Can you see my screen? Can you see the motion? Okay.

Ginny Buccola: Yes, yes, I can see it and my apologies. I think all that was cut off was the top bar.

Kavita Chawla: Kavita here. I might be missing it because there are a lot of drug names here. But the slides that both Beth and Umang presented contained three new FDA approved drugs. And I only see one of them in here. So basically the ones that I don’t see are the Ponesimod or the Ofatumumab.

Leta Evaskus: So those are grayed out. Let me open this back up so you can see the footer. So those are grayed out, which means that they are not reviewed by OHSU and so they're not eligible to be preferred. So there's the two grayed out new drugs.

Kavita Chawla: And what does that mean that they were not reviewed by OSHU?

Ryan Pistoresi: So this is this is Ryan. So this is kind of our way of making sure that the P&T committee is able to review the outcomes, the safety and efficacy of the actual trials before a drug can be considered for preferred status on the Washington PDL. So even though it was included in today's surveillance document, it didn't have the level of evidence necessary for the P&T committee to make a recommendation on its safety and efficacy relative to the other drugs in this class or whether therapeutic interchange or any other types of considerations should be considered when evaluating it for the preferred drug list. So even though it's not today, it would be included in the updated report that Curtis mentioned that we'll get in 2022. So we would be

able to reevaluate it then and it would be eligible to be considered preferred or not on the Washington preferred drug list.

Leta Evaskus: This is Leta. I'll scroll back down. I'm going to close this footer so you could see the whole past motion together.

Kavita Chawla: Hey, Ryan, sorry, I'm just getting my clarifications here. Kavita again. So I'm sorry, I'm going to use a brand name here. The Kesimpta on the PDL excel sheet that was sent out. If I'm reading it correctly, it is listed as a preferred drug.

Leta Evaskus: This is Leta. So as the P&T motion, as the P&T committee, you are making selections for the Washington PDL, which applies to uniform medical plan and Labor and Industry. After this motion, you'll do the Apple Health motion, which corresponds with the Excel sheet that I sent you.

Alex Park: Ryan, It's Alex here. I'm glad that Leah brought up the stakeholder letter and I guess we don't necessarily have that stakeholder here with us in person. But they were recommending that the three new drugs, one of which I guess is already going to be included. It's not grayed out, but the other two drugs are grayed out. And so we know that that means can't be preferred. But can we confirm that there is a mechanism in some policy at HCA for those drugs to be used at this point if it's clinically indicated?

Ryan Pistoresi: This is Ryan and yes, even if a drug is grayed out, it still has a pathway to coverage through our health plan. So if it were medically necessary and they met the criteria for that, they certainly could take it even if it were a nonpreferred drug. So as I mentioned I haven't checked our clinical policy or checked with our third party administrator about this issue, but I understand that if a clinician were to have those concerns and request it and can demonstrate that it did meet that policy and was medically necessary that they would be able to receive it.

Alex Park: Okay, thank you. So Leta, shall we copy and paste the verbiage from October 2020 into the above?

Leta Evaskus: So last year this drug was just left out, or these two drugs, so they were added back in. So I don't need to copy and paste that part. All the drugs are listed in here now.

Alex Park: Great. And can we add the grayed out drugs or are we not allowed to do that because they were not included in the review?

Leta Evaskus: Yeah, we cannot add those.

Alex Park: You can't put those in. Okay. So then Ryan, so if we can't include those two new drugs in the motion, we as the committee are saying they're not considered safe and efficacious. But you're saying clinically, there is a pathway for approval in light of some of the clinical situations mentioned in the letter that was sent to the committee by the stakeholder.

Ryan Pistoresi: So this is Ryan and I wouldn't say that if you were to not include those drugs, that wouldn't be saying that they aren't safe and efficacious. I would say that it just means that you haven't had the opportunity to review that body of evidence in light of everything else for the class. And really the motion here is trying to say, here are the drugs that can be considered for preferred status or that can have therapeutic interchange or have these similar characteristics. And until we get that full evidence report, we don't allow these drugs to be eligible to be preferred. Now, there still is a mechanism for coverage, it's just that they can't be one of the preferred drugs.

Alex Park: Got it. Okay. And that review is coming in 2022, you said.

Ryan Pistoresi: Yes, it sounds like we will be getting this. And from the sound of this discussion, when we have conference next week, I can emphasize that it sounds like our P&T committee would like to prioritize this review and hopefully we can get it commissioned sooner rather than later.

Nancy Lee: This is Nancy. I'm going to do my best with the pronunciations for this drug class of meds. After considering the evidence of safety, efficacy, and special populations for the treatment of multiple sclerosis, I move that alemtuzumab, cladribine, diroximel fumarate, Siponimod, daclizumab, HYP, mitoxantrone, natalizumab, dimethyl fumarate, teriflunomide, fingolimod, glatiramer, ocrelizumab, monomethyl fumarate, ozanimod, interferon beta 1B SC, peginterferon beta 1A SC, interferon beta 1A IM, and interferon beta 1A SC are safe and efficacious. A product that is safe for use during pregnancy should be made available. The MS drugs cannot be subject to therapeutic interchange in the Washington preferred drug list for the treatment of multiple sclerosis. An oral agent should be included in the list of preferred drugs on the PDL.

Alex Park: This is Alex Park congratulating Nancy on the pronunciations and seconding that motion.

Ginny Buccola: This is Ginny Buccola, committee chair, all those in favor, please say aye.

All: Aye.

Ginny Buccola: Are there any opposed? The motion carries and Nancy gets a gold star. And now I'll look at the DUR motion.

Kavita Chawla: I move that all products in the Multiple Sclerosis agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All nonpreferred products require a trial of at least two preferred products with the same indication before a nonpreferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Alex Park: This is Alex Park. I second that motion.

Ginny Buccola: This is Ginny Buccola, committee chair. All those in favor, please say aye.

All: Aye.

Ginny Buccola: Are there any opposed? This motion carries. That brings us to a break. Leta, do you have? I have 10:43 on my clock.

Leta Evaskus: Yes. So let's just take a 10 minute break so we can come back at, let's just make it a round number and say 10:55.

[break]

Ginny Buccola: Hello, everybody. Welcome back. This is Ginny, committee chair. We are going to move right into antihyperlipidemic and Umang will be presenting for us.

Umang Patel: Okay, so the next topic we'll be going over is the lipotropics, other. Just to remind the committee, sometimes Washington State's PDL has different sub

categories than Magellan's. And so they usually tend to do, the top line, Lipotropics, Other is what the Magellan has it categorized as the antihyperlipidemic MTP inhibitors and PCSK-9 inhibitors are the subgroups that the Apple Health PDL breaks them down into. So on the next slide here, again, we'll just do a little bit of background. The National Health and Nutrition Examination Survey reported that in 2015 to 2018, approximately 11% of adults have high total cholesterol defined as greater than or equal to 240 milligrams per deciliter and 18.4% had low HDL, which is defined as less than 40. There are higher prevalence in women compared to men, 12% versus 10. Many clinical trials have demonstrated that a high serum concentration of LDL and low levels of HDL are major risk factors for coronary heart disease. On the next slide here, there were some updates in terms of clinical guidelines. And I just wanted to kind of give a high level summary. First one being the American Association of clinical endocrinologists in American college of endocrinology 2020. Although CV outcome trials with colesevelam or bempedoic acid are not published, outcome trials with [indistinct] and ezetimibe or PCSK-9 inhibitor suggests further reduction in LDL, though any combination of drugs would provide ASCVD benefits. Thereby, the algorithm advocates for progression of therapy intensity in order to reach LDL targets. The 2019 approval of icosapent ethyl marked the first FDA approval for medication that lowers triglycerides and reduces ASCVD as reduced at trial used for approval showed a triglyceride decrease of 18%. The 2020 algorithm states that CB outcome benefit does not appear to be related to the reduction of triglycerides. For patients with hypertriglyceridemia who do not have established ASCVD or diabetes with two or more risk factors of are not at the triglyceride goal of less than 150 with statin therapy then a fibrate, omega-3 fatty acid, or niacin can be considered. In order to decrease the potential for acute pancreatitis, all patients with severe hypertriglyceridemia, which is defined as greater than 500 milligrams per deciliter, should receive a fibrate prescription grade omega three fatty acid and/or niacin. According to the American College of Cardiology in 2021, they published an expert consensus decision pathway for the management of ASCVD risk reduction in patients with persistent hypertriglyceridemia. This is defined as triglyceride levels greater than or equal to 175 milligrams per deciliter after a minimum of four to 12 weeks of lifestyle intervention, a stable dose of maximally tolerated statins when indicated in management of secondary causes. The guidelines emphasize the necessary lifestyle interventions for hypertriglyceridemia and recommended low fat diet and consideration of fibrates and prescription grade omega three fatty acids. They also note that fibrates provide benefit as monotherapy but

not when combined with status. The next slide here in February 2021, the FDA approved Evkeeza as an adjunct to other LDL lowering treatments for adults and pediatric patients 12 years of age or older with homozygous familial hypercholesterolemia. As you can see, there are some limitations for the use. The safety net efficacy have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia. And the effects on cardiovascular morbidity and mortality have not been determined yet. There is a warning precaution for embryo fetal toxicity based on animal studies. It is recommended to advise patients who may become pregnant of the risk to the fetus to consider obtaining the pregnancy test prior to initiating treatment and to advise patients to use effective contraception during treatment and at least five months following the last dose. The dosage as you can see here is weight-based. It's 15 minutes per kilograms, administered the IV infusion once monthly. And it is available in an injection formulation in various strengths here in single dose vials. On the next slide here, we have Praluent where in April 2021, FDA approved a new indication as an adjunct to other LDL lowering therapies in adult patients with homozygous familial hypercholesterolemia to reduce LDL. Again, no additional changes to the indications of dosage for this new indication. It is recommended to be taken 150 milligrams once every two weeks subcutaneously. There were no other changes in formulations here. In terms of other populations for this medication, safety and efficacy has not been established in pediatric patients. There's no dosage adjustment necessary for mild or moderate renal impairment or mild or moderate hepatic impairment. And there is limited data for patients who have severe renal or severe hepatic impairment. I'll go ahead and pause there for the committee.

Ginny Buccola: Thanks Umang. This is Ginny. Any questions from the committee? Okay, we have two stakeholders that I see, Akima Harrigan with Regeneron and Ben Droese with Amgen, If there are any other stakeholders that didn't hear their name called please just raise your hand so that we know you're here. Akima when you're able to be unmuted, you'll have three minutes to present.

Akima Harrigan: Good afternoon. My name is Akima Harrigan with field medical affairs at Regeneron. Evkeeza is for patients with homozygous familial hypercholesterolemia. HOFH is an ultrarare genetic disease of lipid metabolism. Untreated, LDL levels are severely elevated, often greater than 400 milligrams per deciliter, and this is from birth. We estimate the US prevalence is approximately one in 250,000 people and there's several genes

that are involved in the LDL receptor mediated pathway of cholesterol removal from the blood. HOFH patients have inherited mutations in one or more of these genes. This often results in significantly or completely dysfunctional LDL receptors. And that's why there's diminished efficacy from agents that rely on this pathway. Evkeeza, however, lowers LDLC independent of the LDL receptor pathway. Instead, it targets angiopoietin-like 3 protein or ANGPTL3. By inhibiting ANGPTL3, the production of VLDL remnants is increased and then rapidly cleared by the liver through remnant receptors. This all happens upstream of LDL production. So what you get is a shift away from the LDL receptor pathway, little LDL is produced, and serum LDL-C is lowered. This new mechanism is important because many of the available agents that do work through the LDL receptor can have diminished efficacy in these patients. In Ellipse, the pivotal phase three clinical trial that was published in the New England Journal of Medicine, Evkeeza 50 milligrams per kilogram given by IV infusion once a month, produce decrease LDL-C of about 49% versus placebo from baseline to 24 weeks and even out to 48 weeks. And this was on top of other background lipid lowering therapies including statins PCS k-9 inhibitors Ezetimibe and the like. Irrespective of genotype, phenotype, whether they had low or no LDL receptor activity, or whether or not they were on [indistinct], the effect was the same. Overall, it was well tolerated with very few patients discontinuing due to adverse events across a clinical trial program. Common AEs include the common cold, flu-like illness, dizziness, runny nose, and nausea. Infusions can be given at an institution, at an IV infusion center, or at home. The indications were previously read to us and I respectfully ask the committee to make it available for these difficult to treat patients. Thank you.

Ginny Buccola: Thank you, Akima. Are there any questions from the committee? Okay, our next stakeholder is Ben Droese, I believe, with Amgen. Go ahead, Ben, you'll have three minutes.

Ben Droese: Great. Thank you. So this is Ben Droese. I am a pharmacist with Amgen medical affairs. Thank you for the opportunity to provide clinical comments for Repatha or evolocumab. Please refer to the full Repatha PI for product details which is available online or can be provided upon request. As a reminder, Repatha is indicated to reduce MI stroke and coronary revascularization in patients with established cardiovascular disease as well as indicated for LDL reduction in patients with primary hyperlipidemia or homozygous FH. Also importantly, in September of 2021, the Repatha label was updated with a new indication to reduce LDL in pediatric patients with

heterozygous FH, age 10 years and older. In addition, the indication for homozygous FH was also updated to include pediatric patients aged 10 years and older. These updates are based on data from the Hauser study described in Section 14 of the PI. Importantly, this safety profile in pediatric patients was generally consistent with the adult population. Of note, Repatha is the only PCSK-9 inhibitor approved for pediatric patients with FH. Two additional studies that were recently published and are also unique to Repatha within the PCSK-9 class include a long term open label extension study that included about 1200 patients treated with Repatha for up to five years. Key results demonstrated consistent mean LDL reduction of about 56% over each of the five years of follow-up. In addition, no new safety signals were observed over five years, with a low rate of discontinuation due to adverse events of 1.4% per year. The second study included 451 patients with hyperlipidemia and HIV called the [indistinct]. This study included a 24 week randomized placebo controlled phase followed by an open label phase through 52 weeks. Key results included sustained 58% LDL reduction with Repatha as well as no new safety signals. These results are notable given potential challenges with first line statin therapy in patients with HIV, which is reflected by about 20% of patients in the trial, not on statin due to intolerance or contraindication. Overall, real world evidence has demonstrated considerable unmet need with regard to achievement of guideline recommended lipid targets even in those receiving statin treatment. Repatha has demonstrated CV risk reduction in appropriate high risk patients. And based on the unmet need and supporting data, I respectfully request of the committee consider reinstating Repatha on the PDL. Thank you for your time and I welcome any questions.

Ginny Buccola: Thank you, Ben. Are there any questions, committee members? Okay. Leta, if you could move us to the motion.

Leta Evaskus: Yes, I do not see any other hands raised.

Ginny Buccola: Great. Thanks.

Alex Park: This is Alex Park. So we are only voting on the two antihyperlipidemic classes listed on the prior slide. Is that right? Because I saw many other classes in the TCR that Umang sent out.

Leta Evaskus: This is Leta. Marissa is not at this meeting today. So I don't know if Ryan or Ryan could answer that.

Ryan Pistoresi: So this is Ryan Pistoresi. I believe that what you have here is just these two classes. But I can see if I can get any clarification on that. Yeah, I believe it's just those two because those are the only ones that we have the slides ready for.

Alex Park: Okay.

Ryan Pistoresi: Yeah, and I just got confirmation. So yeah, it's just those two. So each of the drugs that have slides prepared today are the ones that the motions were prepared for.

Alex Park: Okay.

Kavita Chawla: So that's to say that Evkeeza is not one of the drug classes we're reviewing today? Because that looks like it's a different receptor inhibitor, right? ANGPTL3?

Ryan Pistoresi: Yeah, I believe so.

Kavita Chawla: So is that something we will be approving in the future or is that a different meeting?

Ryan Pistoresi: So this is Ryan. I believe that we will see it in the future. I'm not sure if it will have a clinical policy attached with it. I'd have to check with Marissa kind of when that was planned for review.

Alex Park: This is Alex Park. So Umang, the only drug I know of in that other class that's on slide four is [indistinct]. Is there anything that the committee needs to know about that drug before we go to the motion?

Umang Patel: Nope. I mean, nothing significant. Nothing potentially different within at least the last two years, so no. And you are correct that that is the only one in that class.

Alex Park: Okay. I move that all products in the drug classes listed on slide four are considered safe and efficacious for the medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least 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.

Nancy Lee: I second that motion.

Ginny Buccola: And this is Ginny, committee chair. All those in favor, please say aye.

All: Aye.

Ginny Buccola: Are there any opposed? And the motion carries. And we'll move to antivirals for the influenza agents.

Umang Patel: So the next the next class we'll have here are antivirals. I apologize. Leta, there's a question in the chat here and I wasn't sure how, since it's regarding the previous class, I didn't know if we needed to address it now.

Leta Evaskus: This is Leta. Yeah, go ahead. Thank you.

Umang Patel: Okay, so the question is from a Akima Harrigan that states, is there any opportunity to modify the class name of Evkeeza. There is not yet classification for it. That's why. This probably would be a question I would need to kind of pass over possibly to Ryan. I know that the subclasses on the Apple Health PDL are different, as I stated, than Magellan's. So I'm not sure if there's discussions on creating a different class name for Evkeeza. So Ryan, if I pass this over to you?

Ryan Pistoresi: So this is Ryan. And as far as I know, if it wasn't up for review on the slide motion, then it may be created in a separate class and have a separate policy attached to it. Again, I'd have to check with Marissa on what the plan was for that.

Umang Patel: Perfect, okay. So we'll go right on forward to antiviral oral. Just a little bit of background here, common illness is affecting most people at least once in their lifetime. It's uncomplicated illness, typically resolves after three to seven days, often self-limiting. Persons at higher risk for influenza complications are, again, there's a litany, just to read off a few, patients less than two years of age or greater than or equal to 65 years old, immunocompromised patients, patients who are pregnant or postpartum patients, and so on and so forth. Influenza vaccination is a primary method

for preventing influenza. Inactivated influenza vaccines are available in quadrivalent and trivalent formulations, while recombinant influenza vaccine and live attenuated influenza vaccine for are available in quadrivalent formulations. There's also a high dose of inactivated influenza vaccine and adjuvanted inactivated influenza vaccine available in trivalent formulation. For the 2020-2021 season, inactivated influenza vaccines, recombinant influenza vaccines, and live attenuated influenza vaccines are available. The virus strains include - and these are extremely long, so I'm not going to fumble over these and make the committee to try to listen to me list all these off - but as you can see, there are numerous various virus strains included in this last 2020-2021 cycle. And there are also cell culture based inactivated and recombinant influenza vaccines, which contain and then the following strains listed as well. On the next slide here, in 2020, the CDC stated there are three FDA approved neuraminidase inhibitor antiviral drugs recommended. There's Tamiflu, Relenza, and Rapivab. The fourth recommended FDA approved product is a cap dependent endonuclease inhibitor, which is Xofluza. Amantadines, such as amantadine and rimantadine are not recommended for use in the US due to resistance to these drugs by many influenza a and influenza B viruses. Empiric antiviral treatment without waiting for a laboratory confirmation is recommended as early as possible for any patients with confirmed or suspected influenza who have severe, complicated, or progressive illness, is hospitalized, or is at high risk for influenza complications. In addition, empiric antiviral treatment of nonhigh risk outpatients with suspected influenza can be started based on clinical judgment without an office visit. According to the CDC, oseltamivir is the recommended antiviral for patients with severe complicated or progressive illness or who are hospitalized. There's insufficient data for Relenza, Rapivab, or Xofluza in patients with severe illness and coinfection with influenza A or B with SARS-CoV-2 can occur and should be considered particularly in hospitalized patients with severe respiratory disease. On the next slide here, moving over to Xofluza, in December 2020, FDA approved an expanded indication for Xofluza tablets to include post exposure prophylaxis of influenza in adult and pediatric patients 12 years of age or older. Additionally, that same time, the FDA also approved a new formulation, which is a 40 milligram per 20 milliliter oral suspension for constitution to a final concentration of two milligrams per milliliter. Again, no additional changes to warnings and precautions. Dosing is weight based and indication based now as well, due to the additional indication. And the only update in terms of availability was the oral suspension there. Keep in mind Xofluza already had an approved indication for treatment of uncomplicated acute

influenza in patients 12 years of age or older who have been symptomatic for no more than 48 hours. On the next slide here for Rapivab, in February of 2021, FDA approved an expanded indication for the treatment of acute uncomplicated influenza in patients six months of age or older - previously, it was limited to two years of age or older - and who had been symptomatic for two days or less. Again, no changes otherwise to warnings, precautions, dosing, or availability. It is now the indication has been expanded just to patient six months of age. I'm going to pause right there. There's no additional update for this class. And I'll go ahead and pause for any questions from the committee.

Ginny Buccola: Thanks, Umang. Any questions from the committee?

Kavita Chawla: Again, not sure if it's in the scope of this particular review but do we understand any positives or any benefits that [indistinct] have over Oseltamivir? Were there any head to head trials or any benefits that your agents have over the oseltamivir?

Umang Patel: So you were asking if there were any head to head studies between Rapivab and which medications?

Kavita Chawla: So there are two [indistinct]. There's an Armavir and a peramivir, which [indistinct]. Do we know if they offer and additional benefit to oseltamivir, what has already existed long term?

Umang Patel: No. I mean, the indications are very similar. The only difference is some of these medications have different age restrictions. And so Tamiflu is indicated for patients two weeks of age and older. And so it has the broadest age indication out of the other medications. Relenza, which you were mentioning is only seven years of age or older. And prophylaxis is limited to five years. Short story, Tamiflu has a wider range of coverage for prophylaxis and treatment compared to the other two. In terms of head to head studies, we usually put the PubMed, head to head studies at the end of the TCRs. I don't see specifically head to head for those, but I can look into that as well.

Kavita Chawla: And similar question about Xofluza, whether that has any superiority over oseltamivir for any indication or any illness severity.

Umang Patel: The only specific thing that Xofluza has that is unique that I mentioned is now a post exposure prophylaxis indication where I don't believe the other agents in this class currently have that indication.

Kavita Chawla: Oh, I thought it oseltamivir had that indication. Or maybe that's an off label use.

Umang Patel: I can check if that's an off label if you give me one second, but from what I see FDA approved indication isn't -- yeah. In terms of FDA approved indications, I only see prophylaxis as a treatment for Tamiflu.

Ginny Buccola: Any other questions before we look at the motion?

Leta Evaskus: This is Leta. I do not see any hands raised for stakeholders.

Ginny Buccola: Thank you for checking.

Susan Flatebo: This is Susan Flatebo. I move that all products in the Influenza Agents drug class are considered safe and efficacious for the medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least two preferred products of the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Michael Corsilles: This is Michael Corsilles. I second the motion.

Ginny Buccola: This is Ginny Buccola, committee chair. All those in favor, please say aye.

All: Aye.

Ginny Buccola: Are there any opposed? The motion carries. And we'll go to cardiovascular agents, the sinus node inhibitors. Back to Umang.

Umang Patel: Well, this will be a very quick one because there are no significant clinical updates for this class. I will pause right there.

Ginny Buccola: Perfect. Thank you. But still, any questions? I don't see stakeholders listed and so Leta, please let me know if there's any that I'm missing.

Leta Evaskus: I do not see any hands raised.

Ginny Buccola: Okay. Yeah, so let's look at the motion.

Diane Schwilke: This is Diane Schwilke. I moved at all products in the cardiovascular agents sinus node inhibitor drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least two preferred products with the same indication before non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Catherine Brown: Catherine Brown, I second.

Ginny Buccola: This is Ginny Buccola. All those in favor please say aye.

All: Aye.

Ginny Buccola: Are there any opposed? And this this motion carries. And next up is pituitary suppressive agents LHRH. And that goes to Umang.

Umang Patel: So the next class will have our pituitary LHRH pituitary suppressive agents. In the Apple Health PDL, this is broken down into endocrine and metabolic agents, specifically pituitary and suppressants and oncology agents, which are LHRH analogs, specifically injectable forms. Just so the committee knows, if you were to look at the TCRs that we provide in the SharePoint for this specific class, there's a wide range of disease states that kind of fall into here. I only am going over the disease states that correspond to the new clinical information. I'm not reviewing any of the other disease states that have no new clinical information and no new meds or no new guideline updates just out of respect for the committee's time. So focusing specifically on prostate cancer, from 2013 to 2017, the median age of diagnosis of prostate cancer in the US are 66 years. The estimated number of new cases in the US is 191,000, with estimated deaths at about 33,000. Treatment options depend on several factors, such as the patient's assigned risk group at the time of initial diagnosis, the patient's projected survival based on age and comorbidities, and the benefit and potential side effects of treatment. Treatment options consist of active surveillance, radiation therapy, hormonal therapy,

chemotherapy, or a combination of two or more of these. Active surveillance, which is also referred to as watchful waiting is the monitoring of cancer progression before initiating treatment. Radiation therapy uses high powered energy to kill cells. Hormone therapy, also called androgen deprivation therapy is the mainstay of treatment for metastatic prostate cancer. It lowers androgen, which is testosterone and dihydrotestosterone levels, which cause a prostate tumor to shrink or grow more slowly. Luteinizing hormone releasing hormone, LHRH agonist prevents signaling of the testicles to make testosterone, therefore decreasing circulating testosterone levels. This class of drugs includes GNRH agonists such as Eligard, Lupron Depot, Zoladex, Trelstar, and Vantas along with Firmagon as well. Anti-androgen such as Casodex, flutamide and Nilandron are given in conjunction with LHRH agonists as these prevent testosterone from reaching the cancer cell. Chemotherapy treatment is used to kill rapidly growing cancer cells. And surgery involves the removal of the prostate gland which is a radical prostatectomy, some surrounding tissues, and a few lymph nodes. On the next slide here in terms of clinical updates, we have Camcevi. So in May 2021, the FDA approved this medication which is a GNRH agonist for the treatment of adult patients with advanced prostate cancer. In terms of warnings and precautions, there can be tumor flare, which is transient worsening of bone pain, ureteral obstruction, spinal cord compression, or the occurrence of additional signs and symptoms of prostate cancer which may develop during the first few weeks of treatment. It is recommended to monitor the patients closely and manage symptoms. Hyperglycemia and diabetes, which go hand in hand, so it is recommended to monitor blood glucose levels. Cardiovascular disease, there is an increased risk of an MI, sudden cardiac death, and stroke has been reported men receiving GNRH agonists. Monitor for cardiovascular disease and manage accordingly. And embryo fetal toxicity, it can cause fetal harm as well. Recommended dosage, 42 milligrams sub Q every six months and it is available in an injectable emulsion. In terms of other populations, safety and efficacy has not been established in pediatric patients nor in patients with hepatic impairment here. For this specific class, that is the end right there. I'll pause there for any questions from the committee.

Ginny Buccola: Thanks, Umang. Any questions at all? I see us one stakeholder. I see Margaret Olmon with AbbVie. And if there are any other stakeholders, please make sure your hand is raised so that we know you're here. And Margaret when you're ready you'll have three minutes.

Margaret Olmon: I'm Dr. Margaret Omen with medical affairs at AbbVie. As you know, AbbVie has two newer medications to treat women's health issues were listed to treat the pain of endometriosis and also Oriahnn, an oral treatment specifically approved for heavy menstrual bleeding associated with uterine fibroids in premenopausal women. I would be happy to provide any updates that you need with regard to these two medications and answer any questions. If there aren't any, I'd be happy to give my time back to the committee.

Ginny Buccola: Thanks Maggie. This is Ginny. Are there any questions? So we're ready to look at the motion for these oncology agents, pituitary suppressive agents.

Leta Evaskus: This is Leta. Just for the record, I do not see any other stakeholders.

Ginny Buccola: Thank you.

Leah Marcotte: This is Leah Marcotte. I move that all products in the drug classes listed on slide 11 are considered safe and efficacious for the medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Jordan Storhaug: This is Jordan Storhaug. I second.

Ginny Buccola: All those in favor please say aye.

All: Aye.

Ginny Buccola: Any opposed? And the motion carries. And our next topic is GI agents. Back to Umang.

Umang Patel: Thank you. So again, Magellan TCRs categorize it as ulcerative colitis agents, the Apple Health PDL has it sub listed as GI agents, specifically irritable bowel agents. So on the next slide, little bit of background here. Ulcerative colitis is a chronic inflammatory disease, primarily affecting the colon and rectum. It affects approximately one million people in the US and the incidence continues to increase worldwide. The CDC estimates the current

prevalence is at 238 per 100,000 adults. It may present at any age, but onset typically peaks between 15 and 30 years of age. The disease is characterized by superficial infiltration of the bowel wall by inflammatory white cells, resulting in multiple mucosal alterations and crypt abscesses. The predominant symptom of ulcerative colitis is diarrhea, which is usually associated with blood in the stool. Additional symptoms may include pain in the lower quadrant or rectum along with systemic features including fever, malaise, weight loss. The initial attackable of ulcerative colitis may be fulminant with bloody diarrhea, but the disease more commonly begins indolently with non-bloody diarrhea progressing to bloody diarrhea. It can present initially with any extensive anatomic involvement ranging from disease confinement to the rectum, to the entire large intestine defined as panniculitis. And most commonly, it follows a chronic intermittent course with long periods of quiescence interspersed with acute attacks lasting weeks to months. However, a significant percentage of patients suffer a chronic continuous course. On the next slide here we have just treatment guideline updates for the American Gastroenterology Association in 2020. The next slide please. For moderate severe ulcerative colitis, they recommend to consider patients to be those who are dependent on or refractory to corticosteroids, exhibit ulcers upon endoscopic assessment, or are at high risk for colectomy. In terms of long term management, it can include medications from the following classes: TNF alpha antagonists immunomodulators, the anti-integrated agent, such as vedolizumab, and JAK inhibitors, such as tofacitinib. If the agent selected for inducing remission is effective it is usually continued as maintenance therapy. The exception to this would be when corticosteroids or cyclosporin are used for induction of remission. The following agents are recommended over no treatment for adult outpatients with moderate to severe ulcerative colitis listed in order of FDA approval: infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab. In patients who are biologic naive, infliximab and vedolizumab are suggested rather than adalimumab for induction of remission. However, patients with less severe disease who value the convenience of self-administration over the relative efficacy of therapy may select adalimumab instead. For induction of remission, thiopurine monotherapy suggested against use however, it is suggested over no treatment for maintaining remission. Methotrexate monotherapy is suggested against use for induction as well as maintenance of remission. The combination of TNF alpha antagonists is suggested with thiopurines or methotrexate over biologic monotherapy, or thiopurine monotherapy. Early use of biologics with or without immunomodulator therapy is suggested,

rather than gradual step up for those agents following failure [indistinct]. Additional recommendations for adult outpatients with moderate to severe ulcerative colitis are provided regarding the use of tofacitinib and the management of nonresponders to infliximab. For patients who achieve remission with biologic agents and or immunomodulators or tofacitinib, it is just against continuing [indistinct] for induction and maintenance of remission. There are additional guidelines that are over a year old and I put those in the appendix of this slide for the committee's leisure if they wanted to peruse those as well. On the next slide here we have Zeposia. So in May 2021, FDA approved Zeposia for the treatment of moderate to severe active ulcerative colitis in adults. It was already indicated for adults with relapsing form of MS to include clinically isolated syndrome as well. So nothing else has changed No changes to the limitations. The dosing is recommended still to be .92 milligrams once daily and availability is in capsule form. It just now has a new ulcerative colitis indication as well. In terms of specialized populations, there's no clinically pharmacokinetic differences for patients who have renal impairment. And the use is not recommended in patients who have severe hepatic impairment as well. Those are all the clinical updates for this class. I'll go and pause there.

Ginny Buccola: Thanks, Umang. We have a stakeholder with AbbVie again --

Leta Evaskus: So we are actually going to have Umang also do the next two classes as a presentation and we'll do a motion for all three. So irritable bowel, Gi motility, and then also phosphate binder agents. And then --

Ginny Buccola: Okay, thanks. I'll be quiet.

Umang Patel: Sounds good. Thanks. Thanks, Leta. Perfect, so we'll pivot right over to chronic GI motility. Again in the Apple Health PDL it’s defined as GI agents, irritable bowel syndrome agents/GI motility. A little bit of background here as well. Constipation is a syndrome that is defined by bowel symptoms specific to the difficult passage of stool and frequent passage, abnormal hardness or feeling of incomplete evacuation after a bowel movement. Though constipation can occur secondary to another disease such as Parkinson's or spinal cord injury, idiopathic constipation occurs independent of any other underlying disorder. Chronic idiopathic constipation, I’ll abbreviate as CIC moving forward, is diagnosed if there are three or less spontaneous bowel movements per week, with symptoms occurring six or more months and at least two of the previously mentioned bowel symptoms.

On the next slide here, irritable bowel syndrome is a functional bowel disorder which can be chronic relapsing and often lifelong. It occurs in up to 15% of population and is up to two and a half times more common in women than men. It's characterized by symptoms of abdominal pain or discomfort associated with abnormal stool frequency, abnormal stool consistency, abnormal stool passage, and or bloating or abdominal distension, which may or may not be relieved by the defecation at least three days per month in the past three months. It can also present with non-colonic features such as functional urinary and gynecologic problems, gall bladder and stomach symptoms, back pain, migraine, and depression, which can lead to inappropriate patient referrals. Patients present with combination of symptoms that are typically constipation predominant, diarrhea predominant, and/or alternating between both, which is defined as mixed. Causes have not been fully identified, but could potentially include hypersensitivity, disturbed colonic motility, post effective bowel dysfunction, or a defective anti nociceptive system. There also may be factors that are contributing such as stress, food intolerance, abnormal GI flora, which can hinder the effectiveness of treatment if left unresolved. On the next slide, in January 2021, the FDA approved the first authorized generic for Mallinckrodt's Amitiza from Par and it's for lubiprostone. Again, there's no changes in indications, limitations, or anything. I'm just keeping it here for the committee's reference. Again, it was indicated for CIC in adults, opioid induced constipation in adult patients with chronic non-cancer pain including patients with chronic pain related to prior cancer or its treatment who do not require frequent opioid dosage escalations, and irritable bowel syndrome with constipation in women 18 years of age or older. Again, no changes in limitation, dosing, or formulations. In terms of specialized populations, based on animal data, this may cause fetal harm and women who are pregnant, and the safety and efficacy has not been established in pediatric patients with IBS constipation, pediatric functional constipation, and OIC. And then we'll move right along to phosphate binders on the next slide. There is no significant clinical update within the last 12ish months for this class. So I will pause there for the committee for these three topics. And if there's any questions that I can answer.

Ginny Buccola: This is Ginny again. Thanks, Umang. Sorry for cutting you off earlier. Any questions from the committee? Okay, as I had mentioned before, it looks as if we just have one stakeholder. I see Maggie Olmon with AbbVie listed. If there are any other stakeholders, raise your hand so we know that you're here. And Maggie, when you're ready, you'll have three minutes to present.

Margaret Olmon: Hello, I'm Dr. Margaret Omen with AbbVie medical affairs. AbbVie has two medications for the treatment of irritable bowel syndrome: Linzess for IBS with constipation, and Viberzi for IBS with diarrhea. Today I'd like to focus your attention on Linzess, which is a guanylate cyclase c agonist indicated for the treatment of irritable bowel syndrome with constipation or IBSC and chronic idiopathic constipation or CIC in adults. Linzess acts locally in the gut and is thought to work in two ways: to increase fluid secretion and gastrointestinal motility and to reduce visceral hypersensitivity. Linzess is dosed once daily with three flexible dosing options approved in three strengths, once daily 290 micrograms for adult IBSC patients and once daily 145 micrograms and 72 micrograms for added dose and flexibility for adult CIC patients. Although constipation is the predominant symptom in IBSC, abdominal symptoms including abdominal pain, discomfort, and bloating are also reported as extremely bothersome in a large proportion of patients. In December of 2020, the FDA approved a label update based on the results of a phase three B study evaluating the efficacy and safety of Linzess on the overall abdominal score, which included assessment of abdominal discomfort, pain, and bloating. 34% of patients treated with Linzess experienced a reduction in abdominal score compared with 18.5% of patients on placebo, demonstrating a statistically significant and clinically meaningful reduction in discomfort, pain, and bloating. Improvement in overall abdominal symptoms occurred as early as week one. Safety data were consistent with a known safety profile of Linzess. What is this has been associated with high overall treatment satisfaction. The contour study, a real world longitudinal study assessed IBSC and CIC burden and treatment experience. Patients treated with Linzess reported higher overall treatment satisfaction at all time points as compared with other prescriptions and OTC treatments. Also based on real world data, patients started on Linzess showed significant lower rates of discontinuation over a 12 month follow up period when compared to patients on Emmatiza. I urge the board to retain Linzess as a preferred agent in this category. I want to thank you for your time, and I'd be happy to answer any of your questions.

Ginny Buccola: Thank you very much. Are there any questions from the board? And are there any other stakeholders.

Leta Evaskus: This is Leta. There's Sara Hovland.

Sara Hovland: Good morning. Again, this is Sara Hovland. I'm part of the field health economics and outcomes research department at Bristol Myers Squibb. Once again, I'm providing testimony for Zeposia or ozanimod, which as a reminder is a once daily oral sphingosine one phosphate receptor modulator. As Umang mentioned earlier, Zeposia was first approved in March of 2020 in the US for the treatment of relapsing forms of MS. And in May of this year, Zeposia did receive a second indication to treat moderately to severely active ulcerative colitis in adults. For this particular discussion, I'll be focusing on the phase three placebo controlled registration trial called True North, which evaluated the efficacy and safety of Zeposia in adult patients with moderately to severely active UC. The results of the True North trial showed that the clinical remission rate was significantly greater with Zeposia versus placebo during both the induction phase, which was assessed at week 10 and the maintenance phase, which was assessed at week 52. Also, a greater proportion of patients treated with Zeposia versus placebo achieved all key secondary endpoints including clinical response, endoscopic improvement, and mucosal healing at week 10 and 52, as well as maintenance of remission, cortical free steroid remission, and durable remission at week 52. The results of a subgroup analysis of patients who were naive to prior tumor necrosis factor inhibitors use showed that a greater proportion of patients on Zeposia achieved primary and secondary endpoints that I just mentioned, compared to the placebo group at week 10 and 52. In the patients with prior TNF inhibitor use, the Zeposia cohort showed a significant improvement in clinical response at week 10 and a greater proportion of Zeposia group achieved primary and secondary endpoints at week 52. The most common treatment emergent adverse events were anemia, nasopharyngitis, and headache during the induction period, in addition to an increase in ALT during the maintenance period. Given Zeposia as a once daily oral product with clinical evidence, demonstrating superior efficacy outcomes compared to placebo, we respectfully request that Zeposia be added to the PDL in accordance with the FDA approved label. I appreciate your time and am certainly happy to address any questions that anyone might have.

Ginny Buccola: Thank you very much. Are there any questions for Sara from the committee? Okay, any other stakeholders?

Leta Evaskus: This is Leta. There are no other hands raised.

Ginny Buccola: Okay. So we can go to the motion.

Catherine Brown: This is Catherine Brown. I move that all products in the drug classes listed on slide 14 are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least two preferred products with the same indication before a non preferred drug will be authorized and less contrary indicated, not clinically appropriate, or only one product is preferred.

Michael Corsilles: This is Michael Corsilles. I second that motion.

Ginny Buccola: This is Ginny Buccola, committee chair. All those in favor please say aye.

All: Aye.

Ginny Buccola: Are there any opposed?

Kavita Chawla: Hi Ginny, Kavita here. Just a super quick question. So on the drug list, I'm looking at, am I referencing the Excel sheet for the Apple Health preferred drug list to see which agents we approved? Do we see which agents were all included?

Ginny Buccola: So I know at least the motion is referring to slide 14. And so I don't know if Leta could go back.

Kavita Chawla: So for under Inflammatory Bowel Agents, one of the agents that Umang reviewed was Zeposia and I don't see Zeposia on the apple PDL. And so I'm just wondering whether that is included in these agents.

Ginny Buccola: I'll turn that question over to the experts.

Leta Evaskus: Ryan, are you able to answer that? Or Joey?

Ryan Pistoresi: Hey, this is Ryan. I'm just checking the Excel list right now. Sorry, I was having trouble getting off mute. So I did actually get an answer on the previous question on the Abkezza and so I can answer that soon, too, but I'm wondering if maybe, is this drug an infused drug? Is it infused by a provider?

Alex Park: I think it’s a capsule, Ryan.

Ryan Pistoresi: It is a capsule? Okay. Because for the Abkezza, the reason that it's not in the Apple Health preferred drug list is that it is an infused drug. And so it's not being included here, which is on the pharmacy side. So that's being managed, kind of like our other medical drugs. But let me continue to do research on this and see if I can get an answer on where it may be.

Ginny Buccola: Kavita, do we need to hold off on completing this motion?

Kavita Chawla: If the motion only includes the drugs that's on the PDL then that was my only question. If the motion applies to, as you said, just the slide prior, because it only contains the parent drug classes, I don't know if that includes all of the agents. Hence, I was hesitating.

Ginny Buccola: So I wonder if we should table that until there's enough time to get an answer for it. Table it until this afternoon, perhaps. What does everybody think about that?

Ryan Taketomo: This is Ryan Taketomo and I looked it up. It looks like Zeposia is in the MS multiple sclerosis class.

Ginny Buccola: That was fast research. Thanks, Ryan. Is that satisfying? Does that help, Kavita?

Kavita Chawla: Yes. Maybe for some reason it's not showing up on my sheet. But yes, that satisfies me.

Ginny Buccola: Okay. I don't want you to feel pressured to fit if we need more time to get the question answered. So I just want to return to a vote. I think we had started but all those in favor of passing this motion as proposed by Catherine and seconded by Michael, say aye.

All: Aye.

Ginny Buccola: Are there any opposed? Okay, the motion does carry. And we do have one more on our topic list before a break and that's the GU agents, the overactive bladder agents. So, Umang will update us on that.

Umang Patel: Perfect, thank you. So yes, the next topic we will review is our bladder relaxant preparations, specifically in the Apple Health PDL there under GU agents overactive bladder agents. A little bit of background real quick.

Overactive bladder is a chronic and debilitating syndrome that is characterized by urinary urgency with or without urge incontinence, usually in combination with urinary frequency, defined as eight or more voiding episodes within 24 hours, and nocturia, which is awakening one or more times per night to void. It's a problem with about 16% of men and 17% of women, 20% in those older than 60 years of age. Treatment essentially, according to the American Neurologic Association, first line is behavior therapy, second line are oral antimuscarinics such as darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium. Surgery is reserved for patients with severe refractory OAB symptoms who were not candidates for oral therapy. Keep in mind, these guidelines are from 2014, and it has not been updated since. On the next slide, we have Gemtesa. In December 2020, FDA approved Gemtesa, which is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults. As you can see, in terms of precautions or contraindications, it is contraindicated in urinary retention, pediatric use, end-stage renal disease with or without hemodialysis, and severe hepatic impairment, as well. The recommended dose for this is 75 mg tablets once daily, and it is available in tablet form. The only special population missing for this medication here are women who are pregnant, and there is insufficient data to correlate any form of risk benefit scenario. On the next slide here, we have Myrbetriq. In April 2021, FDA approved this medication for the treatment of neurogenic detrusor overactivity in pediatric patients aged 3 years of age or older. Previously, it was only approved for use in patients in adults with overactive bladder. Additionally, in that same timeframe, they approved the needed dosage form specifically for this younger population. They approved granules and extended-release oral suspension with the strength of 8 mg/mL following reconstitution. It was already approved for an extended-release tablet for the adult population. As you can see, an expanded indication and a new formulation for that expanded indication. Otherwise, no changes in precautions or contraindications or dosage there. On the last slide here, we have Toviaz. Where in June 2021, FDA approved Toviaz for the treatment of neurogenic detrusor overactivity in pediatric patients 6 years of age and older and greater than or equal to 25 kg. Previously, it was only approved for the treatment of overactive bladder in adults. Again, no additional updates or precautions in terms of dosage. The NDO in pediatric patients is recommended to be 4 mg orally once daily. If needed, dosage may be increased to 8 mg. This is weight-based, so that dosing was 25-35 kg. Pediatric patients 35 kg or greater are recommended to take 4 mg daily, as

well. Formulations again extended-release tablets here. Very quick update for this class. I'll pause there for any questions from the Committee.

Ginny Buccola: Thanks, again, Umang. Any questions, Committee members? And are there any stakeholders?

Leta Evaskus: This is Leta. There are no stakeholders, and I don't see any hands raised.

Ginny Buccola: Okay. I guess we can go to the motion then.

Nancy Lee: This is Nancy. I move that all products in the Genitourinary Agents: Overactive Bladder Agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least 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.

Alex Park: I second the motion.

Ginny Buccola: And this is Ginny Buccola, Committee Chair. All those in favor, please say Aye.

Multiple speakers: Aye.

Ginny Buccola: Are there any opposed? And the motion carries. And it looks like we're scheduled for a 15-minute break.

Leta Evaskus: This is Leta. Yes, let's come back at 12:15.

Ginny Buccola: Okay, great. Thanks.

Leta Evaskus: Thank you.

[break]

Ginny Buccola: Hey, everybody. This is Ginny. Just reconvening after our break. We are scheduled to go back to Umang to review hematologic agents. You ready to go, Umang?

Umang Patel: I am. Perfect.

Ginny Buccola: Okay, great. Thanks.

Umang Patel: Thank you. Alrighty. So, the next class we'll be reviewing will be HAE Treatment Medications. Going on to the next slide here. Just a little bit of background. So, hereditary angioedema is a rare dominant autosomal genetic disorder that affects about 6,000 individuals in the US. It's characterized by recurrent episodes of nonpruritic, nonpitting, subcutaneous or submucosal edema involving the skin or mucosal tissues of the upper respiratory and GI tracts. Although swelling can resolve spontaneously in several days without treatment, laryngeal edema may be fatal, and the pain of GI attacks can be incapacitating. Symptoms can begin as early as 2 years of age and persistent through life with unpredictable severity and frequency of attacks. It is thought that minor trauma and stress can lead to an attack; however, many attacks can occur without any apparent trigger. There are two types of C1-INH deficient hereditary angioedema, the first being Type I, which is the most common, in which the body does not produce enough C1-INH, occurs in about 85% of patients with the condition. Type II is characterized by the presence of normal or high levels of dysfunctional C1-INH. HAE prophylaxis is needed to reduce potential edema caused by stressor or procedure likely to precipitate an attack. So, short-term prophylaxis or decrease the number and severity of angioedema attacks, defined as long-term prophylaxis.
On the next slide here, the US Hereditary Angioedema Association recommendations state that an accurate diagnosis must be established prior to discussing treatment options. It may be accomplished by a measurement of serum C4 and assessment of C1-INH activity, so that would be both functional and quantitative. Additionally, treatment options, treatment strategies should be individualized based primarily on patient's specific factors, such as age, comorbidity, and access to emergency medical facilities. The goal of treatment of children with HAE is to prevent mortality, minimize morbidity, and to allow for a normal childhood. Guidelines include four guiding principles: Available on-demand acute therapy for all patients, early treatment to prevent attack progression, treatment of attack irrespective of the site of swelling, and individualized long-term prophylaxis. The guidelines recommend a single dose of Cinryze or Haegarda or a course of anabolic androgen as a treatment of choice for children and adults for short-term prophylaxis prior to medical, surgical, or dental procedures. For long-term prophylaxis in children and adults, the guidelines recommend IV Cinryze, subcutaneous Haegarda, and Takhzyro as first-line therapy. If first-

line therapy is not available, or the patient will only accept oral therapy, anabolic androgen and antifibrinolytics can be utilized as second-line treatment options. For on-demand acute therapy in children and adults. The guidelines recommend one of the four medications FDA approved for use to treat HAE attacks. We have Berinert, Ruconest, Kalbitor, and Firazyr. On the next slide, we have updates to the Haegarda medication. In October 2020, the indication had been expanded to include pediatric patients 6 years of age or older for routine prophylaxis to prevent HAE attacks. No changes to the warnings and precautions. The dosage is still the same where it's 60 IU/kg body weight twice weekly, and it is available as a single-dose vial containing 2,000 to 3,000 IUs. On the next final slide, in December 2020, there was FDA-approved Orladeyo, which is a plasma kallikrein inhibitor indicated for prophylaxis to prevent attacks of HAE in adults and pediatric patients 12 years of age or older. The limitation here is it should not be used for treatment. Again, it is for prophylaxis. In terms of warnings and precautions, there is an increase in QT-prolongation that can occur at higher doses, and additional doses higher than 150 mg once daily are not recommended. Dosage adjustment is needed in patients with moderate or severe hepatic impairment, with chronic Pgp or BCRP inhibitors due to DDIs and persistent GI reactions. The recommended dose here is 150 mg, which is one capsule taken orally once daily with food. And it is available in capsule form. There is insufficient data for this medication on pregnant women to inform a drug-related risk at this time, as well. I'll go ahead and pause there for any questions from the Committee.

Ginny Buccola: Thanks, again, Umang. Any questions, Committee members? And are there any stakeholders?

Leta Evaskus: This is Leta. I do not see any hands raised.

Ginny Buccola: Okay. Thanks, Leta. Let's go ahead and look at our motion then.

Michael Corsilles: This is Michael Corsilles. I move that all products in the Hematological Agents: Hereditary Angioedema Agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of the HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least 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.

Catherine Brown: Catherine Brown. I second.

Ginny Buccola: This is Virginia Buccola, Committee Chair. I wonder if there could be a repeat. I don't know if we got --

Catherine Brown: Yeah. Who got that?

Ginny Buccola: I heard Catherine and somebody else. I wasn't sure who got it first.

Leah Marcotte: I think Catherine and I keep seconding at the same time.

Catherine Brown: Yeah, I think so.

Ginny Buccola: Any of you want to claim it?

Catherine Brown: I'll claim it.

Ginny Buccola: It got claimed. Okay, thank you. So, all those in favor, please say, "Aye."

All: Aye.

Ginny Buccola: And are there any opposed? And the motion carries. Next topic is substance use disorder. Back to Umang.

Umang Patel: Actually, the next topic is Potassium Binders.

Ginny Buccola: Oh! Thank you! Jumping in there. That [cross-talk] you.

Umang Patel: No problem.

Ginny Buccola: Okay.

Umang Patel: However, there is no significant clinical update for this class for 2020 or 2021, so I will pause it right there for the Committee.

Ginny Buccola: Perfect. Any questions, Committee? And I don't see any stakeholders listed. Are there any stakeholders present or hands raised?

Leta Evaskus: This is Leta. I don't see any hands raised.

Ginny Buccola: All right. Let's look at the motion then.

Alex Park: This is Alex Park. I move that all products in the Miscellaneous Therapeutic Classes: Potassium-Removing Agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least 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.

Nancy Lee: This is Nancy. I second that motion.

Ginny Buccola: This is Ginny Buccola, Committee Chair. All those in favor, please say, "Aye."

All: Aye.

Ginny Buccola: Are there any opposed? And the motion carries. And now we're going to Substance Use Disorder.

Umang Patel: Perfect.

Ginny Buccola: Thanks.

Umang Patel: No problem. And our final class for review will be opioid dependence treatments. As you can see in the Apple Health PDL, this encapsulates substance use disorder for agents for opioid withdrawal. opioid antagonists, subcutaneous opiate partial agonists, and transmucosal opioid partial agonists. So, to give a little bit of background here, prescription and illicit opioid abuse and misuse has reached national interest and was declared a national public health emergency by The Department of Health and Human Services, acting Secretary in 2017. The 2019 National Survey on Drug Use and Health reported that there was an estimated 36 million Americans aged 12 years and older who were current (past month) illicit drug users. There are approximately 1.6 million people aged 12 years of age or older in the US who misused opioids in the last year. Approximately 20 million people aged 12 years of age or older in 2019 were considered to have a substance use disorder in the past year, including about 15 million people with an alcohol use disorder, 8.3 million people with an illicit drug use disorder, and 1.6

million have an opiate use disorder. In 2020, the US Preventive Services Task Force issued a final recommendation statement on screening for unhealthy drug use. For adults, they recommended screening implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. For adolescents, the current evidence is insufficient to determine the benefits and harms of screening for unhealthy drug use. On the next slide here, the American Society of Addiction Medicine released an update in 2020. I know there's a lot of information here, so please bear with me. They state that the choice of medication, whether it be buprenorphine, methadone, naltrexone should be a shared decision between the clinician and patient and should consider patient preferences, treatment history, concomitant medical conditions, and treatment setting. Additionally, all FDA-approved medication should be available options to all patients with individual needs taken into consideration for deciding to take buprenorphine, methadone, and naltrexone in conjunction with psychosocial treatment services. Although, they do provide some additional context to treatment selection. There is no recommended time limit for the pharmacological treatment of opioid use disorder. Methadone is recommended for patients who may benefit from additional supervision in an opioid treatment program. Buprenorphine may be dispensed in an OTP or in office-based opioid treatment, while naltrexone may be prescribed in any setting. Oral naltrexone requires special attention to medication adherence and may require observed administration for some patients. The combined use of benzos and sedative hypnotics increases the risk of serious adverse effects when administered with methadone and buprenorphine. However, the harm of untreated opioid use disorder may outweigh the risks. Buprenorphine and methadone are the standard treatment options for managing acute withdrawal from opioids. When buprenorphine is selected for managing opioid withdrawal, it should not be initiated until there are objective signs of opioid withdrawal and at a dose to suppress the withdrawal symptoms. These guidelines note that methadone and buprenorphine are more effective in decreasing symptoms and aiding in the completing withdrawal. Additionally, the group states that alpha-2 adrenergic agonists, such as clonidine -- again, not approved for this use -- and lofexidine are safe and effective to manage opioid withdrawal. The focused update also includes recommendations for special populations, such as pregnant women suffering from pain, adolescents, patients with current psychiatric conditions, and patients in the criminal justice system because this may impact drug selection, psychosocial services offered, and overall care planning. These guidelines recommend that now naloxone for the

reversal of opioid overdose and training for patients and significant others should be provided if patient is being treated for, or with a history of opioid use disorder. On the next slide, the World Health Organization in partnership with the United Nations Office of Drugs and Crime in 2020 updated their international treatment, international standards for the treatment of drug use disorder. They recommend tapered doses of opioid agonists, such as methadone and buprenorphine for opioid withdrawal, although alpha-2 adrenergic agonists may be used. Naloxone should be on hand for people with opioid dependence, and their families in the event of an opioid overdose, and they should be trained to manage opioid overdoses. Detoxification followed by relapse prevention treatment using the opioid agonist naltrexone is useful for patients motivated to abstain from opioid use. In some groups of individuals with OUD may require specialized tailored care, such as women and pregnant women, children and adolescents, elderly, indigenous populations, migrants, sex workers, people with different sexual orientations and gender identify, disabilities, people with limited education, comorbid health conditions, in contact with the criminal justice system, homeless or unemployed people who lack social support. On the next slide, the FDA released a 2020 drug safety communication and a MedWatch for opioid pain relievers and opioid use disorder agents. They require manufacturers of all opioid pain relievers and OUD treatments to add recommendations on naloxone to the product labeling for healthcare practitioners to discuss and prescribe naloxone. They recommend healthcare practitioners discuss and consider naloxone use with all patients at the time of prescribing. They recommend healthcare practitioners consider prescribing naloxone when a patient has a household member, such as a child or a close contact who may be at risk for accidental ingestion or opiate overdose. In addition, for patients who are not receiving a prescription for an opioid analgesic or OUD treatment, consideration should be given to prescribing naloxone for them if they are at a higher risk of opioid overdose. When these meds are prescribed or [indistinct], the FDA is recommending the potential need for a naloxone prescription to be evaluated. On the next and final slide here, in April 2021, FDA approved a new higher dose naloxone hydrochloride nasal spray that delivers 8 mg of naloxone to treat opioid overdose, named Kloxxado. Previously, it was approved as a 2 mg and 4 mg naloxone nasal spray product. So, now it is an 8 mg, as well. The indications, limitations, and dosage haven't changed. But just to quickly go over it. It is indicated for the emergency treatment of known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression for adults and pediatric patients. It's intended for immediate

administration as emergency therapy in settings where opioids may be present, and it is, again, not a substitute for emergency medical care. That is all is have for this class. I'll pause right there for any questions from the Committee.

Ginny Buccola: Thanks, Umang. Any questions? I don't see any stakeholders listed, and I wonder if there's any that I'm missing?

Leta Evaskus: This is Leta. I do not see that anyone has raised their hand, so I will pull up the motion.

Ginny Buccola: Okay.

Kavita Chawla: Kavita here. I had a question about the formulations of naloxone and naltrexone that are listed. I don't see the Vivitrol formulation, so the injectable naltrexone. That's the once-a-month injection. Do we know anything about that? Maybe it's a question for Ryan about whether that is going to be included in the Apple PDL list in the future or [cross-talk]?

Ryan Taketomo: This is Ryan again. I do see Vivitrol listed in the version that I pulled from our website. So, I do see it.

Kavita Chawla: Maybe I just have a faulty version here. [laughter]

Ryan Taketomo: Yeah, it could be. Yeah. Don't feel bad for asking these questions just to make sure that you do feel comfortable if you do find certain drugs that are missing or that you have questions on, because I did not know about the Evkeeza on why it wasn't on the Apple PDL and wondering about it's going to be managed as a medical drug. So, these are good questions.

Kavita Chawla: Thank you.

Kavita Chawla: All right. I move that all products in the drug classes listed on slide 23 are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of at least 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.

Leah Marcotte: This is Leah Marcotte. I second that motion.

Ginny Buccola: And this is Ginny Buccola, Committee Chair. All those in favor, please say, Aye.

All: Aye.

Ginny Buccola: Any opposed? And the motion carries. We have one more topic on our agenda, and it's Ryan Taketomo to read the alcohol policy on the PCSK-9 inhibitors.

Leta Evaskus: Yes. This is Leta. Give me just a second to pull that up. Okay, Ryan. Whenever you are ready.

Ryan Taketomo: Hi. This is Ryan Taketomo. Thanks, Leta. I can see it now. So, good afternoon, Committee. Today, I'll be presenting an update to the existing PCSK-9 inhibitor policy. Currently, there are two drugs in this class including Repatha, which is evolocumab, and Praluent, which is alirocumab. As it was discussed before that these drugs are used to lower cholesterol levels. And so, I'll start off by just going over the updates that have changed since the previous version. Starting off with the medical necessity box, there were changes to the language to update it to our most recent language talking about medically, and its necessity is met based off when the criteria listed in the clinical policy below is met. And if we can scroll down, please. Okay, so starting off with the first indication, which is primary hypercholesterolemia and heterozygous familial hypercholesterolemia, there were a few changes here based on the most recent at the time cholesterol ACC/AHA guidelines. So, with criteria 1, there used to be two criteria based on age and LDL. Specifically, it was age greater than or equal to 20, and LDL greater than or equal to 190 mg/dL on maximally tolerated statin therapy prior to adding a PCSK-9, and age less than 20, and LDL greater than or equal to 160 mg/dL on maximally tolerated statin therapy prior to adding PCSK-9 inhibitor. Both of these criteria were removed as it was redundant to the criteria listed in number 2. So, with criteria number 2, the only change was the addition of [indistinct] based to incorporate adults with known coronary heart disease or diabetes. They have a less than 70 mg/dL LDL threshold that they must not meet in order to qualify for criteria 2. And then there is one last criteria, which was 4, and that criteria was specifically prescribed by or in consultation with a provider specializing in lipid management. After

discussion with our medical director and review of current utilization, we did not feel like that particular prescriber requirement was necessary anymore, so we removed that. And then those wrap up the updates for this first indication. So, we can move down. So, the second indication, which is secondary prophylaxis in adults with established cardiovascular disease. The major changes that were made were with criteria 2 and what was in criteria 4. So, in criteria 2, there used to be an option of inability to achieve LDL cholesterol less than 100 mg/dL. This was updated to less than 70 mg/dL This is mainly based off of what we've seen that most clients, if not all, had that very high-risk categorization, and so having just that lower threshold ultimately will just increase who is eligible and makes it less burdensome to prescribers. And then the other criteria that was removed was one major ASCVD event and multiple high-risk conditions. Again, most clients met that, so we removed that as an option, and we expect the lower mg/dL LDL cutoff will encompass all those patients. And then the last change that was made was the removal of the prescribed by or in consultation with a provider specializing in lipid management.

Kavita Chawla: May I ask a question about those [indistinct]?

Ryan Taketomo: Yep.

Kavita Chawla: The requirement here of being on the highest tolerated statin I get. The requirement to also be on ezetimibe is that -- I'm trying to understand the reasoning for that -- the requirement for them to also be on ezetimibe.

Ryan Taketomo: At least from my understanding and interpretation of the guidelines, ezetimibe was reasonable to add on to statin. Ezetimibe is also significantly cheaper than a PCSK-9, and we felt like it would be a reasonable drug to require prior to PCSK-9 for this particular indication.

Kavita Chawla: Okay. And I feel like I saw the verbiage somewhere else where if they didn't tolerate ezetimibe or the highest-tolerated statin or just statins in general. Is that verbiage somewhere else? I guess it's maybe at the bottom. If they're just not able to tolerate statins but they do require secondary prophylaxis? Does the question make sense?

Ryan Taketomo: Can we look at the definition and maybe we can highlight the one you're focusing on. Is it the highest-tolerated statin dose definition?

Kavita Chawla: No. Just if they've had a cardiovascular event and they're just not able to tolerate statins, period, and they move onto a PCSK-9 inhibitor.

Ryan Taketomo: Okay. I got it. And I think it's listed in the definition that if they can't tolerate statin, then there should be [indistinct] bridge should be with or without ezetimibe, I believe.

Ryan Pistoresi: Yeah. This is Ryan. If we can scroll down, I do remember that there is a section on statin intolerance below this policy section. Maybe that will --

Kavita Chawla: As I understand is the definitions section -- what is the term? What is this criteria listed as one of the qualifying criteria, like if you have statin intolerance, you can go onto a PCSK-9 inhibitor?

Ryan Taketomo: Right. Yeah. And in criteria 2, it specifically is worded concomitant with the highest tolerated statin, there should be one of these definitions, I believe.

Kavita Chawla: Oh, okay. I see.

Ryan Taketomo: So, if they don't need it, then I don't think the ezetimibe would be a requirement to PCSK-9. But I might guess based off of how it's worded right now since it was updated a little bit, that the ezetimibe statement looks like it's gone, so we can add that in just to specify, if that helps.

Kavita Chawla: Yes. Since we're listing ezetimibe as a requirement, too, for secondary prophylaxis. Then maybe also including similar verbiage as the statin intolerance, that they can forego ezetimibe if there is intolerance to it. It's not a common issue, as common as the statin intolerance, but just so that patients have that option available.

Ryan Taketomo: Yep. Okay. I have noted that too --

Leta Evaskus: Well, can you tell me where that is? And I can add it in.

Ryan Taketomo: Yeah. I would just highlight criteria 2.

Leta Evaskus: Okay, hang on just a second. Let me make sure this is in track changes. Okay, so this one?

Ryan Taketomo: Yeah. You can just highlight the whole thing and add a comment.

Leta Evaskus: Well, why don't we just add it in right now? Can we do that?

Nancy Lee: Would adding or changing the saying "and/or" identified -- would that encompass what you're looking for?

Ryan Taketomo: Okay. If we want to add it in now, then I think updating the definition would be the best. I think adding -- we try to avoid and/or for these policies just to keep it as straightforward as possible. So, if we want to add it right now, let's just give it a definition to highest tolerated statin dose. And add under C, which says statin tolerances, define below add another bullet point. And then you can add a statement [indistinct] clients who have statin intolerance are not required to use ezetimibe prior to PCSK-9.

Leta Evaskus: Tell me the drug again.

Ryan Taketomo: Ezetimibe, E-Z-E-T-I-M, as in Mary, I-B, as in boy, E, as in elephant. Yep, prior to a PCSK-9 inhibitor. Maybe add an "a" after "to."

Leta Evaskus: Oh, to "a".

Ryan Taketomo: Yeah.

Leta Evaskus: Okay.

Ryan Taketomo: Does that satisfy what you're asking about or inquiring about?

Kavita Chawla: Yes, that's the bigger chunk, for sure, yeah. I'm just wondering if the Committee thinks that we -- should there be any verbiage here for ezetimibe intolerance? Meaning that they tolerated the maximum dose of statin, for whatever reason they can't tolerate ezetimibe, then you can forego the ezetimibe and move on to a PCSK-9 inhibitor.

Ryan Taketomo: I think that's reasonable to add. Let me think where that would be the best to add.

Kavita Chawla: I wonder if that would just be a new row stating --

Ryan Taketomo: A new definition?

Kavita Chawla: Mm-hmm.

Leta Evaskus: Can we repeat that one more time, Kavita.

Kavita Chawla: I think that would just be a new definition altogether, so it would be a new row.

Leta Evaskus: Oh. Okay, gotcha. Okay.

Kavita Chawla: And that would be ezetimibe intolerance. I guess I would copy the language from statin intolerance.

Leta Evaskus: All of it?

Kavita Chawla: Ryan, feel free to take control here.

Ryan Taketomo: Yeah. Mainly, I think for the ezetimibe we can keep this one simpler and just say, ezetimibe intolerance is defined as not being able to tolerate ezetimibe or is found to be contraindicated. Let me see. Let's delete some [indistinct]. It should be "or is contraindicated." And then we can remove the -- yeah.

Leta Evaskus: And do we [cross-talk].

Ryan Taketomo: [cross-talk]

Leta Evaskus: Yeah, go ahead.

Ryan Taketomo: I was just going to say, how does that look?

Kavita Chawla: Yeah, that looks good. And so, then do we just say similar to the point of the clients who have ezetimibe intolerance are not required and can move on to a PCSK-9 inhibitor? Or that's not [cross-talk].

Ryan Taketomo: Oh, yeah [cross-talk].

Kavita Chawla: That's redundant.

Ryan Taketomo: Yes.

Kavita Chawla: While being on maximally tolerated statin. Does that look okay, Ryan?

Ryan Taketomo: Yep, that's fine. Looks good to me. Thanks.

Kavita Chawla: Thank you.

Leta Evaskus: Okay. Do you want to go back up?

Ryan Taketomo: Yes, please.

Leta Evaskus: I think we were here.

Ryan Taketomo: Okay. Let me just see here. It's going up on my version really quick. Okay. So, I guess to recap -- for criteria 2, we updated the definitions below to incorporate if ezetimibe is not tolerated that a client can move on to PCSK-9. And if they are not able to tolerate statin, then they are not required to use ezetimibe prior to PCSK-9. In addition to that, again, was the update to the LDL threshold, which condensed it down to pretty much inability to achieve LDL cholesterol level less than 70 mg/dL or at least the criteria 2, which has not changed. Other than that, there was the removal of the prescriber requirement, which was specifically prescribed while in consultation with a provider specializing in lipid management. And that wraps up the updates to this indication. So, we can move on down to the last one. So, yep. That was it. Okay. The last indication is homozygous familial hypercholesterolemia. The main updates around this indication are related to expansions of the existing indication for Repatha and the new indication for Praluent. So, with criteria 1, language was added specifically for children, and that's because Repatha is now indicated in a pediatric population 13 years of age or older. And then the next update was with criteria 2. b. And so, LDL threshold was added for children. Criteria 3 was updated to incorporate the new age range for Repatha. And criteria 4 was added as alirocumab is now indicated for homozygous familial hypercholesterolemia. Previously, it was not. And criteria 6 was added, as we now have a non-preferred product that is indicated. And that wraps up the updates for homozygous familial hypercholesterolemia.

Leta Evaskus: Okay. Ryan, this is Leta. Do I need to scroll through anything else on this, or should I go to the form?

Ryan Taketomo: I believe it's okay to go to the form.

Leta Evaskus: Okay.

Ryan Taketomo: And just for the Committee, well, we kind of did it like it was just the dosing limitations, and so, if you would like to go back and look at that, we can do that. Otherwise, I'll quickly go through the form really quick. So, the form is used to help facilitate the prior authorization process and supplements the clinical documentation submitted. I'll leave a few minutes for the Committee to look over it, and then I'll open it up for questions.

Leta Evaskus: This is Leta. If one of the Committee members can let me know when you're ready for me to scroll down.

Ginny Buccola: Oh, you can scroll.

Leta Evaskus: Okay.

Kavita Chawla: Kavita again. I'm so sorry to be the squeaky wheel here. I'm just looking at the FDA indications for -- I'm just looking for Repatha as one of the representatives. So, PCSK-9 inhibitors and ezetimibe, and I'm seeing that for PCSK-9 inhibitors the FDA has specifically approved it for reduction of risk of MI, stroke, and coronary revascularization. So, the actual outcomes that we want versus with ezetimibe, it's only that it reduces LDL level. So, I'm still grappling a little bit with even though ezetimibe lowers cholesterol levels, is anyone aware of actual cardiovascular outcome data that it lowers and, hence, it makes it reasonable to ask for ezetimibe prescription before approving a PCSK-9 inhibitor?

Nancy Lee: This is Nancy. I can't remember. I have to refresh my memory in looking at the Journal of Medicine Repatha study. I believe the patients that were in that trial that had the cardiovascular benefit were on the highest tolerated statins and Zetia, I believe. We'll have to double-check that. I wonder if that's where the ACC/AHA guidelines are coming from. Not necessarily saying that ezetimibe itself has the cardiovascular outcome benefits, but in that study that they used the PCSK-9s that the patients were on that prior, I believe. Not just --

Ryan Taketomo: Okay. So, this is Ryan, and I did do a quick search through Google Scholar, and I do see that there are some studies that do measure cardiovascular outcomes for ezetimibe, but I haven't prepared reading through the studies to see what the quality of evidence is, or how these populations compare. But

it does look like there are some studies. It just wasn't any studies that were submitted to the FDA for review for updating their label.

Kavita Chawla: Okay. I guess I now go with the majority here if the rest of the members feel that it's reasonable. I'm on board.

Jordan Storhaug: This is Jordan Storhaug. I know that they have done some studies, as there was kind of talk about that it was looking at people who are at max-tolerated statin and adding ezetimibe to it did reduce a cardiovascular risk. I think that was mostly looking at people who were at a highest risk. But I did have another question that I wanted to bring up because we had taken out the language about needing to consult a specialist. But it looks like our paperwork still is asking those questions, which I just have the concern that that would lead to the misconception that those questions need to be answered in a certain way in order for the authorization to be approved. I'm sorry. I think it's probably just question 9 in general that could be deleted.

Ryan Taketomo: Thanks, Jordan. I agree with your move. Number 9. Thanks for calling that out.

Leta Evaskus: This is Leta. Both parts? Or just the first part of 9?

Ryan Taketomo: Yes, both.

Leta Evaskus: Okay.

Ryan Taketomo: Thank you.

Ginny Buccola: This is Ginny. Just chiming in because it sounds like we're at a lull. And I'm wondering if everybody's had a chance to make comments, ask questions? Leta, I see we have stakeholder input just listed on the agenda, but I didn't know if there were any --

Leta Evaskus: Sorry. This is Leta. Nobody signed up, and I don’t see any hands raised.

Ginny Buccola: Okay. All right. So, here's the motion.

Jordan Storhaug: This is Jordon Storhaug. I move that the Apple Health Medicaid Program implement the clinical criteria listed on policy 39.35.00-3 as recommended.

Nancy Lee: This is Nancy. I second that motion.

Ginny Buccola: And this is Ginny Buccola, Committee Chair. All those in favor, please say Aye.

All: Aye.

Ginny Buccola: Are there any opposed? And the motion carries. That's our last motion for today. So, we're going to adjourn to DUR Board Meeting and see everybody again, I guess, in December, unless there are any other announcements, Leta.

Leta Evaskus: Nope. This is Leta. I will see you guys' December, I believe, it's the 15th. Mm-hmm.

Ginny Buccola: Okay. Great. Thanks, everybody. I always appreciate all of you. Appreciate all your thoughtful questions and responses.

Leta Evaskus: Yes. Thank you very much.

Ginny Buccola: And keeping me on track. Yes.

Nancy Lee: Have a good Thanksgiving, everybody!

Ginny Buccola: Yeah. Same here. Bye.

[end of file]