

**Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
Meeting Transcription
June 15, 2022**

Leta Evaskus: All right, Jordan, why don't you get us started.

Jordan Storhaug: Okay. So I'm Jordan Storhaug, the Chair of the P&T Committee. We will now convene the P&T Committee Meeting. I will read off the names of the participating attendees. Please say "here" when I call your name for the P&T Committee Members. Laura Beste.

Laura Beste: Here.

Jordan Storhaug: Virginia Buccola.

Virginia Buccola: Here.

Jordan Storhaug: Kavita Chawla.

Kavita Chawla: Here.

Jordan Storhaug: Michael Corsilles.

Michael Corsilles: Here.

Jordan Storhaug: Susan Flatebo.

Susan Flatebo: Here.

Jordan Storhaug: Jon MacKay.

Jon MacKay: Here.

Jordan Storhaug: Alex Park. Diane Schwilke.

Diane Schwilke: I'm here.

Jordan Storhaug: And then Leah Marcotte is absent today. From the Health Care Authority, Laura Crocker.

Laura Crocker: Here.

Jordan Storhaug: Luke Dearden.

Luke Dearden: Here.

Jordan Storhaug: Leta Evaskus.

Leta Evaskus: Here.

Jordan Storhaug: Amy Irwin.

Amy Irwin: Here.

Jordan Storhaug: Ryan Pistoresi.

Ryan Pistoresi: Here.

Jordan Storhaug: Donna Sullivan.

Donna Sullivan: I'm here.

Jordan Storhaug: Marissa Tabile.

Marissa Tabile: Here.

Jordan Storhaug: Ryan Taketomo.

Ryan Taketomo: Here.

Jordan Storhaug: Joey Zarate.

Joey Zarate: Here.

Jordan Storhaug: From Labor & Industries, Jaymie Mai.

Jaymie Mai: Here.

- Jordan Storhaug: From the Drug Effectiveness Review Project, our DERP presenters, Leila Kahwati.
- Leila Kahwati: Yes, I'm here.
- Jordan Storhaug: Gerald Gartlehner.
- Leta Evaskus: I think he will be joining later [cross-talk] before his presentation.
- Jordan Storhaug: And Beth Shaw.
- Beth Shaw: Good morning.
- Jordan Storhaug: Perfect. Thank you. Next, from Magellan Medicaid, Administrator Presenter, Umang Patel.
- Umang Patel: Here.
- Jordan Storhaug: And then for our last members of the Managed Care Organizations, we won't make you be part of the roll call, but we have Greg Simas from Molina Healthcare, Heidi Goodrich from Molina Healthcare, Petra Eichelsdoerfer from United Healthcare, Omar Daoud from Community Health Plan of Washington, and Jeffrey Natividad from Community Health Plan of Washington. Now I'm going to turn it over for Leta a little bit to update us on some meeting logistics.
- Leta Evaskus: Thanks, Jordan. This is Leta Evaskus. The median logistics, the Committee, and presenters can mute and unmute themselves. Please mute yourself when not speaking to limit background noise. Presenters, please share your webcams while presenting, and Committee members please share your webcams during discussions and motion consideration. For stakeholder participation, the Chair will read the list of stakeholder names who pre-registered to speak, please raise your hand so we can find you and unmute you. After, the Chair will ask if there are any other stakeholders. Raise your hand. We will call on you and unmute you. You can also use the Q&A box. We will address your questions during the stakeholder time. We will be turning off the chat after each drug class stakeholder testimony time period concludes for the Committee to make a motion. And lastly, the meeting is

being recorded. So please state your name every time you speak. Okay.
Jordan, do you want me to just go into [cross-talk] --

Jordan Storhaug: Yeah, I think we just if you want to update on the Open Public Meetings Act requirement or two.

Leta Evaskus: Okay. So I'm going to go over some changes to the Open Public Meetings Act that is effective June 1 of this year. Due to the COVID pandemic, in March 2020, the Governor signed a proclamation prohibiting public agencies from conducting meetings subject to the Open Public Meeting Act unless they can be held remotely. The Governor recently rescinded this proclamation. Now, governing bodies can choose, 1.) to hold hybrid meetings in person with a remote option or, 2.) to continue to hold fully remote meetings. After a full briefing and consulting with other agency heads. HCA's Director, Sue Birch, is asking that all meetings HCA supports or facilitates that are subject to the Open Public Meeting Act continue to be held fully remote. Factors considered in Sue's decision are there is still a declared Public Health Emergency, COVID infection rates are on the rise with highly infectious variants, and HCA employees and contractors are required to be vaccinated, yet HCA is not able to verify the vaccination status of individuals who attend open public meetings. So this introduces an unnecessary health risk to everyone at the meeting. Fully remote meetings have been successful for over two years, and we will continue to continue to revisit this in the future. Another consideration is that the Conference Center at SeaTac, where we hold the in-person meetings, is not set up for hybrid meetings. HCA would have to bring in cameras and technology to create a hybrid meeting. So I will now turn it over to Jordan for the Committee to vote on whether to continue holding fully remote meetings or whether to hold hybrid meetings with both an in-person and remote option.

Jordan Storhaug: Thank you, Leta. So I will summarize a little bit that we do have to make a formal motion on this, but we don't really have more than one thing to decide between, essentially, as it would be very difficult to be able to do a hybrid option, which would be the only option going forward, and we have been pretty successful with these virtual meetings. I will just give a little bit of time if anybody has questions on that process. So if not, I will go ahead and make the motion that we continue to hold our meetings virtually until we decide otherwise. Is there a second?

Virginia Buccola: This is Ginni, and I'm happy to second that motion.

Jordan Storhaug: Thank you. All in favor, please say "Aye."

Multiple speakers: Aye. Aye. Aye. Aye. Aye.

Jordan Storhaug: Any opposed? Okay. I will go ahead. And Alex Park is -- he did communicate to us that he is here today. I can see him on screen, as well. So he is part of that roll call, as well. But with that, then I think we're ready to move on to our first topic, which is on plaque psoriasis and psoriatic arthritis. And Leila Kahwati will be presenting for us.

Leila Kahwati: Great. Thank you very much. Let me just get my slides queued up here. Are you all seeing the full screen? [cross-talk] Yes? Okay. Great. Thank you. Thank you, everybody, and good morning. My name is Leila Kahwati. I am an investigator with the RTI University of North Carolina Evidence-Based Practice Center. We are a partner to the Drug Effectiveness Review Project coordinated out of the Center for Evidence-Based Policy at OHSU, and today, I will be giving you an update. This is actually an encore presentation on the topic of Targeted Immune Modulators for plaque psoriasis and psoriatic arthritis. It's an update of a topic that I think I have come to you before to present. The original presentation was designed for a full hour, and we have less time than that. So I'm going to go through some of the slides pretty quickly and skip over others in order to focus on what's new for the update and to help you stay on time for your meeting today. So with that, this is just a brief overview of today's presentation. It's a fairly standard DERP presentation format. And first, a little background just to get everybody on the same page. So plaque psoriasis is a chronic inflammatory disease affecting the skin, scalp, and nails, and plaques or scaling skin lesions are the hallmark of the disease. Psoriatic arthritis is a chronic inflammatory arthritis that is often associated with plaque psoriasis. And TIMs are biologic agents used to treat both conditions by selectively blocking the mechanisms involved in the immune response in those conditions. And the first TIM was approved for psoriasis in 2003. The first TIM was approved for psoriatic arthritis in 2002. And since that time, many additional agents, including biosimilars, have been approved for both conditions. On slide 4, are the drugs that we included in the DERP review that we recently conducted. And this graphic is organized according to mechanism of action, which is listed in the top green boxes at the top. And just as a note, there were no new drugs included in this update compared to the review we conducted for DERP in

2020. The drugs that are colored in blue boxes are approved for both plaque psoriasis and psoriatic arthritis. The drugs that are in the light green boxes are only approved for plaque psoriasis. And the drugs that are in the very light yellow boxes are only approved for psoriatic arthritis. The drugs that are in white, which are bimekizumab and deucravacitinib and are not yet FDA approved. And I will note that the manufacturer for bimekizumab recently, within the last month or six weeks or something like that, received a complete response letter to their submission based on some pre-approval inspection issues. So to our knowledge, neither of these two pipeline drugs are up for immediate FDA approval. Here were the scoping parameters for the updated review in terms of population interventions, etc. The criteria were largely the same as previous reviews that we have done, except that we required cohort studies to be adjusted for confounders to have at least 1000 participants, and so that was a slight change from prior. And just as a reminder, for this review, we only are including head-to-head TIM comparisons for the FDA-approved agents. But for pipeline drugs, we do allow placebo comparators. Here are the key questions for the update. The first was on comparative effectiveness of the various TIM agents. The second is on comparative harms. The third question was around variation in effectiveness or harms by subgroups. And the fourth one was to characterize ongoing studies for these two conditions. Very briefly, we use standard DERP methods, which are summarized here on slide 8. Of note, our update search did go through August of 2021. And then we have been conducting active surveillance through March of this past year to identify any late-breaking studies that we didn't pick up in our search. For the sake of time, I'm going to skip over the rest of the Methods slides. They are there for your reference. But again, we used standard DERP methods. So we'll go right into the findings. So here is our steady flow diagram. We screened just over 1100 new citations and assessed 108 full-text articles. We carried forward 33 studies from the previous report to end up in this update with 70 included articles that represent 51 unique studies. So some studies have two or three publications associated with them because they are reporting on either longer-term outcomes in a subsequent publication or they are reporting on subgroup findings or additional outcomes that were in the primary study publication. Here is an overview of the 51 unique studies that were included. As I mentioned, 18 are new for the update, and 33 were previously included. In terms of study design, 40 were randomized trials, the other 11 were cohort studies. In terms of risk of bias, we rated 46 of the 51 as a moderate risk of bias, and five we considered high risk of bias. In terms of condition, most of them are focused on plaque psoriasis, 42. Only nine were focused on

psoriatic arthritis. And in terms of the comparators evaluated, 43 of these studies are head-to-head comparisons of TIM agents, and then eight of them are comparisons of pipeline TIM agents. And within that group of eight, some of those are placebo-controlled comparisons, but some of them are head-to-head comparisons. So let me just quickly outline how the following slides are structured. I am first going to start out by reviewing the evidence on the plaque psoriasis studies, and then I will transition to the psoriatic arthritis studies. For each condition, I am going to go through the comparative benefits, and if there is any evidence on variation by outcomes by subgroup, I will cover that. But for the most part, there is not too much of that. Then I will review comparative harms. I'm not going to go over comparative harms from observational studies in this presentation. All of that information is available in the full report. And then lastly, I will quickly summarize the comparative benefits and harms for the pipeline drugs. And, briefly, before we get into the results, I wanted to just point out some of the common outcomes used in this evidence base. So here at the top is the (ACR), the American College of Rheumatology response. This is a measure of a multitude of symptoms or signs, and ACR20, 50, and 70 represent a 20%, 50%, and 70% reduction in the ACR score, respectively. The Dermatology Life Quality Index is a measure of the impact of the skin condition on somebody's quality of life. A score of 0 or 1 basically is no impact on quality of life. The Psoriasis Area and Severity Index (PASI) 50, 75, 90, and 100 again represent the respective reduction in the PASI score from baseline. So a PASI 90 or a PASI 100 is often seen as a measure of disease remission. And then lastly, there is a global assessment measure that goes by a couple of different names depending on whether it's the physician or investigator doing the rating or whether it is the patient themselves doing the rating. But a score of 0 or 1 represents disease remission. And then lastly, at the bottom are several common abbreviations that you'll see throughout the rest of the slides for your reference. So onto Findings. First, we are going to start with comparative effectiveness from the trial evidence for plaque psoriasis. This slide is an evidence map showing the number of RCTs and their risk of bias and the specific comparisons that are represented in the body of evidence. So overall, there were 28 studies that represent 18 different head-to-head comparisons. So the studies that are bolded and have an asterisk, like this one here and this one here, are either studies that are new to the update or they have new data for this update. There are a couple things to note on this map, and first is that most of the possible pairwise comparisons don't actually have any RCTs to provide direct evidence, so there is a lot of empty white cells on this map. Second, the majority of trials are comparing TIM agents to etanercept. So you see a lot of

comparisons with etanercept here. Or you see a lot of comparisons to ustekinumab here vertically. There are only six pairwise comparisons other than that that don't include etanercept, ustekinumab. For example, adalimumab versus guselkumab up here. There are three RCTs for that comparison. All of the studies were sponsored by industry and had extensive industry involvement in study design, execution, and reporting, which is why they were all downgraded to at least a moderate risk of bias. There was one study here, the study comparing it etanercept to infliximab that we did rate as high risk of bias because of insufficient blinding and switching of treatments that occurred during the study. And then lastly, I will just note that all of these studies are enrolling participants with moderate to severe psoriasis, usually based on at least a 10% body surface area involvement and/or a certain threshold of PASI score, and a duration of at least three to six months. In addition, some of the studies also require participants to be naive to biological agents, but that's not always universally criteria for enrollment. And then on the next series of slides, I'm going to quickly walk through the evidence for each of these comparisons, but I am going to spend more time on the comparisons that are new for this update. And I'm going to go a little bit faster on the comparisons that are not new, and then I will circle back with a summary slide for the 18 comparisons. So let me just orient you to the setup here for all these result slides. In this green box at the top is the TIM agents that are being compared and the number of studies and the number of participants in those comparisons. So here we have a study comparing apremilast to etanercept that had 166 participants. The bullets down below in the box describe the outcome types that we evaluated with grade for certainty of evidence. I note that the full report often includes other outcomes that may have been reported by the study, but for this presentation, I'm only including the outcomes that we created certainty of evidence for. So in this example, we graded Disease Remission and Quality of Life. And below the outcome domain is a summary of what was found, what measure was used, and the timeframe over which it was measured. So in this example, this study reported no difference in disease remission as measured by the PASI 75 at 16 weeks of follow-up. This study also reported no difference in change in the Dermatology Life Quality Index (DLQI), again, at 16 weeks, and we graded both of those findings as low certainty of evidence. So, again, for the sake of clarity and time, I'm really only going to go through the findings that are new in this update, and I'm not really going to go through the rationale for the grade ratings, but all of that information is available in the full report. What I can say is that, in general, over the entire body of evidence, the grade ratings were downgraded from high to either

moderate or low when that happened, usually for imprecision, which, as you know, is a function of the study sample size. Downgrading for other reasons like inconsistency or risk of bias was rather infrequent. So on the bottom panel of this slide includes a comparison between brodalumab and ustekinumab which we had before, but this update, we identified new data for quality of life and new longer-term data for disease remission. So in the two RCTs that had over a total of 3000 participants, brodalumab was more effective at both the 12-week and the 52-week follow-up points as measured by the PASI 100 measure. We saw absolute risk differences of between 18 and 22 percentage points between the two drugs for the PASI 100, and for quality of life, we saw absolute risk differences between 14 and 15 percentage points for the DLQI. And we graded both of those findings as having high certainty of evidence. We identified a new comparison with one new study for certolizumab versus etanercept. This was one RCT of 502 participants. The study looked at two doses for certolizumab, 400 mg and 200 mg, and it reported that the 400 mg dose was more effective than etanercept as based on the PASI 75. The risk ratio, there was 1.2, and this was at 12 weeks of follow-up. But there was no statistical difference between the 200 mg dosage etanercept at that same follow-up point. So we graded the certainty of evidence for this finding as moderate. We did not identify any new data or studies for the two comparisons that are on this slide -- etanercept versus infliximab and etanercept versus ixekizumab. For both comparisons, the etanercept was less effective than either drug as measured by the PASI 75, and it was also less effective than ixekizumab for improving quality of life. However, our certainty for the infliximab comparisons was very low, and you can see this was a very small study, so the findings were quite imprecise. We also did not identify any new studies or data for the comparison list on this slide -- etanercept versus secukinumab. In summary, etanercept here was less effective for achieving disease remission and improving quality of life as compared to secukinumab. And as you can see, our certainty for these outcomes was high and moderate, respectively. We didn't identify any new data. In our studies comparing etanercept with tofacitinib for disease remission, clinical improvement, and quality of life outcomes, etanercept was more effective than a 5 mg dose of tofacitinib but was no different compared to a 10 mg dose, and all of these outcomes were rated as moderate certainty. We didn't identify any new data or studies for either of the two comparisons on this slide either. In summary, etanercept was less effective for disease remission compared to ustekinumab at 12 weeks, and that was low certainty of evidence. And in the bottom panel, guselkumab was more effective than adalimumab for achieving disease

remission and improving quality of life over 16 weeks, and this was based on high and moderate certainty evidence, respectively. We did identify some new data. Specifically, it was a new subgroup analysis for one study that was previously included, comparing guselkumab with secukinumab. In the RCT for this comparison, guselkumab was more effective than secukinumab at 48 weeks, but was non-inferior at a combined endpoint of 12 and 48 weeks and had a numerically lower response at 12 weeks. But there was no statistical testing performed for that based on the statistical analysis plan design for that study. So that is not the new data. That was in the previous report. What is new is this subgroup analysis here at the bottom of the panel that was based on where they looked at age, weight, body mass index, severity of disease, body area affected by psoriasis, and prior medication use. They looked at each of these factors to see if there was variation in effectiveness, and what they found was across all of these various subgroups, guselkumab remained superior compared to secukinumab across all the subgroups within these factors that they evaluated. We identified two new comparisons, each having one study each as shown on this slide. So the first one in the upper panel here was a new study comparing ixekizumab with guselkumab. It was evaluated in one RCT with over 1000 participants. In this study, ixekizumab was more effective at 12 weeks, as measured by the PASI 100. The relative risk was 1.7 for achieving a positive 100 score. But there was no difference at 24 weeks. The relative risk was 0.96, and the confidence interval included one, so no statistical difference at 24 weeks. [Indistinct] observed similar findings for the quality of life measure, which was a DLQI score of 0 or 1, so superior at 12 weeks, but no difference at 24 weeks. And we rated both of those outcomes as moderate certainty. In the lower panel was an RCT comparing ixekizumab with secukinumab. It had 54 participants so quite small. This study enrolled participants specifically with genital psoriasis, and they found no difference in disease remission at 24 weeks as measured by a patient's global assessment. And then they also saw no difference in clinical improvement as measured by the Genital Psoriasis Severity Score at 24 weeks, and we rated both of these outcomes as moderate certainty. We identified new data for a previously included study that compared to ixekizumab, with ustekinumab that provided longer-term outcomes and additional quality of life outcomes and outcomes that were specific to nail psoriasis severity. So ixekizumab was more effective at achieving disease remission and improvements in quality of life at 12, 24, and 52 weeks of follow-up, and we rated this evidence as moderate certainty. In the new articles that we identified, ixekizumab was also more effective in achieving disease remission, specifically, of nail psoriasis among those

participants who had nail involvement at baseline. We did not identify any new studies or data for the comparison of risankizumab to adalimumab. As you can see from the slide, which is slide 27, that risankizumab was more effective at achieving disease remission and improving quality of life. And those outcomes we graded as having moderate certainty of evidence. We identified one new study for a new comparison, risankizumab and secukinumab. This was an RCT of 327 participants and found that risankizumab was more effective for achieving disease remission as measured by a PASI 90 score. The absolute risk difference between the two drugs was 8.2 percentage points at 16 weeks, and at 52 weeks, it was even larger. It was 29.8 percentage points. And we rated this evidence as moderate certainty. We identified some new data for a previously included comparison of risankizumab and ustekinumab. Previously, we had reported that risankizumab was more effective for achieving disease remission at 12 and 16 weeks. The new article provides consistent results at 52 weeks for its superiority. And it also provided data on quality of life outcomes specifically for the DLQI response and the proportion achieving a minimally clinically important difference on the EQ-5D measure which is a measure of health utility. The two quality of life measures were consistent in demonstrating that risankizumab was more effective. And we graded both the disease remission and the quality of life outcomes as having high certainty of evidence. We also identified some new data for the comparison between secukinumab and ustekinumab. Previously, we had reported that secukinumab was superior to ustekinumab for disease remission and quality of life at 16 weeks. And one of the two RCTs had also reported at 52 weeks the new data that we identified that provided data for the 52 weeks for the other RCTs. So now we have 52-week data from both RCTs, and the findings are consistent in terms of secukinumab being superior early on, like at 16 weeks, but really, for disease remission, also superior at 52 weeks for both disease remission and quality of life. So now both RCTs have those one-year outcomes suggesting superiority. We identified new data for a previously included comparison for tildrakizumab and etanercept. Specifically, it was a new subgroup analysis, and what we had reported before was that etanercept was less effective at both 12 and 28 weeks compared to tildrakizumab for achieving disease remission and improving quality of life. In the new data, subgroup analysis authors analyze outcomes within subgroups defined by metabolic syndrome status -- so either people with metabolic syndrome or people without -- and they found no difference in effectiveness of this comparison between people with metabolic syndrome or people without. So secukinumab was more effective than etanercept

regardless of whether participants had metabolic syndrome. So that sums up the comparative effectiveness. Now, I'm going to briefly go through the comparative harms for plaque psoriasis. And this is a shorter number of slides because there is not that much to say for comparative harm. So overall, all of the RCTs that I just went through that were included for key question one on comparative effectiveness also reported comparative harms. The focus of the next few slides is really just on comparisons from studies where there was a statistically significant difference in either adverse events overall or in serious adverse events, and that our certainty of evidence was at least low. So we did not identify any new data on harms for the existing comparisons that were already included in the previous report. So none of the new data. All the new data for previously included studies was around effectiveness. There was no new harm data for previously included studies. And then secondly, none of the newly identified studies that are new for this update reported any significant differences in adverse events or serious adverse events. There were 10 cohort studies that we identified that also did report harms, and six of those studies are new to this update. Any significant differences from that body of evidence we ended up grading is very low certainty, and so those are available in the full report. There are a lot of comparisons, so for the sake of time, we're not including them in the presentation, but those are available in the full report if you are interested. So again, these findings that I'm going to go through right now are not new for this update. These were all previously presented. So I'm going to go through them kind of fast. But basically, in one RCT comparing apremilast to etanercept, there was a lower incidence of AEs for apremilast. The relative risk was 0.75, and you can see it's a fairly wide confidence interval. In one of the three studies that compared risankizumab to ustekinumab, there was a lower incidence of AEs observed for risankizumab during weeks 17 to 52. In one of the three studies, there were no significant differences in the other two studies. And then for serious adverse events, there was a lower incidence for risankizumab during weeks 1 to 16 in one study, but there were no significant differences in the other two studies. Some studies choose to report their adverse event data by time periods, so it's a little funky to try to make a bottom-line conclusion, but this is what the studies reported. Okay, the only other comparison with any significant differences in adverse events is depicted here for the tildrakizumab versus etanercept comparison. There was a lower incidence for the 100 mg dosage of tildrakizumab during weeks one to 12, and during weeks 13 to 28. There was also a lower incidence for tildrakizumab for the 200 mg dosage, but only during the second time period, the week 13 to 28 time period. All right. So here is a slide that completely

summarizes the comparative benefits and harms for the 18 comparisons in this update regarding plaque psoriasis that I just went through. As a reminder over here, these are all the comparisons, the ones that are bolded, and it might be a little bit hard to see on the slides, but the ones that are bolded are comparisons that either are new to this update or have new data in this update. The certainty of evidence is represented by the circles here in the cell. So four circles mean high certainty of evidence, three circles mean to moderate, two circles mean low, and one circle means very low. And then the color of the cell, a green color means that the first, so for example, up here, this brodalumab versus ustekinumab, the green color means that the first TIM listed is favored or is more effective for a benefit outcome. Or for a harm outcome, it means the first TIM has fewer harms. So green means the first TIM is favored, red means the second TIM is favored that's listed and the yellow means there is no there was no difference between the two agents. So that's the overall scheme for this graphic. Overall, what I will point out to you is you can see there is very few differences in harms between the TIM agents and most of these boxes are yellow. For benefits, you can see some patterns emerge. For example, if you just look at things that are based on moderate or high certainty of evidence, etanercept, which the studies are located here -- there is a lot of red here -- which means that etanercept is generally seems less effective than at least five of the comparator agents, so certolizumab, ixekizumab, secukinumab, tildrakizumab, and ustekinumab. So etanercept is worse than those agents, and the only thing it is more effective than is tofacitinib, and that is just the lower dose of tofacitinib 5 mg dose. The other pattern that emerges from this is there looks to be about four agents that are more effective than ustekinumab, specifically, brodalumab, which is up here, ixekizumab, which is in this row right here, risankizumab, which is down here, and secukinumab, which is here. So ustekinumab is less effective than those four agents. There are really not enough other direct comparisons of most of the other drugs to make a grand pattern. So etanercept and ustekinumab were the only drugs where there are enough other comparisons to other drugs to come up with a bottom line, I think, interpretation Okay, really quickly, this is a one-slide summary of the pipeline treatments for plaque psoriasis. We identified seven trials. Four of them are new to this update. Three of those are head-to-head comparisons. So you can see there are three head-to-head comparisons of bimekizumab. There are four studies that are placebo-controlled comparisons of bimekizumab, and then there is one placebo-controlled study of deucravacitinib, which was included in the previous report, so that is not new. One of these studies, and I can't remember which one, was both a head-

to-head comparison. It had three arms, so it had a placebo arm, bimekizumab, and then an active comparator, and that's why you see actually eight studies listed here on the table when only seven are included. It is because one of them was a three-arm study. Overall, both pipeline agents were more effective with respect to disease remission and clinical improvement and quality of life. But if you look at the placebo-controlled studies, they also had more adverse events than placebo. Bimekizumab appears to be more effective for disease remission and quality of life compared to the three active agents. And there was no difference in AEs or serious adverse events for those head-to-head comparisons. Alright, I'm going to move on to psoriatic arthritis. It is a little bit shorter than plaque psoriasis, so hopefully everybody is still with me. Here is the evidence map. So there is a total of seven RCTs. The three studies that are bolded and have an asterisk are ones that are new to this update or have new data. Two of the studies were high risk of bias, five or moderate risk of bias, and as you can see from the evidence map, six of the studies are comparisons to adalimumab. The seventh study compares ustekinumab to TNF-alpha inhibitors. The comparisons here, the TNF-alpha comparisons were selected by participants and their providers. So this was not a blinded study, which is one reason it is high risk of bias. The other study that was high risk of bias up here was not well described. It also allowed for dose adjustments of infliximab during the trial. So that was another reason we evaluated that as high risk of bias. So we will go through each of the comparisons now in this body of evidence. So for this comparison, adalimumab versus etanercept versus infliximab -- so there are three arms here -- there was no new studies or data identified for this comparison. In this study, there was no statistical significance testing done, and a numerically similar response on the ACR20 was seen across the three agents, and so we ended up grading this evidence as very low certainty. Also, not a new comparison for this update, and also this is a study that did not report statistical testing, so this is adalimumab versus tofacitinib. It would appear that the higher 10 mg dose of tofacitinib is more effective than adalimumab, but there is no difference with the 5 mg dose, at least for clinical improvement in skin remission and probably no differences at all for quality of life. And we graded all three of these outcomes as low certainty. Again, this is not new data or a new study for the update. This was in the previous report. We did identify one new study for the comparison of ixekizumab and adalimumab for the update. This there were two trials here. One of them enrolled 417 participants but didn't do any statistical testing on the comparisons we were interested in, since the primary study aim was to compare ixekizumab to placebo. As far as the

arthritis clinical improvement goes at 24 weeks, there were minor numerical differences in the ACR20 response. You can see the ixekizumab every two-week dose group had a response of 62%, the dose group that was every four weeks had a numerical response of 58%, and the adalimumab group had a response of 57%. Again, there was no statistical testing done. In the other study, the relative risk for ACR20 response was 0.96, and the confidence interval did include the null result. In terms of skin disease remission, ixekizumab was more effective than adalimumab in both studies, and we rated this evidence as moderate certainty. So the bottom line here was probably no difference in arthritis symptoms but more improvement with ixekizumab on skin disease. This comparison of secukinumab and adalimumab is new for this update. We identified one RCT for this comparison. There was no difference in the ACR20 at 52 weeks between the two agents. And in terms of skin disease, secukinumab was more effective in terms of the PASI 90 measure. The relative risk was 1.5. So again, sort of a similar story, no difference in arthritis symptoms but more improvement in skin disease with secukinumab compared to adalimumab. This comparison was also new for this update compared to upadacitinib with adalimumab. At 12 weeks, a larger proportion of people taking the 30 mg dose of upadacitinib showed improvement in arthritis. I think there is a typo on this slide. It says, "no difference for either the 15 or 30 mg doses," but there was a small difference for the 30 mg dose. The relative risk was 1.2, with a lower confidence found of 1.1, so no difference with the 15 mg dosage, though. There were similar findings in the quality of life as measured by the HAQ-DI Quality of Life measure at 12 weeks. So for both doses, upadacitinib had a higher improvement in quality of life compared to adalimumab. There was no difference, and that was for both the 15 mg and the 30 mg difference. And this is the last comparison. It's not new for this update. Briefly, this was a small trial of 47 participants, all of whom had active enthesitis, which is a narrow subset of the population of people with psoriatic arthritis, and it compared ustekinumab with various TNF-alpha inhibitors. We graded this evidence is very low certainty for ustekinumab being more effective for enthesitis remission and for skin disease remission but no difference for arthritis remission. And similarly, ustekinumab was slightly more effective as measured by the SF-36 PCS, the physical component score but no difference measured in the mental component score, and that, again, is also a very low certainty of evidence. All right. Moving on to Comparative Harms. So six of the seven RCTs included for psoriatic arthritis also reported comparative harms. We did not identify any new data on harms for previously included comparisons. One of the newly identified studies did report on a significant

difference in AEs or SAEs, and I will cover that on the next slide. And there was only one cohort study. It is not new to this update. It reported a significantly higher risk of tuberculosis with infliximab compared with etanercept or adalimumab, and that has very low certainty of evidence. So again, this is the only significant difference in AEs or SAEs that we identified. It was from a new study comparing the upadacitinib to adalimumab. It did report a higher incidence of adverse events with the 30 mg dosage. You can see the relative risk just barely excludes the null effect. There was no difference in serious adverse events between these two agents. And there was no difference in adverse events or serious adverse events for that matter in the 15 mg dosage. So the higher dosage did have a slightly higher incidence of adverse events. So here is a summary of the RCT evidence for Benefits and Harms for Psoriatic Arthritis. Again, the studies that are bolded here are the new studies or new data for this update. As you can see, it's a bit of a mixed picture. For the comparisons with at least low certainty of evidence, which is everything in these middle rows, basically excluding the top and the bottom row. You can see that compared to adalimumab, ixekizumab, and secukinumab are more effective at improving skin disease, but there is really no difference for improving arthritis symptoms, and there is no difference in adverse events. Upadacitinib does seem to be more effective than adalimumab at improving both arthritis and improving skin disease. However, it does have more adverse events compared to adalimumab. All right. Here is the one slide summarizing the pipeline treatments for psoriatic arthritis. So we identified only one study comparing bimekizumab to placebo. As you can see, bimekizumab was more effective for clinical improvement quality of life compared to placebo, and there was no difference in adverse events. And lastly, during surveillance after we completed the report, we identified a late-breaking Phase 2 study comparing various doses of deucravacitinib with placebo. Those results were too late to be incorporated into the report in our presentation. The bottom line summary is that deucravacitinib was more effective than placebo for improving arthritis, but it had more side effects. And so, that study will get incorporated into the next update of this topic. So that pretty much covers the waterfront for TIMs for psoriasis. Just a few limitations of our review and overall the evidence base. So as you can tell, for some comparisons, we still have a lot of direct evidence lacking for head-to-head comparisons, and we don't really have much data beyond a year for most drugs, and for some drugs, we don't have much data beyond 12 to 16 weeks. Manufacturers sponsored nearly all the trials. Studies are not powered for harm outcomes, so they are often limited to be able to detect differences particularly in serious adverse events. And

limitation of the cohort studies is that many of them -- some of them use claims data, which may not be entirely valid for some types of harm outcomes. And as a reminder, this review did not include a trial shorter than 12 weeks, cohort studies smaller than 1000 participants, data from conferences, abstracts, or press releases, and studies published in languages other than English. A real quick summary of ongoing studies. So these are studies that have a registry entry in clinicaltrials.gov. As of February this past year, we identified 17 studies of these TIM agents for these conditions, and 12 are trials, five are observational. Half are in plaque psoriasis, half are in psoriatic arthritis of the trials, and almost nearly all are sponsored by the drug manufacturers. So in conclusion, the largest body of comparative direct evidence is for etanercept and ustekinumab compared to other TIM agents. For clinical improvement or disease remission outcomes, etanercept is less effective than ixekizumab, secukinumab, tildrakizumab, certolizumab, ustekinumab, so these are comparisons that have at least moderate or high certainty. Ustekinumab is less effective than brodalumab, risankizumab, secukinumab and ixekizumab. And again, these are the comparisons that have at least moderate or high certainty. For other TIM comparisons other than that included etanercept or ixekizumab, they are not random, but they are sort of idiosyncratic as comparisons because can't really come up with a solid pattern here. But basically, adalimumab is less effective than guselkumab, and it also seems less effective than risankizumab. Guselkumab is more effective than secukinumab for maintenance therapy, but less effective than ixekizumab. And then finally, secukinumab is less effective than risankizumab but is not different compared to ixekizumab. There are few differences in harms among the TIM agents, but most of the evidence is based on very low to low-to-moderate quality evidence. And for psoriatic arthritis conclusions limited head-to-head comparisons available much more limited than for plaque psoriasis. Upadacitinib may be more effective than adalimumab for improvement in arthritis and in skin disease, and that is a moderate certainty of evidence. Ixekizumab and secukinumab are no different than adalimumab for improvement in arthritis but are more effective for improving skin disease. And that was my last slide. I'm happy to take any questions from anybody at this point.

Jordan Storhaug: I don't think we have any questions. So with that then, we will move on to our stakeholder input, and first up on the list is Nathan Blake of AbbVie. We will give each speaker three minutes.

Nathan Blake: Good morning. Can you guys hear me?

Jordan Storhaug: We can. Thank you.

Nathan Blake: Perfect. Good morning. My name is Nathan Blake with AbbVie Medical Affairs. I really want to provide the Committee with a couple of updates today regarding a few AbbVie products. So you will hear from me throughout the meeting. As it relates to TIMs for psoriatic arthritis, I will start with upadacitinib with the brand name or Rinvoq, which is an oral JAK inhibitor that was just reviewed, has several new indications over the past year, one of which is in adults with active psoriatic arthritis who have an inadequate response or intolerance to one or more TNF blockers at a dose of 15 mg once daily. Additionally, risankizumab, with the brand name Skyrizi, which is an Interleukin-23 antagonist, is also indicated for the treatment of active psoriatic arthritis in adults. Risankizumab is dosed similarly for psoriatic arthritis as it is for plaque psoriasis with 150 mg administered subcutaneous injections at week zero, week four, and every 12 weeks thereafter. I encourage you to read the full prescribing information for more details on the use, dosing, efficacy, and safety of you upadacitinib and risankizumab. However, I'm available today if you guys have questions on these products. I would like to ask the Committee to maintain formulary status for both upadacitinib and risankizumab and add the new psoriatic arthritis indications for these products. I appreciate the time today.

Jordan Storhaug: Thank you. Next up, I will have Shirley Quach from Novartis Pharma. After that, we'll have Carrie Johnson from Amgen. Shirley, if you're ready.

Shirley Quach: Yes. Can you hear me?

Jordan Storhaug: We can hear you.

Shirley Quach: Okay, great. Well, good morning. My name is Shirley Quach, and I am a population health MSL with Novartis Pharma. I just want to first thank you for the thorough and thoughtful review for the TIMs class and for this opportunity to provide some updates regarding Cosentyx. Cosentyx is the first and only fully human interleukin-17 inhibitor that's indicated for plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, and in May 2021, approved for pediatric psoriasis age 6 and up and more recently in December 2021 for juvenile idiopathic arthritis that includes age 4 and up enthesitis-related arthritis in age 2 and up for Juvenile Psoriatic Arthritis (JPsA). Cosentyx fills an unmet need for

underserved pediatric populations. It is now the first biologic indicated for ERA and the only biologic treatment approved for both ERA and PsA in pediatric patients in the US. Today, Cosentyx has been prescribed to over 500,000 patients worldwide since its launch in 2015, with more than five years of consistent long-term efficacy and safety data, over 100 clinical studies, and a comprehensive head-to-head clinical trial program. ERA and JPsA are subtypes of juvenile idiopathic arthritis, which are autoimmune diseases, and the approval is based on the Phase 3 JUNIPERA study, a two-year, double-blind, randomized placebo-controlled trial that enrolled 86 children and adolescents aged 2 to 18 years old with ERA or JPsA. The study met its primary endpoint by demonstrating that patients treated with Cosentyx had a longer time to flare versus placebo. Safety in this pediatric population was consistent with the known safety profile of Cosentyx when treating of plaque psoriasis, PsA, nr-axSpA, and AS. Thank you for your time and consideration. And I would be happy to answer any questions you have for me. Thank you.

Jordan Storhaug: We will just give it some time if anybody has any questions. But if not, next up will be Carrie Johnson of Amgen.

Carrie Johnson: Hello? Can you hear me okay?

Jordan Storhaug: We can hear you, Carrie.

Carrie Johnson: All right, great. Thanks. My name is Carrie Johnson, and I'm a pharmacist with Amgen Medical Affairs. Thank you for the opportunity to speak in support of Otezla (apremilast). Apremilast was FDA approved in 2014 and is indicated for treatment of adult patients with active psoriatic arthritis, treatment of adult patients with plaque psoriasis, or candidates for phototherapy or systemic therapy, and the treatment of adult patients with oral ulcers associated with Behçet disease. Please see the full prescribing information at amgen.com for further information. A few important reminders and then a couple of updates. Apremilast is not a biologic, and recent published guidelines separated out from biologics the AAD guidelines for psoriasis and ACR psoriatic arthritis guidelines. Apremilast is an orally administered small molecule that works intracellularly to inhibit phosphodiesterase 4, which reduces immune cells production of pro-inflammatory cytokines and increase the production of anti-inflammatory cytokines. It works in intracellular to modulate the future production of cytokines. It's a unique mechanism of action. Importantly, Apremilast has no

black box warnings and no requirement for laboratory monitoring or pre-medication screening. Additionally, there are no warnings or precautions related to infection or malignancy. As an oral small molecule, it does not induce the production of anti-drug antibodies, either. A couple of updates. The most recent update as of December 2021, Otezla is now the first and only oral treatment approved in adult patients with plaque psoriasis across all severities, including mild, moderate, and severe psoriasis. The FDA approval is based on the findings from the Phase 3 advanced trial, in which five times as many adults with mild to moderate plaque psoriasis receiving oral Otezla 30 mg twice daily achieved the primary endpoint of Static Physicians Global Assessment Response at week 16 compared to placebo, a difference that was statistically significant, 21% versus 4%. Otezla also demonstrates statistically significant improvements in key symptoms such as whole-body itch, difficult to treat areas, the scalp as measured by Scalp Physicians' Global Assessment Response at week 16 compared to placebo. An additional label update occurred in 2020. Scalp psoriasis occurs in over 90% of psoriasis patients at some point in their disease, and it's considered a difficult to treat area. And in the Phase 2 study, Apremilast demonstrated significantly greater improvements in scalp psoriasis, scalp and whole-body itch, and quality of life versus placebo at week 16, with improvements continuing out 32 weeks. These data are fully published and were added to the label in April 2020. Additionally, a third update of long-term data are published out to five years on psoriatic arthritis. These data show no increase in incidence or severity of adverse events and no new safety signals over time. In summary, apremilast is not a biologic and is placed in a separate category in recent guidelines. Apremilast does not have a black box warning and no requirement for medication pre-screening or laboratory monitoring. And as an oral small molecule, apremilast does not induce the production of anti-drug antibodies. And as of December 2021, Otezla is now the first and only oral treatment approved in adult patients with plaque psoriasis across all severity including mild, moderate, and severe. Please consider moving apremilast to a preferred position on the PDL as an oral non-biologic option for adult patients with active psoriatic arthritis, plaque psoriasis, or adult patients with oral ulcers associated with Behçet disease. Thank you.

Jordan Storhaug: Thank you, Carrie. So I will make sure to check with Leta and make sure we don't have any other stakeholders for today. And also Leila is going to have to go from my understanding, so just one more opportunity if the panel has any questions. This will be your last chance?

- Leta Evaskus: This is Leta. I don't see any other stakeholder hands raised.
- Jordan Storhaug: Okay. With that then, thank you again, Leila. And we will have our other presentation on our immune modulators, as well, with Gerald presenting on that. I think we're ready for that at this time if you are ready, Gerald.
- Gerald Gartlehner: Okay. Yeah. Thank you. So, thanks again. My name is Gerald Gartlehner from RTI International. And my presentation today will summarize the update of the report on targeted immune modulators for rheumatoid arthritis and ankylosing spondylitis. Next slide, please. This slide just provides an overview of today's presentation. I will briefly talk about background, key questions, and methods but spent most of the time on findings, and I will end the presentation with a brief discussion of the results. Next slide. So, in the slide set, we use several abbreviations. They are all defined here on this slide. And they also cover frequently used outcome measures. And I would like to point out one of these outcome measures and that is the American College of Rheumatology Response or ACR Response. It is probably the most common outcome measures in the studies that we found, and it is a composite measure of several items including number of swollen and tender joints, the patient's global assessment, the physicians' global assessment, and several others. And an ACR20 response means a 20% improvement in measures, and ACR50 and ACR70 response means a 50% and 70% improvement. In the report and in the presentation. we considered ACR20 and ACR50 responses as clinical improvement and ACR70 response as disease remission. Next slide. So our report focused on two conditions, namely rheumatoid arthritis and ankylosing spondylitis. Rheumatoid arthritis is a chronic inflammatory autoimmune disease of the synovial tissues that progressively erodes cartilage and bone, and that can lead to a destruction of the joints and ultimately to disability. Ankylosing spondylitis is a chronic inflammatory arthritis of the axial skeleton with prominent involvement of the spine and the sacroiliac joints. And as you have probably already heard from Leila, targeted immune modulators are a class of biologic drugs that work by selectively blocking mechanisms involved in the inflammatory and immune responses of the body. Next slide. This slide provides an overview of the different TIM agents that we included in this update. We included 15 agents plus three pipeline drugs. The agents in blue boxes are approved for use in both rheumatoid arthritis and ankylosing spondylitis. The agents in green boxes are approved for only rheumatoid arthritis. And one agent, secukinumab, in the yellow box, is approved only for ankylosing spondylitis. The white boxes show the pipeline drugs. For this update, we excluded

studies assessing filgotinib because the producer of filgotinib withdrew the drug application from the FDA but still part of the previous report. Next slide. This slide presents our PICOS and study selection criteria. The populations of interest were adults with rheumatoid arthritis and ankylosing spondylitis. We considered any TIM agent that is FDA approved or is in the pipeline for approval for these two conditions. For comparators, we selected other TIM agents, and for pipeline drugs, we also included placebo or a standard of care. For outcomes, we were interested in health outcomes such as remission, clinical improvement, quality of life, but also adverse events and serious adverse events. And for study designs, we selected randomized controlled trials of 12 weeks or longer in duration. And in addition for harms, we also included cohort studies -- large cohort studies. Next slide. So for the cohort studies, we adjusted the inclusion criteria for this update to focus on larger and more reliable cohort studies. Specifically, we increased the minimum number of participants to 10,000, and we required that results have to be adjusted for [indistinct] and provided direct statistical comparisons. Next slide. Our report addressed four key questions. Key Question 1 was about the comparative effectiveness of the TIM agents. Key Question 2 was about the comparative harms. Key Question 3 addressed differences in subgroups. And Key Question 4 then focused on ongoing studies. Next slide. Just very briefly on the methods. Next slide. So in general, our methods followed standard DERP methods and are presented in more detail in the report. For this update, we searched electronic databases from January 1, 2019 through July 22, 2021. Next slide. And just as a reminder, although Leila probably showed you a similar slide, the DERP Assessment of Risk of Bias results are ratings of low, moderate, and high risk of bias, and you can see on the slide the definitions of these risk of bias ratings. Next slide. And also Leila probably talked about this. We use grade to rate the certainty of a body of evidence. And for this review, we rated five outcomes, and these were disease remission, clinical improvement, quality of life, adverse events, and serious adverse events. And this slide also suggests how each grade rating can be interpreted with respect to the confidence in the findings. Next slide. So now, let's start with the findings. Next slide. So for this update, we screened more than 1500 abstracts, and we included nine new studies. We carried forward 74 studies from the previous report, and because of the changes in inclusion criteria for COVID studies that I mentioned before, we excluded 19 small cohort studies, which were still part of the prior report. Next slide. So, overall, the report now includes 60 studies, and 56 studies address populations with second-line rheumatoid arthritis and two studies address ankylosing spondylitis, and two additional studies have mixed populations.

Next slide. So, now findings for rheumatoid arthritis. Next slide. Before I start with the detailed findings, let me just quickly outline how we structure the results for rheumatoid arthritis in the slide set. I will start out with first-line treatments and then move on to second-line treatments for rheumatoid arthritis, and then I will follow with the pipeline drugs and a summary of harms from observational studies. Within first and second-line treatments, we structured findings in three parts. First, our comparisons with no significant differences in benefits and harms, then second comparisons with some significant differences, and third comparisons with mixed findings regarding differences in benefits and harms. And I will present new evidence from this update with more detail than evidence that was already part of the previous report because we do have 60 studies. Next slide. So rheumatoid arthritis and comparative effectiveness as first-line treatments. Next slide. This slide is an evidence map showing the number of RCTs for specific comparisons and their methodological quality. New RCTs added for this update have a blue frame. For first-line treatments, we now include 19 RCTs in total, representing 15 different head-to-head comparisons, and two comparisons of combination treatments. There are several things to note on this map. First, most of the possible comparisons do not have any RCT to provide direct evidence. And second, the majority of trials are comparing TIM agents to add adalimumab. All studies were sponsored by the industry and had extensive industry involvement, which is why all were downgraded to moderate risk of bias. Next slide. So I'm starting with first-line treatments for which studies show similar benefits and harms. And based on a single study that we included already for the previous report, benefits and risk of adverse events were similar between abatacept and adalimumab. The certainty of evidence for the beneficial outcomes is low for risk of harms and low or very low for serious adverse events. Next slide. Likewise, a large study found no significant differences between adalimumab and certolizumab pegol. The certainty of evidence was high, except for serious adverse events. Next slide. Also, no significant differences between adalimumab versus etanercept, although this comparison is based on a small study, and the certainty of evidence here is very low. Next slide. Furthermore, three RCTs found no statistically significant differences between adalimumab and tofacitinib. The certainty of evidence was high. For this comparison, we added one new publication for this update, which says differences in functional capacity. The new evidence here is shown in the blue frame. And there were no statistically significant differences in functional capacity between adalimumab and tofacitinib. Next slide. Based on one small RCT and very low certainty of evidence, there were similar benefits and harms

between etanercept and infliximab, and two RCTs found no significant differences between etanercept and tocilizumab. Clinical improvement was rated as very low because it was only assessed by a small RCT. The larger of the two trials assessed serious adverse events during four years of treatment. Next slide. A comparison that is new for this update is between abatacept and certolizumab pegol. We added one new RCT with 407 participants, and after 24 weeks, clinical improvements and remission rates were similar between the two treatment groups, and likewise, proportions of participants with overall adverse events and serious adverse events were also similar. We rated the certainty of evidence as moderate for most of these outcomes. Next slide. The second new comparison for this update was between anakinra and TNF-alpha inhibitors as a class. This was a very small RCT with only 39 participants, and there were no significant differences in clinical improvement, remission, and risk for serious adverse events. But findings favored anakinra over TNF-alpha inhibitors. However, because this was a very small study, the certainty of evidence for all of these outcomes was very low. Next slide. So now let's move on to comparisons for which the evidence shows some significant differences in benefits or harms. For abatacept versus infliximab, efficacy outcomes were similar, but abatacept had a significantly lower risk for serious adverse events than infliximab. It was 5% versus 12%, and the strength of evidence here for this comparison was low. Next slide. For the comparison of adalimumab versus sarilumab, one RCT reported significantly greater improvements in efficacy outcomes for sarilumab. For example, clinical improvement was 30% for adalimumab but 46% for sarilumab. And, likewise, remission and quality of life were significantly higher for sarilumab. The certainty of evidence was moderate or low. Next slide. And, likewise, adalimumab was less efficacious than tocilizumab, but the risks for adverse and serious adverse events were similar. So, for example, 28% of participants treated with adalimumab achieved clinical improvement compared with 47% in the tocilizumab group, the certainty of evidence was low. Next slide. Adalimumab was also less efficacious than upadacitinib based on a large, well-conducted trial from the previous report clinical improvement, remission, and functional capacity were significantly better with upadacitinib than adalimumab treatment. And we rated the certainty of evidence as high. The incidence of adverse events, however, was similar between the two treatment groups. Next slide. Combination treatments as first-line treatments did not add any clinical benefit compared with monotherapy. So we found two RCTs that looked at etanercept as monotherapy versus etanercept plus anakinra, or etanercept as monotherapy versus etanercept plus abatacept. So, benefits were similar, but

the proportion of serious adverse events was significantly increased with the combination treatment of the two targeted immune modulators, The risk of serious adverse events, for example, was 3% for monotherapy and 11% for combination treatment. Next slide. For this update, we added one new study comparing abatacept with tocilizumab. The trial included 392 participants. Efficacy outcomes, such as clinical improvement, remission, were similar between the two treatment groups, but participants in the abatacept group had a significantly lower risk of adverse events than participants in the tocilizumab groups. It was 80% versus 95%. The risk for serious adverse events, however, was similar again. We rated a certainty of evidence as moderate or low. Next slide. Another new study for this update compared certolizumab with tocilizumab. It enrolled 391 participants. And here, again, efficacy outcomes were similar between treatment groups, but tocilizumab led to a higher risk of overall adverse events than certolizumab pegol. Next slide. And finally, one study which was already part of the previous report, provided mixed findings regarding benefits and harms comparing adalimumab with baricitinib. Baricitinib was more efficacious than adalimumab, but it also had a higher risk for serious adverse events than adalimumab. Next slide. And so, this slide summarizes all of this information that you have just heard. So the first column that you can see on this slide shows the comparisons. The other columns present outcomes that we created. And the light brown color indicates no significant differences between treatments. The red color indicates results that favor the first drug. The green color indicates results that favor the second drug. So just to give you an overall impression again of the first-line treatments for which we found evidence. Next slide. So I'm now moving on to second-line treatments. Next slide. And this slide again shows an evidence map for second-line treatments. And as you can see, there are even fewer comparisons than for first-line treatments. We included nine RCTs and seven comparisons, two studies assessed combination treatments compared with monotherapy. Next slide. We found four comparisons for which studies showed no significant differences in efficacy and harms. Two of them are abatacept versus TNF-alpha inhibitors as a class, and the other one is abatacept compared with rituximab. Both comparisons are from the previous report. The certainty of evidence varies by outcomes between high and very low. Next slide. The previous report also included one study comparing tocilizumab versus sarilumab. This trial, however, did not assess efficacy outcomes but focused on adverse events only, and adverse events were similar between the two treatment groups. Next slide. Combining two TIMs as a second-line treatment showed is basically a similar picture as combination treatments for first-line

treatments. The combination did not lead to greater efficacy but caused a higher risk for adverse events. Next slide. For this update, we included one new RCT which provided data on rituximab versus tocilizumab. This trial included 164 participants and reported similar clinical improvements after 16 weeks. The study did not provide any information on any outcomes of interest, unfortunately, and we rated the certainty of evidence is very low because of high risk of bias and precision. Next slide. The previous report included data on three comparisons with some significant differences. Abatacept versus tocilizumab showed similar clinical improvements, but the risks were adverse events and serious adverse events were higher for tocilizumab. This finding is also somehow consistent with what we saw for first-line treatments. Next slide. And in one study, abatacept, rituximab, and tocilizumab showed higher proportions of remission and clinical improvement than TNF-alpha inhibitors as a class. Next slide. For second-line treatments, one new study reported significant differences between abatacept and upadacitinib. This was a large RCT with more than 600 participants. After 24 weeks of treatment, participants treated with upadacitinib showed greater clinical improvement than participants on abatacept, and they also had a higher proportion in the upadacitinib group who achieved remission. The risks for adverse events and serious adverse events, however, between the two groups were similar. Next slide. In the previous report, a second study assessed combination treatments of things, namely the combination of rituximab with a TNF-alpha inhibitor compared with TNF-alpha monotherapy, the combination group had better clinical improvement but then, again, the risk of adverse events and serious adverse events were also significantly higher. Next slide. This slide again, provides a summary and overview of the evidence. The brown color indicates no statistically significant differences between treatments. Red and green indicate some statistically significant differences for one or the other TIM agent. Next slide. So now I'm moving on to the pipeline drugs. Next slide. So as I mentioned at the beginning, for this update we excluded filgotinib from the pipeline drugs because the producer [indistinct] withdrew the drug application from the FDA. Next slide. So for this update, we did not include any new evidence on pipeline drugs, the available evidence is still limited to peficitinib which is a janus kinase inhibitor, and it was peficitinib versus placebo or peficitinib versus etanercept. The five placebo-controlled trials showed greater efficacy of peficitinib than placebo. Next slide. The head-to-head comparison with etanercept, however, reported actually lower efficacy for peficitinib than etanercept. Next slide. Another head-to-head trial assessed a combination therapy of certolizumab pegol plus bimekizumab,

which is an interleukin-17 inhibitor, and the study compared the combination treatment with certolizumab pegol monotherapy, the combination therapy led to a higher proportion of response and remission than certolizumab pegol monotherapy. But then, again, like with all the other combination therapies, it also had a higher risk for adverse events. Next slide. In addition to the randomized control trials, we also included data from observational studies for adverse events. Next slide. I mentioned in the beginning that we changed inclusion criteria for observational studies, and as a consequence, we excluded 19 observational studies that were still part of the previous report. Most of the studies reported no significant differences in harms and excluding the studies did not change the overall conclusions, but it made the report a bit tidier and cleaner. Next slide. So the updated report now includes 25 cohort studies, which were mostly based on registry data. The majority of studies did not report any significant differences in mortality, malignancies, and cardiovascular events. There are two notable results though, and these are that studies consistently indicated a higher risk for serious adverse -- for serious infections and opportunistic infections, also tuberculosis and herpes zoster for infliximab compared with other TNF-alpha inhibitors. And we also have two studies which reported a higher risk for gastrointestinal perforations for tocilizumab compared with TNF-alpha inhibitors. Next slide. So now, I'm moving on to ankylosing spondylitis. Next slide. We found no new studies for ankylosing spondylitis. The evidence is still limited to a single high risk of bias randomized controlled trial. Next slide. So this is a head-to-head trial with 50 participants, which compared etanercept to infliximab. The study reported smaller improvements for etanercept than infliximab, but we rated the quality of evidence as very low, mostly because of the very small sample size. Next slide. Pipeline agents for ankylosing spondylitis. Next slide. We added one new study on a pipeline TIM agent, namely bimekizumab, which as I mentioned before, is an interleukin-17 inhibitor. This was a dose-ranging placebo-controlled trial that found statistically significantly greater clinical improvements and improvements in functional capacity for bimekizumab than placebo. The risk for serious adverse events was similar, but the study only had 300 participants. Next slide. So, we also looked into a network meta-analysis, and we summarized three network meta-analyses for TIM agents on rheumatoid arthritis and one network meta-analysis on ankylosing spondylitis in the report. In the report, we present effects of comparisons for which we did not find head-to-head evidence, for the ones where we found head-to-head evidence, estimates of the network meta-analysis are basically similar to what I just presented here. Next slide. So we also looked into ongoing studies.

Next slide. There is still a lot of research going on in this field. We identified 21 ongoing studies of which 18 are head-to-head RCTs, two are comparative observational studies, and one is a placebo-controlled trial on the pipeline drug. The majority of studies are on rheumatoid arthritis, and only four studies are on ankylosing spondylitis. Next slide. Limitations of our review: First, as you saw from the evidence map for most comparisons, we still do not have any direct head-to-head evidence. So the evidence is really limited to a few comparisons and for first-line treatment mostly to comparisons of newer TIMs versus adalimumab. When we found head-to-head studies, few comparisons actually were evaluated by more than one or two studies, and we are still missing long-term data on effectiveness and safety. Drug manufacturers sponsored nearly all included RCTs, and most observational studies addressing harms were of retrospective design and based on national registries. And the quality and completeness of these databases are really hard to assess and basically cannot be determined. And then there are some inherent potential limitations of our methods. So, for example, we focused on studies in English language only. Next slide. Our conclusions: Our conclusions rely on evidence of high or moderate certainty of evidence. Next slide. Adalimumab appears to be less effective than baricitinib, sarilumab, and upadacitinib as a first-line treatment. Abatacept appears to be less effective than upadacitinib as a second-line treatment, lower proportion of overall adverse events with abatacept and certolizumab pegol compared with tocilizumab as first-line treatments. And all the other differences in effectiveness and harms, which we rated as low or very low certainty of evidence, must be interpreted very cautiously, particularly when they are based on single studies. Next slide. And for ankylosing spondylitis, we only have this one small single trial where all the outcomes are rated as very low. So we cannot draw any conclusions about the comparative effectiveness or risk of harms for targeted immune modulators for ankylosing spondylitis. Next slide. And this slide concludes my presentation. Thank you very much for your attention.

Jordan Storhaug: Okay. Any questions from the Committee? Okay, thank you. Then we will move on to our stakeholders. First of all, we have Anthony Hager of Bristol-Myers Squibb. Next, will be Nathan Blake of AbbVie. Anthony, are you ready?

Anthony Hager: Yes. Can you hear me okay?

Jordan Storhaug: Yes, we can hear you. Go ahead. You have three minutes.

Anthony Hager: All right. Thanks everyone. I appreciate this opportunity. My name is Anthony Hager. I'm with PharmD and Medical Liaison for Bristol-Myers Squibb in the Immunology and Rheumatology Division. And I'm very happy to provide testimony, [indistinct] for consideration for Orenzia (abatacept). For Orenzia, its labeled indications include RA, PsA, and polyarticular JIA. These have not recently changed. Orenzia has been approved for a long time. Orenzia does have a new indication, though, for the prophylaxis of acute graft versus host disease in combination with CN1 and methotrexate, and this is in adult and pediatric patients 2 years of age and older undergoing hematopoietic stem cell transplantation from a matched or 1 allele-mismatched unrelated-donor. This is just for an update. It is not necessarily relevant to this particular review, but it is an update to [indistinct]. Orenzia continues to have no black box warnings. On its label, it reveals the only molecule is its mechanism class T-cell co-stimulation modulator. During clinical trials, the most commonly reported adverse events occur in at least 10% of Orenzia treated patients are headache, URTI, nasopharyngitis, and nausea. Recently, Bristol-Myers, the company that I represent, in collaboration with the rheumatology community has uncovered evidence of a clinically meaningful serum biomarker predicting treatment response to Orenzia in adult patients with RA. This biomarker, which is an auto antibody known as (ACPA) anti-citrullinated peptide antibody, is commonly utilized for diagnostic and prognostic value in RA. However, it has recently been shown to correlate within cancer treatments [indistinct]. For example, the AMPLE study. I believe you reviewed this here. This was published in The Annals of Rheumatic Disease in 2014. Initially, in the Phase 3 head-to-head randomized-controlled [indistinct] study comparing subcutaneous abatacept, subcutaneous adalimumab. As a biologic-naive population, the patients reported methotrexate and adequate responders in RA patients. [Indistinct] was shown per the program point of ACR20 response. Post hoc analysis also showed that the subcutaneous abatacept [indistinct] highest accurate concentrations so that higher [indistinct] for. They have higher responses compared with patients with lower concentrations but who are also active positive [indistinct] 1 through 3. This association was not observed in subcutaneous adalimumab cohort. This was published, also, in The Annals of Rheumatic Disease 2016. [Indistinct] given unique mechanism of Orenzia to co-stimulation modulator differential treatment response and seropositive RA patients, and the low volume of utilization in the Washington Medicaid population, I ask you to evaluate coverage policy in this class to have access to Orenzia by adding it as a Preferred drug within the Washington Medicaid

PDL as a unique and targeted option in patients not responding to anti-TNF therapy. Thank you. Sorry I went a little longer. I will now take any questions.

Jordan Storhaug: Thank you, Anthony.

Anthony Hager: Yep, thank you.

Jordan Storhaug: Next, we'll have Nathan Blake of AbbVie. After that will be Sheta Ara of Pfizer. Nathan, are you ready?

Nathan Blake: Yep. I'm ready. Can you hear me?

Jordan Storhaug: We can hear you. Go ahead.

Nathan Blake: Perfect. Again, hello, my name is Nathan Blake with AbbVie Medical Affairs. I mentioned previously that upadacitinib with the brand name Rinvoq has several new indications over the past year. Upadacitinib's rheumatoid arthritis indication was updated last year, now approved for use in adults with moderately to severely active rheumatoid arthritis, who have an inadequate response or intolerance to one or more TNF blockers. Additionally, upadacitinib was recently approved for use in adults with active ankylosing spondylitis who have an inadequate response or intolerance to one or more TNF blockers. Both indications are treated with a dose of 15 mg by mouth once daily. Other new indications for upadacitinib that are not being reviewed today, however, may be of interest for the Committee to be aware of include adults and pediatric patients 12 years of age and older with refractory moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products including biologics or when those therapies are inadvisable and adults with moderately to severely active ulcerative colitis who had inadequate response or intolerance to one or more TNF blockers. Again, please read the full prescribing information for more details on use, dosing, efficacy, and safety of upadacitinib. I'm available for questions. I would like to ask the Committee to maintain formulary access for upadacitinib and add the new AS indications as well as the new indications for atopic dermatitis and ulcerative colitis. And I will give the rest of my time back.

Jordan Storhaug: Thank you, Nathan. Last of all, Sheta Ara of Pfizer. Are you ready?

Sheta Ara: Hi there. Can you hear me?

Jordan Storhaug: We can hear you. Go ahead. You have three minutes.

Sheta Ara: Great. Thanks. Hi, my name is Sheta Ara, I'm a pharmacist and Field Medical Director with Pfizer Medical Affairs. Today, I will be presenting the tofacitinib or Xeljanz prescribing information update that occurred in December 2021. Four sections of the prescribing information were updated, the indications and usage section, box warnings, warnings and precautions, and clinical studies section. Tofacitinib is now indicated for the treatment of adult patients with active ankylosing spondylitis, who have had an inadequate response or intolerance to one or more TNF inhibitors. The recommended dose is Xeljanz 5 mg twice a day or Xeljanz XR 11 mg once daily. The clinical studies section has been updated to include the confirmatory study for ankylosing spondylitis. In a randomized control trial, adult patients with ankylosing spondylitis achieved ASAS20 response rate of 56% in the tofacitinib group versus 29% in the placebo group. In terms of revisions to other indications, such as RA, psoriatic arthritis, and polyarticular course juvenile idiopathic arthritis, tofacitinib is now indicated after the use of a TNF inhibitor. In accordance, the clinical study section has been updated with results of the oral surveillance study. This was fully published in the New England Journal of Medicine in January of 2022 this year. Oral surveillance is a Phase 3 B/4 randomized safety endpoint study required by the FDA at the time when tofacitinib was approved in the rheumatoid arthritis population. RA patients 50 years and older with one or more cardiovascular risks treated with tofacitinib had a higher rate of (MACE) or major adverse cardiovascular events, compared to those treated with a TNF inhibitor. This brings me to the revisions in the box warning section where MACE was added. The box warning also states that current or past smokers are at additional increased risk. Discontinue tofacitinib in patients that have experienced a myocardial infarction or stroke. The warnings and precautions section have also additional details on MACE, mortality, malignancy, and thrombosis. Please refer to the full prescribing information for details at xeljanz.com. Thanks for your time, and I'm happy to answer any questions.

Jordan Storhaug: Thank you very much. Next, we will connect with Leta and see if we have any last-minute stakeholders, and if not, we'll entertain a motion.

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

- Jordan Storhaug: All right. Very good.
- Laura Beste: This is Laura Beste. I have a question on what we are voting on. So are we voting on including them for all indications? That is what it kind of appears. And for both pediatrics and adults.
- Ryan Pistoresi: This is Ryan Pistoresi. Yes, it would be for all the indications as they are approved for these conditions.
- Alex Park: This is Alex Park. I just have a question following up on Laura's question. There are two drugs on this motion, which were not reviewed in the systematic analysis, and I think they are primarily IBD and/or MS drugs. [cross-talk] Go ahead.
- Ryan Pistoresi: This is Ryan Pistoresi. Yes. And yes, that is a good catch. So today, all that we were able to review from the DERP reports were for the arthritis and psoriasis conditions. We are expecting an updated report with evidence on Crohn's and ulcerative colitis to be due next year, and we will likely be reviewing it next June so that we were keeping it year by year. So even though they weren't in the updates today, they are in a class, and they have been reviewed. And so they are part of the motion going forward. We wouldn't want to remove them from this class because we are reviewing the class as a whole. It is just that we don't have any new evidence. And so, I wouldn't anticipate there to be changes to how they would be treated within this class, if that makes sense.
- Donna Sullivan: Hey, Ryan. This is Donna. I'm wondering -- this is the first time we have been reviewing the TIMs class broken out like this. I think that we should limit the motion to the indications that were included in the review that we just had. And then when we review the rheumatoid arthritis indication, we will edit the motion accordingly, removing any indications that were not covered in that, I think, would be my preference.
- Leta Evaskus: This is Leta. Could you tell me the name of the two drugs that were not reviewed for this?
- Alex Park: It's Alex Park here. Let me just take a look here, I can find. It is natalizumab and vedolizumab. Sorry, Leta, it's the "v" as in Victor drug on the bottom.
- Leta Evaskus: Oh, thank you.

- Alex Park: Donna, it's Alex park here. So are you suggesting that when the two drugs that we just called out are reviewed again in their respective classes and they will come back to this motion and add them back in as a complete list? Or are we going to [cross-talk] pull them out into a separate class?
- Donna Sullivan: Well, I mean, we're going to manage the class as a class as a whole. But as far as making a motion and saying they are safe and efficacious based on the evidence that you have reviewed, I don't think it's appropriate to include the indications that were not reviewed in this report. We would then do a very similar motion for the rheumatoid arthritis, Crohn's disease indications and focusing on the drugs that were included in that report. And then any drug that has ever been reviewed for any of the indications will be carried forward in the class, even if it's no longer included in these updated reports because it still has that indication, and they are still considered part of the class from previous evidence that has been reviewed. I don't know. So I think one of the examples is, especially like with the MS class, there are a few drugs that are used to treat cancer and very seldomly used to treat MS anymore. But we have continued to include them in the MS class, even though they are no longer reviewed as part of the updates. And so we would do the same for this class. If a drug has kind of fallen out of the review either because there is no new evidence or no head-to-heads, then we would continue it in the class because it has that indication and there is historical evidence of its safety and efficacy that had been reviewed.
- Alex Park: Makes sense. Makes sense. So it sounds like you're saying the class is the class, but the motion is going to be specific to the drugs that were reviewed today.
- Donna Sullivan: Yes.
- Alex Park: Yeah.
- Laura Beste: I have one comment on the vedolizumab. So that is indicated for Crohn's disease. And even though we didn't speak to Crohn's disease, unless we are updating what we have as this statement here, it does say that the treatment of the following FDA indications it has included Crohn's disease and ulcerative colitis. [cross-talk] --
- Donna Sullivan: I think Leta was editing that motion up above.

Laura Beste: Oh, okay. Got it. I just wanted to confirm that.

Leta Evaskus: So what I could do is start by copying this and just removing those two drugs.

Laura Beste: And then updating the Crohn's disease to make [cross-talk] --

Donna Sullivan: Yeah.

Leta Evaskus: Yeah.

Laura Beste: Okay. Thank you.

Leta Evaskus: And then also take out the juvenile? Is that correct?

Donna Sullivan: Yeah, and rheumatoid arthritis and ankylosing spondylitis and ulcerative colitis [cross-talk] to only keep psoriatic arthritis. Oh, no, never mind.

Leta Evaskus: Yeah. Rheumatoid and ankylosing spondylitis were reviewed.

Donna Sullivan: What about ulcerative colitis?

Leta Evaskus: Not all three of them.

Donna Sullivan: Then I think we also -- I thought then I heard juvenile arthritis. Was that included? I had to jump off the call, so I don't remember.

Laura Beste: That was just one of the representatives that spoke to that.

Donna Sullivan: Okay.

Alex Park: This is Alex Park. The way this is looking, Leta, are these two motions now?

Leta Evaskus: It is. This is the motion for today, and this is the motion from the last meeting.

Alex Park: Oh, I see. I see. Okay. Could I suggest to Donna's point, the way we're breaking this one out based on the evidence we looked at today, can I suggest that we add -- can we make the first sentence read, after considering the evidence of safety -- blah, blah, blah -- for the use of targeted immune modulators for their FDA-approved indications relative to plaque psoriasis

and etc., I think it would just make it clearer. Quick question for you, Donna, on this topic. The evidence didn't go into much of it because there probably just isn't that much evidence, but how has HCA been handling the biosimilars in this class?

Donna Sullivan: They are considered reviewed.

Alex Park: Okay.

Donna Sullivan: We are treating them like they would be a generic so that they would be considered reviewed.

Alex Park: And one last question. At the bottom, it says that these are not going to be subject to therapeutic interchange. Is that because they are immune modulators?

Donna Sullivan: That was a decision made by the Committee, so I believe it was, if I recall the discussion, there was the concern about -- what was it -- antibodies being built up and that switching between the two may or may not be appropriate once you have been established on the particular product?

Alex Park: You know how the PDL overview says that drugs are not subject to therapeutic interchange if they are an immunosuppressant. Does that apply to this class?

Donna Sullivan: That language, I would have to go back and look at the statute again. I believe initially that that meant it was meant to be for like transplant rejection drugs, but I have to go back and look.

Alex Park: Got it. Okay.

Donna Sullivan: A lot of these drugs were not on the market when that statute was passed.

Alex Park: Yeah, the field has moved on.

Donna Sullivan: Yes.

Alex Park: Yeah, and that thing in the overview is I think only applying the refills or continuations.

- Donna Sullivan: Yeah, it is refills.
- Alex Park: This is Alex Park. I'll take a stab at the motion here. After considering the evidence of safety, efficacy, effectiveness, and special populations for the use of targeted immune modulators for their FDA-approved indications relative to rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis, I moved that baricitinib, guselkumab, risankizumab, tildrakizumab, upadacitinib, abatacept, adalimumab, anakinra, apremilast, brodalumab, certolizumab pegol, etanercept, golimumab, infliximab, ixekizumab, rituximab, sarilumab, secukinumab, tocilizumab, tofacitinib, and ustekinumab are efficacious. The PDL must include a drug approved for the treatment of the following FDA indications: Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis and must include a self-administered agent if indicated. These medications cannot be subject to therapeutic interchange in the Washington Preferred Drug List.
- Laura Beste: This is Laura Beste. I second the motion.
- Jordan Storhaug: Thank you. For the Committee, all who approve, please say, "Aye."
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay, thank you. It looks like we are running right on time, so we will go ahead and take a 10-minute break.
- Leta Evaskus: Thank you. We'll return at 11:10.
- [break]
- Jordan Storhaug: Okay. Looks like it's time to be back. So we'll go ahead and move on to our next topic. We're doing Second-Generation Antipsychotics in Children. Our presentation will be from Beth Shaw. Looks like we have our presentation all ready to go. So Beth, if you're ready, I think we are ready to hear your presentation.
- Beth Shaw: Lovely. Thank you. So I'm presenting you today the surveillance on our Second-Generation Antipsychotic Medications in Children and Adolescents. So on the next slide, you can see the format of this presentation. So we'll start with the topic history, moves through the background, the PICOS, key questions, methods, and we'll focus mostly on our findings and the summary.

So just before we move into the meat of the report, I just wanted to show on this next slide, some of the common abbreviations that we'll be using throughout this presentation, so I won't call them all out. And some of them I'm sure you're very familiar with. But I just wanted to focus on the Assessment Scales on the right-hand side. So these are the assessment scales that are used in the trials, and they are assessing things like depression, the global impression, bipolar severity. They are assessing performance as well as positive and negative symptoms and mania. So that will be important when we look at the outcomes in the identified studies that we have found. So on the next slide, you can see the topic history. So in September 2020, we presented a systematic review of second-generation antipsychotic medication in children and adolescents. So this is the first surveillance that we have conducted since that systematic review was published. So moving on to the background, in 2006, risperidone became the first second-generation antipsychotic medication. It was FDA-approved for treatment in pediatric patients, and that was specifically for the treatment of irritability in children and adolescents with autism. Since then, there have been a number of newer drugs that have been approved -- so that's seven -- and they have been approved for treatment of a range of mental health disorders in children. And those indications include schizophrenia and psychotic disorders, bipolar disorders, autism spectrum disorder, as well as disruptive behavior disorders, impulse control disorders, and conduct disorders in children. So looking at our PICOS. So for this population, you can see that we were looking at both adolescents and children in those different age groups with a range of diagnoses. We were looking really for studies that had a diagnosis that was based on the DSM-5 criteria, but studies did not always use that diagnostic criterion. So in the absence of DSM-5 criteria, we also accepted investigator-defined diagnostic criteria for these range of both ages as well as a range of different disorders. So moving on to our table of interventions. You can see here in the table on the left-hand side we have got the generic name, the brand names in the next column, along with the formulation. We also show you the initial year of FDA approval as well as the details of the approved indications in this population of children and adolescents. So the range of interventions we were looking for were aripiprazole, asenapine, lurasidone, olanzapine, paliperidone, quetiapine, and risperidone. You can see different brand names, different formulations, and different approved indications. In terms of the comparators, we were looking for head-to-head trials, and then in this specific population, so bipolar disorder, autism spectrum disorder, disruptive behavior, impulse control, or conduct disorder. We were also looking for placebo-controlled trials. We

were looking for a range of efficacy and effectiveness outcomes to those things like symptom response. So we talked earlier about those outcomes, scales for things like mania, depression. We were also looking for measures of quality of life, functional capacity, so you know how these symptoms, how these conditions are affecting people's activities of daily living, education, achievement, etc. We were also looking for resource use, so things like hospitalization and emergency department visits as well as persistence and mortality. And on the next slide, we were also looking for evaluations of harms. So those are things like overall adverse events, withdrawals due to adverse events, and time to withdrawal, as well as specific adverse events. So we were looking for general adverse events such as these incidents of clinically-important weight change and the severity of adverse sexual events. And we were also looking for major adverse events, things that were life-threatening that resulted in long-term morbidity or required medical intervention to treat that major adverse event. For this surveillance, we're really only looking for randomized control trials. So the key questions that we were hoping to address looking at studies that might address these questions in our surveillance report, we were looking at whether the different drugs differ from each other in terms of benefits and harms, and for those specific populations whether the drugs differ from placebo in terms of benefits and harms. And we were looking for them in these four different groups, children and adolescents with autism spectrum disorder, adolescence with schizophrenia and other psychotic disorders, children and adolescents with bipolar disorder, and then children and adolescents with these different disorders: disruptive behavior, impulse control, or conduct disorders. So in terms of our methods, we used our standard surveillance approach where we were looking for the registered trials in the online trial registries, so that is clinical trials.gov and the ISRCTN Registry. We use the information from those trial registers to look in Ovid, MEDLINE, and Google Scholar to see if any of those randomized control trials had subsequently been published. And we also looked at a number of websites for FDA actions, including the FDA website, CenterWatch, IPD Analytics, and a Google search. And for this particular surveillance report, the searches covered from April 17, 2020 -- so that was the date of the search conducted in the original systematic review -- and we searched through to November 2, 2021. So what did we find? So moving on to the next slide, you can see that in terms of published studies, we identified two new eligible randomized controlled trials in children. And these were both head-to-head studies in children with bipolar 1 disorder. We also identified one new eligible randomized controlled trial in adolescents and adult populations that was again a head-

to-head study in adolescents and adults with schizophrenia. So on the next slide, you can see a bit more information about these published studies. So on the left-hand side, you can see the citation, the trial number, and the number of people that were enrolled in the trial. In the middle column, you can see more detail about the population, the duration of the trial in those treatment groups. And then in the final column, you can see the eligible outcomes. So these are the two head-to-head trials looking at treatment in children with bipolar 1 disorder. As you can see, both of these trials are very similar. They include the same population, the duration is the same of six weeks, and both trials compared quetiapine 400 mg to 600 mg with lithium-targeted serum level of 1 to 1.2. So very similar populations, interventions, and comparators. Where they do differ is in those outcomes that they report. So the first trial by Streicher et al is really looking at the performance of people in the trials to change from baseline measured using their identical pairs continuous performance test. In the second trial by Patino et al, they are looking at mania symptoms as well as depression and bipolar severity. On the next slide, you can see them the third of the three trials. So this is the one that is been conducted in adolescents and adults. They enrolled 546 people, so these are people aged 16 to 45 years with schizophrenia, and it was a one-year open-label trial looking at the effectiveness of risperidone, aripiprazole, and olanzapine. And in terms of the outcomes, they were looking in the change from baseline of symptoms using the PANSS score. They were looking also for adverse events as well as changing cognitive performance between these three interventions. In terms of the ongoing studies, we identified three ongoing studies that would be relevant for this report if and when they were published. So there is one head-to-head randomized controlled trial of risperidone and aripiprazole. This is being conducted in children under 17 years of age with autism spectrum disorder. The sample size is 350, and the expected completion date is in July 2025. The second trial is again a head-to-head randomized controlled trial of these listed interventions, and it's being conducted in individuals aged 16 to 40 with a diagnosis of intellectual disability and psychosis. The sample size is 114. And that's expected to be completed in around February 2024. The final trial is a placebo-controlled trial of quetiapine in individuals aged 15 to 24 with bipolar disorder or DMDD, disruptive mood dysregulation disorder, and that's a sample size of 19, so significantly smaller than the other trials, and that was completed in April 2021. And at the time of the surveillance reports, we didn't identify any publications reporting on the outcomes of this trial. So moving on to new drugs, formulations, and indications in this surveillance report, we didn't identify any new drugs, formulations, or indications for these drugs since the

searches in the last systematic review. However, we did identify some new serious harms or warnings. So on this next slide, you can see a box that lists the drug on the left-hand side, the new serious harms or warnings in the middle, as well as the date when these were added to the prescribing label. So I'll just leave this up for a few seconds just so you can look at some of those so you can see there were harms for lurasidone, olanzapine, paliperidone, the quetiapine ER, and risperidone. So moving into the summary. So, in summary, you can see here that we identified those three new randomized control trials that have been published since the systematic review. They are all head-to-head trials. We also have the three ongoing randomized control trials, again two head-to-head trials, and one placebo-controlled trial. We didn't identify any new drugs formulations, indications, or serious harms, but we did identify six new warnings that have been added to those drugs, and you can see the details there. Thank you.

Jordan Storhaug: Thank you. Any questions from the Committee? With that, then we'll go on to our stakeholders. First off, is Madeline Shurtleff from Otsuka. Madeline, are you there?

Leta Evaskus: This is Leta. Madeline, you need to unmute yourself, as well. Madeline, are you able to unmute yourself on your computer? All right. I'm going to try promoting her to panelist for a minute. Did she drop off, Laura?

Laura: I don't see her listed in attendees, and I don't see her listed in panelists, either.

Leta Evaskus: Okay, I think she dropped off.

Laura: Nope.

Leta Evaskus: Is she calling back in?

Laura: I just allowed her.

Leta Evaskus: Okay, there we go.

Madeline Shurtleff: [Cross-talk] I'm sorry. Can you guys hear me?

Leta Evaskus: Yeah. There you are!

Madeline Shurtleff: Okay, I'm so sorry. It wasn't letting me unmute and then it dropped me. But I apologize.

Leta Evaskus: Oh, we lost her again.

Madeline Shurtleff: Hello?

Leta Evaskus: Hello?

Jordan Storhaug: You know, Madeline, I think we can hear you now.

Madeline Shurtleff: Okay. I'm going to go ahead and get started then.

Jordan Storhaug: Go ahead and get started. Thank you.

Madeline Shurtleff: Okay. Hello, my name is Madeline Shurtleff, and I am the Managed Market Liaison with Otsuka. Thank you for this opportunity to provide an indication of Rexulti. Rexulti is an atypical antipsychotic indicated for use as adjunctive therapy to antidepressants for the treatment of major depressive disorder in adults and the treatment of schizophrenia in adults. On December 27, 2021, the FDA granted approval for Rexulti for treatment of schizophrenia in pediatric patients 13 years of age and older. Use of Rexulti in this population is supported by evidence from adequate and well-controlled studies in adults with schizophrenia, pharmacokinetic data from adults and pediatric patients, and safety data in pediatric patients 13 to 17 years of age. Adverse reactions reported in clinical studies for this age group were generally similar to those observed in adults. In the long-term open-label study in pediatric patients with schizophrenia, 0.5% of patients discontinued due to weight increase. The mean increase in weight from the open-label study from baseline to last visit was 3.8 kilograms. To adjust for normal growth, Z-scores are derived, measured in standard deviation, which normalized for natural growth of children and adolescents by comparisons to age and gender match population standards. A Z-score change of less than 0.5 standard deviation is considered not clinically significant. In this trial, the mean change in Z-score what from baseline to last visit was only 0.1 standard deviation for body weight. When treating pediatric patients, weight gain should be monitored and assessed against that expected for normal growth. Shifts in baseline fasting total cholesterol from normal to high were reported in 7% of patients taking Rexulti and shifts in baseline HDL cholesterol from normal to low were reported in 12.9% of patients taking Rexulti. Of patients with normal

baseline triglycerides, 8.5% experienced shifts from normal to high, and 2.7% of pediatric patients with normal baseline fasting glucose experienced a shift from normal to high while taking Rexulti. Based on an interim analysis of an ongoing study, brexpiprazole appears to be a well-tolerated potential treatment option for adolescents with schizophrenia with the safety profile consistent to that observed in adults. Long-term open-label treatment with brexpiprazole was associated with continued improvement in efficacy. In fair balance, I call your attention to the box warning for Rexulti of increased mortality in elderly patients with dementia-related psychosis and suicidal thoughts and behaviors in children, adolescents, and young adults. In closing, Rexulti is indicated for the adjunctive treatment of MDD in adults and treatment of schizophrenia in pediatric patients, and we request Rexulti be included on the Preferred Drug List. Thank you.

- Jordan Storhaug: Thank you, Madeline. Yeah. Thank you. All right, Leta, I will just check with you to make sure that we don't have any more stakeholders. And if not, then we'll take a look at a motion.
- Leta Evaskus: This is Leta. I do not see any other hands raised. [Indistinct] the motion. And this is Leta. You'll see that we have subtitles under each of these. So, the next time all of the drugs are reviewed, we will include all three of the motions moving forward. And Jordan, first the Committee should vote if they accept the surveillance as an adequate update.
- Virginia Buccola: This is Ginni. Just again, I think, Leta, you just said this, but I want to be sure. For today, we are just accepting that surveillance is adequate for use in children. Correct?
- Leta Evaskus: Correct.
- Virginia Buccola: Okay, thank you.
- Jordan Storhaug: So, this is Jordan Storhaug. I'll just encourage the community along. Does anybody have any concerns regarding their surveillance as it was performed?
- Virginia Buccola: This is Ginni Buccola. I don't hear concerns. I will go ahead and propose that we accept the scan as adequate.
- Jordan Storhaug: Do we have a second for that motion?

- Diane Schwilke: Diane Schwilke, I second.
- Jordan Storhaug: All in favor, please say, "Aye."
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay. Thank you.
- Leta Evaskus: This is Leta. I'm just going to start putting this together, but if you want to leave out any of these drugs, let me know. I will edit it.
- Virginia Buccola: This is Ginni. Leta and Committee, I think we can we keep that sentence about a drug that is preferred in pregnancy for child and teen use?
- Leta Evaskus: Yes.
- Virginia Buccola: Thank you.
- Laura Beste: Okay, so this is Laura Beste, and I have a question. So some of the medications listed below in the previous motion are approved in pediatrics, but we're not including them in this review. How does that affect prescribing?
- Ryan Pistorosi: This is Ryan. And because today was a surveillance document, we didn't get the new evidence about how some of these other drugs that may be approved are efficacious relative to each other. So essentially, the surveillance documents are more to show we are continuing to monitor this class, look for new evidence, and as DERP states, when we saw that there were only a few new randomized trials, we decided to not move forward by commissioning a new report at this time. We will wait until there is more evidence, so that way we have a more substantial update to bring to you. So essentially, the surveillance document today does not really change and add some of these new drugs. But in the event for a prescriber to potentially request this, it still may be covered by the different programs. It's just that they may not be as part of this motion to be a preferred drug for that specific pediatric population, but they still may be preferred in an adult population, and still may be preferred as a prescribed medication.

- Virginia Buccola: Laura, this is Ginni, just adding as a provider, these types of medications I have not found, and I work primarily with a Medicaid population, I have not found difficulty if I need to move off label or to a non-preferred product.
- Laura Beste: Okay.
- Virginia Buccola: As it stands, I know that that's just one provider's experience, but I haven't had difficulty with that.
- Laura Beste: Okay. I just was concerned because I noticed ziprasidone and some of these other agents can be used in pediatrics but are not included in this list. I didn't want to make it so that if there was a child on that medication to make it that they weren't able to fill that prescription or have that option. So, okay. Thank you.
- Virginia Buccola: This is Ginni. I'm happy to go ahead and make the motion for use of these medications in children. After considering the evidence of safety, efficacy, and special populations for the treatment of schizophrenia, bipolar disorder in children, and bipolar disorder in children with autism spectrum disorder, or disruptive behavior disorders. I move that aripiprazole, asenapine, lurasidone, olanzapine, paliperidone, quetiapine, and risperidone are efficacious for their approved FDA indications and should be preferred on the Washington Preferred Drug List. Second-Generation Antipsychotics cannot be subjected to therapeutic interchange on the Washington Preferred Drug List. The Preferred Drug List should include at least one medication that is considered safe in pregnancy.
- Michael Corsilles: This is Michael Corsilles. I second that motion.
- Jordan Storhaug: All in favor, please say, "Aye."
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay. Thank you, Committee. Next, we will look at newer diabetes, medications, and other surveillance, and that will be back to Beth Shaw.
- Beth Shaw: Thank you. I'm just waiting for the presentation.
- Leta Evaskus: Yeah, this is Leta. I'm opening it up here.

Beth Shaw:

Okay, thank you. Thank you very much. So I will be presenting next to you the latest surveillance report on newer diabetes drugs and cardiovascular outcomes. So on the next slide, you can see the same format that we've used in the previous presentation. So we'll just move straight on to the abbreviations section. Again, for this particular topic, there are a lot of them. Many of them I'm sure you'll be familiar with and will pick up on them as we move through the presentation. So in terms of topic history, the first systematic review on this topic was conducted in February 2011. And since then, there have been three updates with the latest being presented in February 2020. In December of 2020, we also conducted a surveillance report that looked through the search dates that you can see on the left-hand side. So there has been one surveillance report since the most recent systematic review. So this is the second surveillance report on this particular topic. So in terms of the background, as you will know, several new drugs for treating adults with Type 2 diabetes have been approved in recent years, and these are primarily in the three classes. So we have got the GLP-1 agonist, the DPP-4 inhibitors, so they are kind of [indistinct], and the SGLT-2 inhibitors. And in 2008, the FDA released guidance requiring new diabetic drugs to demonstrate that there was no association with an unacceptable increase in a risk of cardiovascular events, and they define that as being greater than a 30% increase. So there were safety concerns around these particular drugs. However, in March of 2020, the FDA issued a draft guidance that said they no longer required drug manufacturers to demonstrate cardiovascular safety for Type 2 diabetes drugs in cardiovascular outcome trials, hence the interest in the impact of these newer diabetes drugs on cardiovascular outcomes. So moving on to our PICOS, we are looking specifically at the population of adults with Type 2 diabetes, and we're looking at a range of interventions. So our first class here is the GLP-1 agonists. So you can see on the left-hand side, we've got the class and whether it's alone or in combination, then we have the generic names, followed by the brand names, and the FDA approval. So in this class of GLP-1 agonists, we've got oral formulations, we have subcutaneous injectables, and we also have a combination of a GLP-1 agonist with a long-acting insulin. So moving on to the next slide, we continue with the DPP-4 inhibitors. Again, you can see these are oral drugs, either alone or in combination with [indistinct] 33:52 or with metformin. On the next slide, you can see the interventions included in the SGLT-2 inhibitor class. Again, these are oral drugs, either used alone or in combination with a DPP-4 inhibitor or with metformin. Moving on to the comparators. Again, we were looking for comparison of these drugs against another of the drugs, so those

head-to-head comparisons. And we were also looking for comparisons of those combination therapies, so with another of the newer diabetes drugs on metformin versus monotherapy of that specific drug. And we were also looking for placebo-controlled trials and cohorts. In terms of outcomes, we were looking for mortality, and that was both all-cause mortality as well as cardiovascular-related mortality. Specifically for this report, we were obviously looking for cardiovascular disease outcomes, so those are things like fatal or non-fatal myocardial infarction as well as hospitalization for heart failure and MACE. So those are those major adverse cardiovascular events. It is a composite outcome, and it does vary between studies, but it often includes things like heart failure, recurrent angina pain, repeat PCI, CABG, etc. We were also looking for harms for serious adverse events. Both investigated determined treatment-related serious adverse events and pre-specified events of interest, such as pancreatitis. But this particular report, we were looking for both randomized controlled trials as well as large prospective and retrospective cohort studies. And for this particular topic, we defined large as being a sample size of 10,000 or more participants. The key questions that we were looking for in this report around the efficacy of newer diabetes drugs for cardiovascular events and adults with Type 2 diabetes. And we were also looking for whether that efficacy buried looking at things like monotherapy versus combination therapy, patients with or without prior cardiovascular disease. We were looking for class effects as well as different harms between these drugs, either individually or on a class level. We were also looking for ongoing studies of newer diabetes drugs, where they were looking for those cardiovascular disease outcomes. So in terms of our methods, again, standard methods here we talked about in the last presentation. So I really just want to know the differences here. As I mentioned, we were looking for randomized controlled trials and those large cohort studies. And for this particular surveillance report, so the second one in the series, our searches covered November 2, 2020 through to October 19, 2021. So moving into the findings, you can see that we identified no new randomized control trials, but we did identify 20 new cohort studies. And the sample sizes range from just over 11,000 to over 714,000 participants. And there's a range of comparisons that were being made in these cohort studies. You can see that they were either comparing the classes directly against each other or they were comparing these classes against other diabetic treatments that are used in standard care. They were looking at these classes as add-on therapies mainly to metformin as well as on their own. So you can see all the different types of comparisons, and we'll go through them in a bit more detail on the next slides. So moving on to the next slide, you can see the first two of

five cohorts that were looking at the comparison of GLP-1s versus SGLT-2s. So again, you can see on the left-hand side the details of the trials, so the number and the trial name, then we have the enrollment, and the study country, then we have the treatment groups. And on the right-hand side, you can see the eligible outcomes. So these first two trials are based in Sweden and Denmark. Like I said, they are comparing the GLP-1s versus SGLT-2s, and you can see the range of outcomes there. So things like MACE, cardiovascular death, stroke, hospitalization for heart failure. On the next slide, you can see the next two of these. Again, both large studies by definition, one conducted in the US and one in Denmark. Again, looking at that comparison of GLP-1s versus other treatments and, again, the range of cardiovascular outcomes on that right-hand side of the slide. And on the next slide, you can see the final one in this series. So this is a large study, again, over 370,000 conducted in the US. Looking at those GLP-1 agonists versus the SGLT-2 inhibitors and, again, outcomes of the composite outcomes looking at those cardiovascular outcomes, myocardial infarction, stroke, mortality. So moving on to the next comparison, this is a group of studies looking at the SGLT-2 versus other diabetic treatments. So the first study here, the OBSERVE-4D study conducted in the US, and this was looking at a range of the SGLT-2 inhibitors versus other treatments, including things like the [indistinct], 39:46 the sulfonylureas as well as insulin. And they had pretty specific outcomes. They were looking primarily at hospitalizations for heart failure and the number of below-knee lower extremity amputations. The next three of this group of comparators are conducted in South Korea, Japan, and again, South Korea. Again, you can see the comparisons there, the SGLT-2 inhibitors compared with DPP-4 inhibitors. And the outcomes, again, a range of outcomes you can see there, including things like hyperglycemia and the MACE composite outcomes. Moving on to the next slide. Again, we're still in this group of SGLT-2 inhibitors versus other treatments. So for these two particular studies, one in the US and one in the UK, we're looking at the comparison of these inhibitors versus metformin or versus the DPP-4 inhibitors. And again, a range of outcomes on that right-hand side then including things like acute kidney injury as a specific harm in that study. Then on the next side, I think this is the final of this group. Again, three studies, one conducted in Japan, one in Spain, and one in the US. Again, SGLT-2 inhibitors versus DPP-4 inhibitors as well as other glucose-lowering drugs including the sulfonylureas. Again, the range of outcomes there, things like all-cause mortality, chronic kidney disease, and heart failure. So on the next slide, we're moving into the final class. So this is DPP-4 compared with other diabetic treatments. And we have got three studies in this particular

categorization. Both of these studies on this slide were conducted in the US. They were looking at DPP-4 versus other drugs, including sulfonylureas, metformin, and other treatments. However, they did exclude comparisons with pioglitazone or the SGLT-2 inhibitors or GLP-1 agonists. And the outcomes again on the right including acute kidney injury as well as things like angioplasty and CABG procedures. And on the next slide, the final one in this grouping, this was a study that was conducted in Spain. Looking at the DPP-4s against things like the sulfonylureas, the meglitinides, and metformin, again, outcomes including things like MACE, composite as well as the individual outcomes, such as all-cause mortality, heart failure, and peripheral arterial disease. So this is the next category on the next slide. So this is a series of studies, the duplicate series, where they were looking at newer drugs versus a range of other options, and those other options include a mix of those newer drugs as well as sulfonylureas. Again, all of those outcomes are composite outcomes. They do vary, but they tend to be the composite stroke, MI, and mortality. On the next slide, again, this is one cohort that is really looking at comparing people taking either a GPL, one agonist or an SGLT-2 inhibitor, and they're comparing it with other antihyperglycemic agents. And again, there's a range of outcomes there, including things like hospital admission or cerebrovascular disease, lower limb complications, and a range of serious adverse events. Moving on to the next slide. Again, we've got a slightly different comparison here that is looking at those newer diabetes drugs as an add-on therapy to metformin versus other diabetic treatments. So here, it's looking specifically at GLP-1 agonists or SGLT-2 inhibitors as add-ons to metformin versus metformin alone. And the outcomes here are the first major CB composite, including stroke, MI, chronic heart failure as well as stroke, MI, and chronic heart failure. Moving on to the ongoing studies, we identified 31 ongoing studies that would be eligible for this report, if they were published. We identified one head-to-head trial. So this is comparing the combination of insulin glargine and lixisenatide versus dulaglutide, and that's in 40 participants, and the estimated completion date for that trial was December 2021. We identified one trial comparing the newer diabetes drugs with dietary intervention. So this is looking at specifically semaglutide versus dietary intervention in 100 participants with Type 2 diabetes, and the estimated completion date for that trial is March of 2023. And we identified eight trials comparing newer diabetes drugs to the standard of care. So that's five in the SGLT-2 inhibitor class, and three for the GLP-1 agonist class. The sample sizes range from 40 to over 12,000 in these eight trials, and the estimated completion dates range between December 2022 and September 2025.

Within these eight trials, one randomized control trial was noted as having been completed, and one was estimated to have been completed in August 2020. But at the time of this surveillance report, no publications related to those two trials had been identified. So continuing with the 31 ongoing studies, you can see we also identified 12 placebo-controlled trials, nine in the SGLT-2 inhibitors class, and three in the GLP-1 agonist class. Sample sizes range from 52 to around 9500, and the estimated completion dates ranged between November 2021 and June 2024. We also identified nine cohort studies, six in the SGLT-2 inhibitor class, two GLP-1 studies, and one for the DPP-4. The sample sizes range from 20,000 to 232,000, and again, the completion dates range between December 2021 and August 2024. Two of these studies were estimated to have been completed in 2020 and one in 2019. But again, at the time of this surveillance report, no publications related to these studies had been identified. So moving on to kind of the FDA actions part of the surveillance report. In terms of new drugs and formulations, we noted that subcutaneous exenatide extended-release that was marketed as Bydureon and Bydureon pen was discontinued by the manufacturer in March of 2021 due to business reasons. They stated that this was due to business reasons. It was not due to issues of safety, efficacy, product quality, or manufacturing issues. We also found that exenatide extended-release is available on the brand name Bydureon Bcise with the same formulation and a new auto-injector pen that doesn't require titration or reconstitution before use. We also identified two new indications for drugs of interest. So for dapagliflozin, an SGLT1/2 inhibitor, there was a new indication to reduce the risk of kidney function decline, kidney failure, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease with or without Type 2 diabetes. And that indication was approved in April of 2021. For empagliflozin, in the same class, there was a new indication to reduce the risk of cardiovascular death plus hospitalizations for heart failure in adults with heart failure with reduced ejection fraction, again, with or without Type 2 diabetes. And that was approved in August of 2021. We also identified two new harms in interventions of interest. So in June of 2021, the FDA actually removed a warning for risk of increased LDL cholesterol from the prescribing label of the fixed-dose combination of empagliflozin with metformin products, so that was a removal of a harm rather than an addition. However, in June 2021, the FDA also noted that they were evaluating the need for regulatory action for a potential signal of drug-induced liver injury for GLP-1 agonists both alone or in combination with long-acting insulin. On the next slide, you can also see that we also identified a series of other new harms. So both in the

classes of DPP-4 inhibitors, so that is primarily sitagliptin alone or in combination, as well as in the GLP-1 agonist class, so that's semaglutide, liraglutide, and exenatide. You can see the details here of those, and they were approved from around November 2020 through to June 2021. And on the next slide, you can see the new harms that were added for the SGLT-2 inhibitors, primarily empagliflozin, either alone or in combination, and those were all added to the prescribing label in June of 2021. And just of note is that final line at the bottom of the table. They also added a box warning for the combination with metformin around lactic acidosis. So in summary, you can see on this next slide that across the two surveillance documents, we've identified four new published studies since the most recent systematic review, 20 of which were identified in this surveillance document. So overall in the two surveillance documents, we have not identified any head-to-head trials, but we have identified one new published randomized control trial looking at liraglutide as add-on therapy, four new placebo-controlled randomized controlled trials that were identified in previous surveillance reports, and 35 cohort studies in total, of which 20 we have just reviewed in this surveillance document. We also identified 31 ongoing studies, one head-to-head study, one trial comparing these drugs with dietary intervention, eight comparing the drugs with a standard of care, 12 placebo-controlled trials, and nine potentially eligible cohort studies. And on the next slide, you can also see that in terms of the FDA actions, we identified one new drug that was identified in the previous surveillance document. So that is that own comparison of the combination of empagliflozin, linagliptin, and metformin in an extended-release formulation. We also identified six new indications, two of which were included in this surveillance document, and they relate to dulaglutide, semaglutide, dapagliflozin, and empagliflozin. And then on the next slide, you can see we have also identified between the two surveillance documents 11 new warnings. You can see the details in the GLP-1 agonist class, so sitagliptin, semaglutide, liraglutide, exenatide, and then in the SGLT-2 inhibitors around empagliflozin. And then specifically noting that final combination noting the risk of volume depletion with the use of the extended release. And then finally, we also identified two updated safety labels, one in this surveillance document. So in the previous surveillance document, we noted that for empagliflozin, the black box warning of leg and foot amputation was removed. However in this surveillance document, for the combination of empagliflozin with metformin, there has been a black box warning added around the risk for lactic acidosis. Thank you.

- Jordan Storhaug: Thank you, Beth. Any questions from the Committee? Okay. We don't have any scheduled stakeholders, and I don't see any hands raised, but Leta will let me know if there is somewhere else. Otherwise, we'll take a look at the motion.
- Leta Evaskus: This is Leta. I do not see any stakeholder hands raised, and we have these in three different motions so let me -- I'm sorry, this should not be NA here because this is a surveillance.
- Jordan Storhaug: So, does anybody have any problems with their surveillance?
- Diane Schwilke: So not hearing anything. This is Diane Schwilke. I will move to accept the surveillance as adequate.
- Alex Park: This is Alex Park. I will second that motion.
- Jordan Storhaug: All in favor, please say, Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay, then we can turn our attention to our motion. And we have the previous one listed for us already.
- Jon MacKay: This is John here. I just note that we specifically call out the cardiovascular benefits requirement for one therapeutic agent. Should we add something similar to that in terms of renal protective effects, given the new indication?
- Donna Sullivan: I'm sorry, this is Donna, can you repeat that question again?
- Jon MacKay: We called out specifically including one drug with cardiovascular benefits. Should we include something in addition, kind of a corollary to that with the renal protective effects?
- Donna Sullivan: That is completely up to you if you want to do that or not.
- Diane Schwilke: So this is Diane Schwilke.
- Donna Sullivan: Was that in the data?

- Diane Schwilke: That's more going to be with the SGLT-2s, though. Correct? Because we are doing three separate motions?
- Jordan Storhaug: [Indistinct] specifically think of any indication for the empagliflozin.
- Donna Sullivan: This is Donna. So this doesn't update it. This was a surveillance. Is that correct?
- Leta Evaskus: Yes.
- Donna Sullivan: Okay. So was the renal indication included in the original review of the data?
- Ryan Pistorosi: I'll go on the DERP website and look at the last updated report.
- Leta Evaskus: Or if Beth, if you remember.
- Ryan Pistorosi: It looks like this was the February 2020 DERP report. That was probably reviewed in mid-2020.
- Beth Shaw: Yes. Let me just have a quick dig around. I've just lost it. Yeah, so the actual report. Yeah, the latest update was in February 2020. And I don't know specifically if that did include renal. I'm sure it would have done because we saw the renal outcomes in this study. So I'm sure it would have been looking for harms.
- Jordan Storhaug: So I think we do have a little bit of time, as I don't think that applies to the drugs we're currently looking at. So I may suggest that we focus on these ones here and then maybe I'll ask that to give her a formal report before we move on to the SGLT-2 medications.
- Donna Sullivan: Sounds good.
- Kavita Chawla: I think if Committee members agree with not changing anything in the motion, I can start. After considering the evidence of safety, efficacy, and special populations for the treatment of diabetes, I move that the GLP-1 agonists of dulaglutide, exenatide, exenatide ER, liraglutide, lixisenatide, semaglutide in all combinations listed in this subclass are safe and efficacious. GLP-1 agonists can be subject to therapeutic interchange on the Washington Preferred Drug List. Therapeutic interchange is allowed only within each diabetes subclass. At least one drug with cardiovascular benefits

needs to be preferred on the PDL for patients with proven cardiovascular disease. Albiglutide cannot be preferred on the PDL.

Jordan Storhaug: Do we have a second?

Diane Schwilke: This is Diane Schwilke. [Cross-talk] -- I second.

Jordan Storhaug: Thank you. All in favor, please say Aye.

Multiple speakers: Aye. Aye. Aye. Aye. Aye.

Jordan Storhaug: Any opposed? Okay. Now maybe then I think as we pull up the next motion, I'll invite back to kind of update us on whether we have had a report that specifically goes towards a renoprotective benefits of our SGLT-2s.

Beth Shaw: Yeah, I'm just looking at the report now. And certainly it wasn't called out in the grade summary. So this is for SGLT-2 inhibitors. Is that right? Yeah.

Jordan Storhaug: Yes, that would be current.

Beth Shaw: Okay. I can't see. It's not called out in the grade table specifically. There may be some information in the detail of the trial, but I can't really see anything specific about renal protection.

Ryan Pistorosi: This is Ryan. I also have the report open. I do see that there was one study on Invokana that did have it as not the primary outcome but one of the outcomes. Most of the data around renal seems to be either in the inclusion population, so looking for people that did have some renal disease, but the outcomes of those studies were more focused on cardiovascular or all-cause death or that they were excluded from a study and did not have anyone with, let's say, end-stage renal disease or other compromised renal condition. So it really is buried deep in the report. And Beth, I'm looking at page 98, and that's the only time that I can see it included as an outcome.

Beth Shaw: Yes. I completely agree with your summary. I'd say if it's in there, it's pretty buried. Yeah, I can see that trial now.

Ryan Pistorosi: Okay. So Donna, your thoughts?

- Donna Sullivan: Well, normally, we wouldn't include the indication if it hasn't gone through a full review, and it doesn't sound like there is much in the report about the renal effects.
- Beth Shaw: Yeah. I mean, I guess the focus was the cardiovascular outcomes specifically. I know that they are interrelated, but it may well be that that was why it's not been called out specifically.
- Ryan Pistorosi: And this is Ryan. Yeah. Just looking at the search strategy. It doesn't look like it was included within the original scoping for that report. But on that point, Jon, this may be of interest to DERP states in the future. And the reason that we're bringing this as I think a topic brief today is because it did not move forward when the states voted on next year's DERP plans. So that's why we're bringing it today in this state, and we can propose this when we do topic nominations in the future.
- Okay, if everybody is okay with the motion as stands, then I will make a motion. After considering the evidence of safety, efficacy, and special populations for the treatment of diabetes, I move that canagliflozin, empagliflozin, dapagliflozin and all combinations in the subclass are safe and efficacious for the treatment of their approved indications. SGLT-2 inhibitors can be subject to therapeutic interchange in the Washington Preferred Drug List. Therapeutic interchange is allowed only within each diabetes subclass. At least one drug with cardiovascular benefits needs to be preferred on the PDL for patients with proven cardiovascular disease.
- Jon MacKay: This is Jon. I will second that.
- Jordan Storhaug: All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay, very good. Looks like we got through our agenda for the morning, so we'll take a break for lunch. Leta, do you [cross-talk] --
- Leta Evaskus: Hey now, Jordan?
- Jordan Storhaug: Yeah.
- Leta Evaskus: Sorry to interrupt. This is Leta. We have one more motion.

Jordan Storhaug: Oh, yeah. Thank you.

Kavita Chawla: This is Kavita Chawla. After considering the evidence of safety, efficacy, and special populations for the treatment of diabetes, I move that DPP-4 inhibitors linagliptin, saxagliptin, alogliptin, sitagliptin, and all listed combination drugs in this subclass are safe and efficacious. DPP-4 inhibitors can be subject to therapeutic interchange in the Washington Preferred Drug List. Therapeutic interchange is allowed only within each diabetes subclass.

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

Jordan Storhaug: All in favor, please say Aye.

Multiple speakers: Aye. Aye. Aye. Aye. Aye.

Jordan Storhaug: Any opposed? Okay, with that then I think we're ready to go for lunch. Leta, would you like us back at 12:30 or in 30 minutes? Let's do 30 minutes. So let's come back at -- let's just say 12:45.

[break]

Jordan Storhaug: Looks like it's about time for that. So I think we can get everything started. Our first item on the agenda is an update on kind of our process from Donna Sullivan.

Donna Sullivan: Hey, good afternoon. Can you hear me okay?

Jordan Storhaug: We can hear you Donna. Yeah.

Donna Sullivan: Great. Thanks. So, Leta, you can go ahead and go to the next slide. So what I really wanted to do is give you just a brief overview of the DUR Board and the P&T Committee and provide some explanation of the differences of the two bodies, the P&T Committee being one set of one body that you are Board being under a different regulatory process. So I also wanted to do a look at some of the rules and responsibilities of those of us who attend the meetings and staff the meetings. Myself, I'm the Chief Pharmacy Officer for the Health Care Authority. I pretty much oversee prescription drug purchasing strategies, which includes the Drug Price Transparency Program, the Prescription Drug Consortium. Soon we'll be implementing and creating a

Prescription Drug Affordability Board as well as managing the pharmacy benefits for Medicaid and the Public and School Employees Benefits. We have Ryan Pistorosi, who is the Assistant Chief Pharmacy Officer who primarily oversees our PEBB and SEBB Program as well as managing the clinical policy development within both Uniform Medical Plan and Medicaid. And then he also is our representative on the Drug Effectiveness Review Project Governance Board and on that Steering Committee, as well. We have Leta Evaskus, who is the Northwest Prescription Drug Consortium Operations Manager. The Northwest Consortium has actually rebranded. Now, we are called ArrayRx, and we've just launched our new discount card earlier this year. Leta also manages the P&T Committee/DUR Board meetings and the contracts with the Committee members. She schedules the meetings and manages all the logistics. She manages the Preferred Drug List, the Washington Preferred Drug List that's posted on our WPDP website, and then she oversees the cost analysis process that Ryan goes through to determine, which will be the preferred drugs for UMP and L&I after you have made your motions. You can go to the next slide. We also have Amy Irwin, who is our Medicaid Pharmacy Operations Manager. She manages the Fee for Service Medicaid Program. She has a team of about almost 10 people now, I think. And she also assists with the Washington PDL cost analysis with some of the points on the data for us. We also have Marissa Tabile, who is our Apple Health PDL Manager, and she also is the Drug Utilization Review Manager. So she is the one that is doing the day-to-day changes for the Apple Health PDL. So like when new NDCs come to the market, making sure that they get appropriately placed. Or if there is a new strength on the drug, making sure that that gets appropriately placed. There is Luke Dearden, who's one of our Clinical Pharmacists, as well. He helps us do some of the Clinical Policies and presents them to you. In addition to Marissa, we have Ryan Taketomo, also a Clinical Pharmacist that works pretty much on monitoring the pipeline of new products that are coming to market and identifying some high-cost drugs that we carve out of our managed care responsibility. Ryan also helps us with the clinical policies, as well. And then Joey Zarate, who is the Apple Health PDL Coordinator, he assists with the new drug report, as well, and does a lot of the configuration of the PDL drug classes in our Claims Processing System. And we also have representatives from Labor and Industries, Jaymie Mai, who is the Pharmacy Director for Labor and Industries. Doug Tuman, who also works at Labor and Industries. And then Christy Pham from Labor and Industries, as well. Next slide. And then what I didn't mention what we don't have on here, we also have representatives from our Managed Care Plans. We have five managed care

plans, Molina Coordinated Care, Community Health Plan of Washington, United, and Amerigroup. And we have invited their pharmacy directors to attend these meetings, as well. So a background on the Washington Prescription Drug Program. In June of 2003, the Legislature created the Washington PDP, and it really was built around having an evidence-based formulary. And it was a coordinated effort between the health care authorities, our Uniform Medical Plan, our self-funded program, Medicaid, which was in DSH at the time, and then Labor and Industries. And the Washington PDL is a subset of about 35 drug classes now. So it's really a subset of each program's overall formulary or drug list. It's not an all-comprehensive preferred drug list, and that's why we specifically call it the Washington PDL and not labeling it Medicaid or UMP or L&I. And really, the goal of this legislation was to look at the evidence when we were deciding which drugs that we were going to cover. And also at that time prescription drug costs were increasing. In 2003, it was a much different array of drugs that we were looking at. And over time the program has changed a little bit as the drugs have become more expensive and more complicated with multiple indications for that are a wide variety of indications for a single drug as we discussed earlier today with the TIMs class. So next slide. So the WPDP really has two components. Part of it is the Washington Preferred Drug List. So the drugs that are reviewed by Oregon Health Sciences University, those drug classes are the drug classes that make up the Washington Preferred Drug List. It also has the Endorsing Practitioner Therapeutic Interchange Program. We'll go into more detail about that. It established the Pharmacy and Therapeutics Committee, and a subsequent piece of the legislation established the Northwest Prescription Drug Consortium, which is built off of the evidence-based program in the previous legislation. Next slide. So our P&T Committee members, we went with 10 members. The membership really needs to mirror the Medicaid requirements for the DUR Board. The federal requirements for the Drug Utilization Review Board states that the Committee or the Board cannot be more than 51% [indistinct] on physicians or pharmacists. And so we chose to have four physicians, four pharmacists, one physician assistant, and one advanced nurse practitioner on the Committee so that we can make sure that the Committee is well balanced. We also try to make sure that we have an array of provider types or specialties. So focusing on mental health as well as internal medicine so that we have a broad array of representation on the Committee. The rules that we put into place says that the Board or the P&T Committee will meet at least quarterly. However, we chose to meet every two months so that we could do both P&T Committee information or activities as well as the required Drug Utilization

Review activities for the Medicaid Program. The Committee reviews the reports that are prepared by the Drug Effectiveness Review Project, and that's really looking at the comparative efficacy and safety of these medications in special populations. And whenever possible, we really try to look at comparative efficacy rather than just randomized placebo-controlled trials. So we're really trying to look at, is one drug better than the other? The Committee will determine which drugs are equally safe and effective based on that evidence that is presented. And then we'll also be looking at special populations. So I'm going to give a really old example. Back in the day, Ramipril had the HOPE study, and it was found to have cardiovascular outcomes, similar to what we were talking about today. And so we're looking to see is there a special population where if we don't make a drug preferred wide open for everyone, is there a targeted population that we would want to make sure that there is easier access to it for people that meet the criteria of that population? And then the Committee also determines whether or not it is appropriate to do therapeutic interchange within a drug class on the PDL. Next. Okay, so the Drug Effectiveness Review Project, I think the states in here might be a little out of date. I don't remember off the top my head who is all in it.

Leta Evaskus: This is Leta. I updated them.

Donna Sullivan: Oh, great! Thank you, Leta. I wasn't sure. I'm like, I know, there have been some changes, and I haven't been attending recently. So we do have 14 states, most of them are really represented by their Medicaid Programs. Washington is one of the only states that really uses the DERP information to both inform their public employees as well as the Medicaid program. We're trying to have like the One Health Care Authority when we come to clinical policy decision-making. Go ahead, and next slide. The DERP reports. These have changed over time, and we have several different types of reports. We have a new class review, and these types of reports are where new drugs are eligible for inclusion. So how we started it is we would commission a report that would do a full review of the evidence on a particular drug class, and the DERP or the Center would look at all of the studies within a particular period of time and go through. They would grade the evidence, and they would do any comparative efficacy analyses on those particular drugs and really digging into safety and efficacy, and we call them New Class Review, an update to an existing class. There could be a single drug addendum. Let's say a new drug comes out in a class and we just did a full update, but the information was published after the cutoff period of the report. So we want

to really dig into that particular drug so we can add it to the PDL. Or a particular topic brief -- so a topic brief is like looking at the individual studies that are out there, lifting the lid a little bit to see what the efficacy is for the drugs, but it's not a full review of the evidence, like an updated report. But those are the types of reports where a new drug that is identified in that report is then eligible to be on the PDL. If it hasn't gone through that full review or a topic brief or a single addendum, the new products that weren't included in those reports are not eligible to be preferred on the PDL. They can be on the PDL, but they're not eligible to be preferred. We have surveillance reports that we conduct almost every year for each of the drug classes. And this is where if a new drug is identified in a surveillance report, it's not eligible for inclusion as preferred on the PDL. A surveillance report is really just what we saw today summarizing the availability of the new evidence that identifies the new drugs, new indications since the last review. It will summarize. Are there randomized controlled trials that have come out? Is there new comparative efficacy that has come out? Are there new safety information that's come out. But it doesn't go into the specifics of the studies. They don't go in and grade the evidence. They don't do any comparative efficacy or safety comparisons, which is why any new drugs identified are not included or not eligible for the PDL. We want to make sure that this is an evidence-based PDL and not just adding "me-too drugs" into the mix without having them go through a full-blown review. Any questions? I'm going to pause because that's a lot of information. Any questions on the report types? Okay. Go ahead, Leta. And if you do have a question, just raise your hand, or interrupt me, and I will try to answer it to the best of my ability. So what is our process? The P&T Committee makes recommendations on the PDL based on evidence. We then will pull data from Labor and Industries and Uniform Medical Plan, and we'll do an actuary cost analysis looking at the utilization and the net cost of rebates that UMP and L&I pay for those particular drugs. The workgroup, who consists of most of the clinical pharmacists and the L&I staff that I mentioned earlier, reviews the cost analysis. They might make changes to the analysis or ask the actuary to make different scenarios where they are shifting with different drugs being preferred and what would happen. And then they make recommendations for the Agency directors to approve. And then we'll send that memo to the Agency directors with our recommendation and the rationale why, along with a cost analysis. And the Agency directors then approve any changes to the Washington PDL that will be made. The staff then sends out a notice. Usually, it comes from GovDelivery about what changes to the PDL have been made, and then a certain point in the future, usually on the first day of a particular quarter, we

will implement those PDL changes. Next slide, Leta. Oh, I got a hand. Kavita, go ahead.

Kavita Chawla: Hey, Donna. Thank you. So if you could go back to the previous slide, please. So a P&T Committee is an open-to-public meeting. Is the workgroup that reviews the cost analysis, is that meeting open to public? Basically, are any of the other [indistinct] after the P&T meeting, are any of the other [indistinct] open to public?

Donna Sullivan: No. The rebates are confidential and proprietary, so that's why it's done with state staff, and so it can't be open to the public for that particular reason. The Agency Director's memos are publicly disclosable, and then the staff notices of the PDL changes are sent out publicly. So the actual workgroup decision-making is not an open public meeting.

Kavita Chawla: So the cost analysis part of the cycle is what is not open to the public.

Donna Sullivan: Correct. Yeah.

Kavita Chawla: Thank you.

Donna Sullivan: Okay, so the PDL is a list of drugs selected by the Agency. It's really focusing on the drug classes that are reviewed by the Drug Effectiveness Review Project. We began using it in January of 2004, and currently, it's only the Washington specific drugs that are listed as preferred on the Washington PDL are only used preferred for Uniform Medical Plan and the Department of Labor and Industries. Our Medicaid Program follows the P&T Committee's motions, but we do our own cost analysis independent of UMP and Labor and Industries because of the Federal Rebate Program for Medicaid makes the prices for the Medicaid drugs so much different from the prices that are offered to the more commercial-like plans. Next slide. Status of drugs on the PDL. So if a drug is preferred, it doesn't have therapeutic interchange. So it might have a prior authorization to make sure that it's being used for a clinically-appropriate indication, but we don't do therapeutic interchange. Non-preferred drugs are subject to therapeutic interchange under certain circumstances. So if they are included in a new drug class review -- so that list of reports that I said -- an update to an existing class or single-drug agenda or a topic brief, then they would be subject to therapeutic interchange. There are certain classes of drugs that the Legislature determined should not have therapeutic interchange, so they got them refill

protection. So the statute says unless. It's subject to therapeutic interchange unless it is in one of the following classes. So the antipsychotics, the antidepressants, antiepileptic drugs, chemotherapy, HIV medications, immunosuppressants. And, again, at the time that was really targeting transplant rejection medications and hepatitis C drugs. And the hepatitis C drugs is really specific to the injectable drugs the way the statute is written. And then it's allowed in therapeutic interchanges also, we make sure that the Committee determines whether or not it's really appropriate to do therapeutic interchange on other drug classes. We don't want to be changing a medication on a patient if it's not clinically appropriate in order to do that interchange. And then it also has to be allowed by an endorsing prescriber. So I think we're going to go into this in a subsequent slide, but the prescriber has to write "MACE substitution permitted." If a prescriber writes and signs "Dispense As Written" on a prescription, then therapeutic interchange is not allowed, and the non-preferred drug gets dispensed. Next slide. Status of drugs on the PDL. If it's in a PDL class but not included in the DERP report, it's covered according to the program benefit design. Therapeutic interchange doesn't apply, and when therapeutic interchange doesn't apply, DAW does not apply either. So if the Committee says a class cannot be subjected to therapeutic interchange, if a prescriber writes for a non-preferred drug and signs it, "Dispense As Written," we do not honor the "Dispense as Written." They still have to go through the preferred product or through a prior authorization process. Drug classes not on the PDL are covered according to the program benefit design. We also have an archive process. HCA recommends drug classes to be archived. When the Drug Effectiveness Review Project has stopped doing any surveillance on those drug classes -- examples are the beta-blockers, ACE inhibitors, and antihistamines. We no longer review those on an annual basis. The DERP project doesn't have the funding to continue to do surveillance reports on older medications where there is not a lot of new data coming out into being published. The Committee will review the final surveillance report. They'll vote on whether the drug class is appropriate to archive, determine if therapeutic interchange and "Dispense as Written" rules are appropriate to continue without further clinical review. And then we ask that you allow us to make changes to these drug classes if there are changes in cost, but still following the recommendations from the last motion that was given to the agencies. We keep the archived drug classes on the PDL, and then either the Committee or the work group may reactivate any archived drug class if we feel that there are significant changes made in the evidence base for the class or for its indications or any safety issues that might come out. We could bring

them back and then do another evidence review. Next slide. So the Endorsing Practitioner Therapeutic Interchange Program I am going to go into a little bit more detail. It created a process for HCA to have prescribers in Washington sign up to endorse the list. They would review it, they sign up, and we have a file of endorsing providers that we use when we adjudicate claims, and we can identify who has signed up to be an endorsing provider. When the prescription comes through for a non-preferred drug, the pharmacist is directed to automatically interchange the preferred drug for any non-preferred drug and notify the prescriber of the change. And this was really targeted to try to reduce the administrative burden of having a Preferred Drug List, or having the pharmacist have to call and the prescriber prescribed Nexium, and at the time Prilosec OTC was preferred, we didn't want the pharmacist to have to call the doctor to get a new prescription to dispense Prilosec OTC. I remember as a dispensing pharmacist, a lot of times the doctor is like whatever proton pump inhibitor is on the formulary, dispense that one, but we would still have to call to get a prescription. So really the idea was for this to reduce that administrative burden on both the prescriber as well as the dispensing pharmacist, especially when drugs were relatively safe and effective, and it didn't really matter which one you tried, especially if it was a new start. Again, it was therapeutic interchanges allowed unless it's a refill of one of the protected classes, or if the doctor or prescriber writes "Dispense as Written" on the prescription. If so, then they will be allowed to dispense the non-preferred drug. We have about 7200 endorsing practitioners in the state right now, and I get asked all the time, what percentage of all prescribers are endorsing practitioners? And I don't know. I think over 20,000 licensed prescribers, but we don't know if they're actively practicing within the state or if they are retired, but they have an active license. So all I could tell you is how many are endorsing, and it's difficult to give percentages if that was an interest to anybody. Next slide. So we have the DUR Board. The Drug Utilization Review Board is required by Section 1927 of the Social Security Act, and it is specific to Medicaid. And that's why we have really the formal procedural adjourning of the P&T Committee and convening on the DUR Board. The P&T Committee recommendations for the Washington Preferred Drug List are recommendations to the Public Employees/School Employees program, as well as Labor and Industries and Medicaid, all three of those programs. Whereas the DUR Board is specific to Medicaid. So the clinical policies that we're bringing to you or quantity limits that we're talking about, the drug classes that are reviewed by Magellan, those are specific to Medicaid, the Apple Health PDL in our Utilization Management Program. So we use the

same Committee members for convenience, but we want to make sure that we have that procedural separation between the two bodies. So the DUR Board recommends programs or interventions based on data that are provided. I know we haven't looked at a lot of data in a while since the Apple Health PDL has been created. We review and approve DUR Programs proposed by Medicaid, which are the clinical policies that we do bring. We have that collaborative interaction where you're looking at the specific criteria and helping us come up with a good policy that is medically sound. And we ask that you review and approve those so that we're making sure that they have a nice clinical review as well as being reviewed in an open public setting so that we get stakeholder input as well as the Committee input. And then we can also engage in provider education activities when appropriate. And then in the past, we have done opioid-related provider education activities. Next slide. The Apple Health PDL. We began implementing it in January of 2018. We did some quarterly phasing in of the implementation, and we completed the final drug class implementation, I believe, it was April of 2020. We have, I believe, it's more than 484 drug classes now as sometimes we identify we need to split a drug class into two different classes, but we still are participating in the top supplemental rebate pool that is administered by Magellan and Medicaid administration. So our Apple Health PDL process we have Magellan that reviews the drug classes. Those are presented by Umang. And then we will look at its clinical merit. It is relative to the other medications in the same class. Magellan reviews the published literature, and peer-to-peer clinical trials. And then they develop a therapeutic class review, and then the slides that are presented are a summary of that therapeutic class review. They are looking at data regarding efficacy, safety, adverse events, and side effects also compared to other drugs in that class. Magellan presents those class reviews, and then from that analysis, the Board determines an agent's superiority, equivalency, or inferiority relative to those different classes, and we do that through the motions that you make. So if you are concerned that you have the same opportunity in the motion to change the motion as you would from the P&T Committee. The next slide. We also have a financial analysis or cost analysis. So Magellan manages maybe about 200 drug classes, and then twice a year they will do a cost analysis when they get updated rebate offers, and they give to us, they call them cost sheets, and so we will review those drug classes that have either new supplemental rebate bids and then also looking at what their current costs are, and then we'll make any decisions to make any changes to the PDL. And then, again, after we consider the Board's recommendations as well as the P&T Committee recommendations, and we

make sure that any changes that we're making are in compliance with those recommendations. Next slide. And I think this was the last slide. Just a bunch of acronyms that we try to keep adding to our lists so that when we're using them, you have a cheat sheet. And I believe when we were in public, it used to be in the back of your notebooks. But now that we are not meeting in public, we'll just keep this handy for you when we have the meetings. Any other questions? I don't know, Kavita, if you have a new question or if you just didn't put your hand down from before. Okay, great. Any questions?

Jon MacKay: Donna, this is John Mackay. I was just wondering, do any of the MCOs recognize the TIPS Program?

Donna Sullivan: No. Thanks for bringing that up. So the Therapeutic Interchange Program was a good idea, but it did actually exclude the fully-insured managed care plans from the public employees and school employees as well as the Medicaid program. So it only applies to Medicaid Fee For Service, Labor and Industries, and the self-funded ERB programs for PEBB and SEBB. I also don't think it happens in practice. I mean, certain independent pharmacies under collaborative practice agreements were already doing some sort of therapeutic interchange before the law was passed. But it was from our experience, a lot of the larger pharmacy chains had legal advice that prohibited them from doing it, even though it was allowed under the law. There was concern about liability from the pharmacist's perspective of making a change to a prescribed medication without getting the doctor to give an order for a new medication. So I don't think it happens a lot, even though it is a possibility. And we still go through the motions of having the therapeutic interchange edits in our claims processing system, but I don't think it occurs that often. Any other questions? Well, great. Thank you very much. Leta, I'll give it back to you or Jordan.

Jordan Storhaug: Yeah, I think we're ready to start doing some of that work that you're talking about for the DUR Board. So we'll convene the Board and start with our asthma and COPD agents. And we'll start with our presentation from Umang.

Leta Evaskus: And I'm going to turn this over to Marissa.

Marissa Tabile: Okay, this is Marissa. Umang, are you able to see the slides on your screen?

Umang Patel: I can. Yeah.

- Marissa Tabile: Okay. Perfect. I'm ready.
- Umang Patel: Okay. Awesome. Thank you. I'm Umang Patel from Magellan Medicaid. We'll be reviewing a few topics here. If we can go to slide 3, the first one being COPD agents. Just to remind/refresh the Committee's memory. Next slide, please. If you look at the screen and you see COPD agents, sometimes the topic names of the therapeutic classes don't always align one-to-one. The top line will be how Magellan Medicaid refers them to, and then the subsequent asthma, COPD agents, anticholinergics, PDE4 inhibitors, muscarinic agents, and beta-agonist combinations, and long-acting muscarinic agents are the subclasses that are on the Apple Health PDL that fall under this. When we do create these clinical update slides, we look at roughly the past 12 months or so worth of significant clinical updates. That can be new medications, new indications, formulations, recalls, or anything that is significant to prescribers and the public. And if there are no updates within the last 12 or 13 months, then there is no subsequent slide, and it goes right into the next topic. This is the first one that is just like that. So for the COPD agent class, there are no significant clinical updates. Marissa, I will pause because I'm not sure if there is a separate voting that needs to be done or if I just keep going to the next topic.
- Marissa Tabile: Hey, Umang. We do have a separate motion for this. So, actually what we can do is we can just do the motion at the end of the other asthma and COPD agents.
- Umang Patel: Okay.
- Marissa Tabile: So, actually, Leta, I apologize. This was an oversight on my end. Do we have any stakeholders for this particular section on the agenda?
- Leta Evaskus: Let's see. Yes, we do. We have two.
- Marissa Tabile: Okay. I think then, Umang, we'll just continue on with the motion then after this section. So, Leta, we'll go ahead, and I need to actually show the PDL, so let me show the PDL.
- Jordan Storhaug: Okay. No problem.
- Marissa Tabile: Yeah, no worries. Okay. This is Marissa. So, DUR Board, this is the Apple Health PDL. This is just showing you all the drugs that we have preferred and

non-preferred in those anticholinergics, PDE4s, long-acting muscarinic agents, combinations, and the long-acting muscarinic agents class. So as you can see -- I'll just go down the list pretty quickly -- for all the anticholinergics, we have pretty much all of the products in that class preferred. This is not an order. I apologize, it's in alphabetical order -- for PDE4s, we have just Daliresp in that class. So that is the only preferred product. It's preferred on our AHPDL. For the long-acting muscarinic beta agonist combinations right here, we do have Stiolto Respimat is our preferred product on the AHPDL. And then just going to the long-acting muscarinic agents right here, the preferred product in that class is Spiriva HandiHaler. So I'll go ahead and pause if the DUR Board has any questions. If not, we can go ahead, and we'll move over to the stakeholders and then the motion after that.

Jordan Storhaug: Okay, it sounds like we are ready for our stakeholders then of which we have those two. The first step would be Mark Maneval of Boehringer Ingelheim, and then after that would be Carrie Johnson of Amgen.

Leta Evaskus: This is Leta. I do not see Mark on the call. So why don't we move to Carrie Johnson, and then we have a hand raised.

Jordan Storhaug: Perfect. Carrie Johnson. Are you ready?

Carrie Johnson: Can you hear me okay? Yep? [cross-talk] --

Jordan Storhaug: [cross-talk] Yes, we can hear you. [cross-talk] Go ahead and start. [cross-talk] You have three minutes.

Carrie Johnson: Okay, thank you. My name is Carrie Johnson. I'm a pharmacist with Amgen Medical Affairs. Thank you for the opportunity to speak in support of Tezspire (tezepelumab). Tezspire is the first-in-class biologic for severe asthma that acts at the top of an inflammatory cascade by targeting thymic stromal lymphopoietin (TSLP) an epithelial cytokine blocking TSLP that reduces biomarkers and multiple cytokines associated with inflammation including blood eosinophils, IgE, IL-5 and IL-13, among others. Tezspire is the first and only biologic to consistently and significantly reduce asthma exacerbations across Phase 2 and 3 clinical trials and in a broad population of severe asthma patients irrespective of kidney biomarkers, including blood eosinophil counts, allergic status, and fractional exhaled nitric oxide. As such, Tezspire is the first and only biologic for severe asthma that does not have a phenotype, eosinophilic or allergic or biomarker limitation within its

approved label. Tezspire was originally granted FDA breakthrough designation for patients with severe asthma without eosinophilic phenotype in September 2018, then received FDA approval in December 2021 for add-on maintenance treatment of adult and pediatric patients ages 12 years or older with severe asthma following a priority review by the FDA. The recommended dose of Tezspire is 210 mg administered subcutaneously once every four weeks by healthcare professionals. Please see the full prescribing information at [amgen.com](https://www.amgen.com) for further details. Patients with severe uncontrolled asthma represent a small portion of the overall asthma population. However, these patients have a disproportionately high burden of disease. Although other biologics are available, up to 20% of severe asthma patients are ineligible for existing biologic therapies, and approximately 35% of severe asthma patients are uncontrolled. Tezspire represents a novel approach to treating asthma, severe asthma, by inhibiting TSLP, an upstream mediator of multiple downstream inflammatory pathways, Tezspire uniquely addresses the heterogeneity of severe asthma. Within the prescribing information, there are two pivotal registrational trials. Both trials are fully published. PATHWAY was a Phase 2 trial that supported breakthrough designation. NAVIGATOR was the pivotal Phase 3 trial that supported priority review status. Both trials were 52-week randomized, placebo-controlled trials that were designed to evaluate the efficacy of Tezspire on asthma exacerbations in patients with severe asthma. Importantly, there were no restrictions on biomarker status or eligibility. Tezspire demonstrated statistically significant reductions in asthma exacerbations across these two clinical trials, showing a 71% reduction in NAVIGATOR and a 56% reduction in PATHWAY. It is the only asthma biologic to demonstrate statistically significant reduction in exacerbations in patients with eosinophils less than 300 per microliter. The FDA reviewed this as a key differentiator and thus supported the breakthrough designation. From a safety perspective, Tezspire had an adverse event profile similar to that of placebo. The most common adverse events being pharyngitis, arthralgia, and back pain. In summary, Tezspire is the first and only biologic for severe asthma without phenotypic or biomarker limitations and has consistently demonstrated statistically significant reductions in annual asthma exacerbation rates across the registrational trials. Please make Tezspire available to your members per label. Thank you for your time. [cross-talk] --

Jordan Storhaug: [Cross-talk] Thank you so much, Carrie.

Carrie Johnson: [Indistinct] Yep. Thank you.

- Jordan Storhaug: All right. And then next up we have Donna Thomas. We'll have you next if you can just let us know who you are representing, as well.
- Mark Maneval: So thanks. This is Mark Maneval. Can you hear me?
- Jordan Storhaug: Yes, we can hear you.
- Mark Maneval: Awesome. Donna and I work together for Behringer Ingelheim, so I'm going to give stakeholder discussion for BI. Are you ready?
- Jordan Storhaug: Yes. Go ahead.
- Mark Maneval: Super. So again, my name is Mark Maneval. I'm a pharmacist. I was born in Washington, I live in Washington, and I work in Washington. I'm a Value Evidence Liaison for Behringer Ingelheim, and I'm going to talk to you today to draw your attention to some important guidelines and recommendations for the treatment of people with COPD that Dr. Patel mentioned earlier in this discussion. COPD is a heterogeneous condition with wide variation in clinical manifestations that require individualizing the pharmacologic treatment approach based upon exacerbation history, [audio cuts out] systems, side effects, and eosinophil count. In 2020, GOLD released a revision to their 2019 report that provides clinicians with a non-biased review of the assessment, diagnosis, and treatment of COPD. Also in 2020, [audio cuts out] the ATS and ERS, the American Thoracic Society and European Respiratory Society, issued official updated clinical practice guidelines for the pharmacologic treatment of COPD with the following recommendations. LAMA and LAMA/LABA remain the cornerstone of COPD [audio cuts out] maintenance treatment. Triple therapy is not recommended as initial maintenance treatment. Inhaled corticosteroid-containing regimens require assessment of risk versus benefit as regular treatment with ICS increases the risk of pneumonia, especially in patients with severe disease. For initial therapy, GOLD recommends the threshold eosinophil count of 300 to initiate inhaled corticosteroid component in patients in Group D. In follow-up, GOLD recommends to consider the addition of inhaled corticosteroids to long-acting bronchodilators in patients with eosinophil counts greater than 100 cells/microliter, if they had two or more moderate exacerbations, or one severe exacerbation and to avoid ICS in patients with levels below this. Inhaled corticosteroid withdrawal or de-escalation should be considered in those with no exacerbations in the past year. Inappropriate use of inhaled

corticosteroids may be associated with an increased risk of side effects including pneumonia. Not all patients with COPD benefit from the use of inhaled corticosteroids. Several studies have shown extensive use of inhaled corticosteroids in patients for which they may not be recommended. GOLD ATS and ERS are unbiased collaborations of COPD experts reinforcing LAMAs and LAMA/LABAs a preferred treatment for the majority of patients with COPD. Thank you very much. If you have any questions, feel free to go to Behringer Ingelheim.

- Jordan Storhaug: Thank you, Mark. So then I think I don't see anybody else, and Marissa, then do you have a suggested motion for the Committee?
- Marissa Tabile: This is Marissa. Yep. I will go ahead and pull that up right now. Okay. It should be ready to go for you, Jordan.
- Jordan Storhaug: Thank you.
- Alex Park: This is Alex Park. Just a procedural question. Marissa and Jordan, I think the prior stakeholder, the first one who spoke in this section was talking about one of the monoclonal agents. Do we have a separate motion for that, or are we bunching all of these together? [cross-talk] --
- Marissa Tabile: Yeah. Dr. Park, we are actually doing a separate motion for the monoclonal antibodies. There is a different -- we wanted to separate that clinical update, so that's a little bit later, I believe, too. Two reviews after this particular motion. So that [cross-talk] --
- Alex Park: Okay.
- Marissa Tabile: Yeah. [cross-talk]
- Jordan Storhaug: So you're handling the anticholinergics right now and the PDE4 inhibitors, the long-acting muscarinic, including a combination. And then when we finish that, we will do the inhaled corticosteroids including their combinations. And then two away is monoclonal antibodies all covering asthma and COPD.
- Alex Park: Got it. Well, we will remember that stakeholder's comments for that section. I'll make the motion here. I move that all products in the drug classes listed on Slide 2 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 [audio cuts out] indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Diane Schwilke: Diane Schwilke. I second.

Jordan Storhaug: All approve please say Aye.

Multiple speakers: Aye. Aye. Aye. Aye. Aye.

Jordan Storhaug: Any opposed, please say Nay. Okay, we'll move on to our next topic, which is the inhaled corticosteroids. And back to Umang for his presentation.

Umang Patel: Perfect. Thank you. So in this class, we'll be reviewing specifically inhaled corticosteroids, inhaled corticosteroids, and their combinations. A little bit of background. So the prevalence of asthma in the United States continues to rise. More than 25 million Americans have asthma, and over 5 million of them are children. The NAEPP has defined asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role in susceptible individuals. Inflammation may cause recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. These episodes are usually associated with airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an increase in bronchial hyperresponsiveness to a variety of stimuli. And the studies have demonstrated the efficacy of inhaled corticosteroids and improving lung function, reducing symptoms, reducing frequency and severity of exacerbations, and improving the quality of life of patients with asthma. The 2007 National Heart, Lung, and Blood Institute states that inhaled corticosteroids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma. And the 2019 GINA full report advises that all patients with asthma should receive ICS-containing controller treatment to reduce the risk of serious exacerbation and to control symptoms. On the next slide here, a little update to the GINA guidelines in 2021. The guidelines offer a control-based management plan to adjust treatment in a continuous cycle of assessment, treatment, and the review of the patient's response as it relates to symptom control, future risk of exacerbations, and side effects. Equally important in this process is

identifying the patient's own goals regarding their asthma management to ensure improved outcomes in patients whose asthma is not adequately controlled on the preferred controller. Despite good adherence and correct technique, a step up in treatment may be added until control is achieved. This can be a short-term or sustained step-up therapy. If control is maintained for at least three months on the current regimen treatment, it can be stepped down to the lowest step in dosage that maintains that control. Patients should be started on treatment-based symptoms with infrequent symptoms beginning at Step 1, and patients with the most frequent, severe, or debilitating symptoms beginning at Step 4 that will be a reliever. Therapy can be considered for symptom management prior to exercise if needed. And the GINA 2021 guidelines describe two treatment tracks, Track 1, and Track 2, which you'll see on the next slide. But there is a lot on the next slide, so I just wanted to kind of give you a watered-down version. In Track 1, the reliever is an as-needed low-dose ICS-formoterol. And in Track 2, the reliever is an as-needed SABA, in which the alternative approach when Track 1 is not an option or not preferred for a specific patient reason. So on the next slide here, you can see Track 1, Track 2, and other controller options. And so I tried to bold what I had just stated in the previous slide, and Track 1 on line 5, the reliever is an as-needed low-dose ICS-formoterol. And then in Track 2, the reliever is an as-needed SABA, which is the alternative to Track 1, when Track 1 is not an option. So I know there is a little bit of information here. I'm just going to pause right there. Okay. All righty. On the next slide here we have the American College of Chest Physicians in 2020. A 2020 Expert Panel Report on the management of chronic cough due to asthma in non-asthmatic eosinophilic bronchitis in adults and adolescents addressed the role of ICS in these patients. For patients with chronic cough due to asthma as a unique system, they recommend ICS as a first-line treatment. If this is inadequate, the dose may be increased. Treatment can be switched to a leukotriene inhibitor, or an ICS/LABA can be considered. ICS is also recommended for first-line for chronic cough due to NAEB, although they are not FDA-approved at this time. And the NAEPP in 2020 recommended a similar classification of asthma severity and control to guide in the initiation and adjustment of therapy, respectively, asthma severity and control are defined in terms of two domains impairment and risk. The distinction between the domains emphasizes the need to consider separately asthma's effect on quality of life and functional capacity on an ongoing basis along with the risks of adverse events, such as exacerbations and progressive loss of pulmonary function. The group recommends a stepwise approach to asthma management, which is detailed in the table below. In addition, all

asthma patients should have a SABA inhaler for use on an as-needed basis. As needed ICS with formoterol is recommended instead for patients 5 to 11 years of age at steps 3 and 4, but SABA is recommended as an alternative. And lastly, for combinations as an ICS and for patients 5 years of age or older, the group states a single inhaler is preferable. Now on the next slide here, again, just to refresh the committee's memory, whenever there is an update to an existing medication, I try to bold the significant update. If it is a brand new drug, then everything will be bold. So in July of 2021, FDA-approved ArmonAir RespiClick for the maintenance treatment of asthma as prophylactic therapy in patients 4 to 11 years old. Previously, it was only approved for 12 years or older. So again, no adjustments to limitations precautions. In terms of the dosing, it's one inhalation of 30 mcg or 55 mcg twice daily and no adjustment in the availability here. There is a new generic here, the first FDA-approved generic for AstraZeneca Symbicort from Mylan. This occurred in March of 2022 this year, and the product will be marketed under the name Breyna, and the launch is expected later this year. On the next slide, and the final slide for this topic, we have ArmonAir Digihaler. So in April 2022, the FDA approved this medication for the maintenance treatment of asthma as prophylactic therapy in adults and pediatric patients 4 years of age or older. Previously, this also was indicated only in patients 12 years or older. Similar to the previous medication I mentioned, no changes in precautions, dosage, or availability here. I'll go ahead and pause right there for the Committee.

Jordan Storhaug: Marissa, did you want to review the PDL for us?

Marissa Tabile: This is Marissa. Yep, I'm ready to go.

Jordan Storhaug: All right, go ahead. So this is how convenient that you can see the inhaled corticosteroid [audio cuts out] combos and the inhaled corticosteroids on the screen. So just to go through it, we have Advair Diskus and Advair HFA, and also it looks like Budesonide and Dulera, and then some of the generic. Advair is fluticasone. Salmeterol generics. And then we also have Symbicort as our preferred agent. Everything else is non-preferred in the inhaled corticosteroid combinations. And then just for inhaled corticosteroids, we have Budesonide, Flovent Diskus HFA, and Pulmicort Flexhalers are our preferred products in those classes. So I will go ahead and pause for any questions.

Jordan Storhaug: Thanks, Marissa, for running us through that so effectively. We do have a stakeholder for this topic. That is Rochelle Yang, Teva Pharmaceuticals.

Rochelle Yang: All right. Can you hear me?

Jordan Storhaug: We can hear you. Go ahead, Rochelle. Thank you.

Rochelle Yang: Perfect. Thanks so much. My name is Rochelle Yang, and I'm a pharmacist with Teva Medical Affairs. I wanted to first emphasize Teva's shared commitment to improving outcomes in patients with asthma, and we've got your goal in mind. I wanted to provide some information about the portfolio of E-connected inhaler devices called the Digihalers, which are currently non-preferred on the Apple Health PDL. So this platform consists of three different dry powder inhalers. The ProAir Digihaler, which is a short-acting rescue inhaler containing albuterol, the ArmonAir Digihaler, which is a controller inhaler that contains fluticasone, and lastly, and AirDuo Digihaler, which is another controller inhaler containing a combination of fluticasone and salmeterol. And I'll refer to the full prescribing information for each of those products for additional information. But I wanted to focus my comments on the technology and the capabilities. So each Digihaler contains a built-in electronic module, which detects, records, and stores data on inhalation events, such as when and how often the patients use their inhaler. In addition, the Digihaler also measures the peak inspiratory flow rate so that quantifies that an adequate therapeutic dose of medication was delivered to the patient and can provide insight into whether the inhalation was performed correctly since we know that inhaler technique can be an issue for many patients. All of this data is transmitted in real-time via Bluetooth to a free Smartphone app, which also provides notifications, messages, and reports including feedback on inhalation techniques, rescue inhaler overuse, as well as reminders to take their maintenance inhalers. With patient consent, providers can also access to data in a variety of ways, including via a secure online provider portal. So in summary, uncontrolled asthma continues to pose a significant burden to patients and the broader healthcare system. The objective inhaler data that is collected by the Digihaler system can be used to track and monitor patients' inhaler use, including identifying poor technique or overuse of rescue inhalers and non-adherence to controller medication, which can help patients and providers make more informed treatment decisions. So as such, I'd like to request consideration of the Digihaler family as a preferred treatment option on the Apple Health PDL.

And that concludes my prepared remarks. I'd like to thank the Committee, and happy to address any questions.

Jordan Storhaug: Thank you so very much. I don't see that we have any hands raised. So, Marissa, I might ask you to get our motion ready.

Michael Corsilles: This is Michael Corsilles. I would like to make a motion. I move that all products in the drug classes listed on slide 5 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.

Susan Flatebo: This is Susan Flatebo. I second.

Jordan Storhaug: All in favor, please say Aye.

Multiple speakers: Aye. Aye. Aye.

Jordan Storhaug: Any opposed? Okay. It sounds like we have unanimous consent. So just keep on moving along with this topic Asthma and COPD. Back to Umang to talk about the monoclonal antibodies.

Umang Patel: Perfect. Thank you. And since this kind of all falls under asthma, and COPD, there won't be the background guidelines again. We'll just move right into updated drug-specific clinical updates. So the first one we have here is for Dupixent. In the last 12 months, there were two large updates. First, in June of 2021, the FDA approved a 200 mg/1.14 mL single-dose autoinjector or prefilled pen for use in patients 12 years of age or older. It was already approved at a prefilled syringe and autoinjector and prefilled syringe, so just an added formulation here. And in October 2022, the FDA expanded the indication of add-on maintenance treatment with moderate-to-severe asthma with an eosinophilic phenotype or with oral corticosteroid-dependent asthma in patients 6 years of age or older. Previously, this was only indicated in patients 12 years of age or older. So as you can see from my attempt to show you via bolded font a new update to the indications, here is a new availability for this medication. And as you can imagine, the dosage is very patient-specific. It is stratified by indication, age, and weight. So to

prevent overwhelming the Committee, I just refer you to the TCR or the package insert for that. On the next slide here, we have our next medication, Nucala. It also received two new updates in the last year. In August 2021, the FDA approved an expanded indication to the liquid formulation and the subcutaneous autoinjector as add-on maintenance treatment of chronic rhinosinusitis with nasal polyps in adults 18 years of age or older with inadequate response to nasal corticosteroids. And in January 2022, the FDA has approved a new liquid formulation packaged in a safety syringe device for use in children 6 to 11 years old with severe eosinophilic asthma. And the new formulation allows it to be administered to children by a caregiver or a healthcare provider. So similar to the previous medication, we have a new indication here and a new availability. Dosage is again stratified by indication and age, so I refer you to the TCR or the PI for that. And our next slide, we have a Tezspire. Now, in December 2021, the FDA approved this medication, which is a thymic stromal lymphopoietin blocker, indicated for the add-on maintenance treatment of adults and pediatric patients 12 years of age or older with severe asthma. And it is important to note the limitation for this use is not for relief of acute bronchospasm or status asthmaticus. In terms of precautions, there are risks associated with abrupt reduction in corticosteroid dosage. So, it is recommended to decrease it gradually if appropriate. There is a risk of parasitic infections, so it is recommended to treat patients with pre-existing helminth-specific infections before therapy. And if patients become infected while receiving treatment and do not respond to antihelminth treatment, it is recommended to discontinue this medication until the parasitic infection results. And lastly, it is recommended to avoid the use of live, attenuated vaccines. For this, the dosage is 210 mg once every four weeks via subcutaneous injection, and the availability is in injection form. It is 210 mg per 1.91 mL solution in a single-dose glass vial, and 210 mg per 1.91 mL solution in a single-dose prefilled syringe, as well. Since this is a new medication, I will just give a little bit of additional info here. In terms of patients who are pregnant, there are no available data on this medication for use in pregnant women to evaluate a drug-associated risk. In terms of hepatic and renal impairment, there are no formal (PK) pharmacokinetic studies that have been conducted in patients with hepatic or renal impairment. I'll go ahead and pause right there as that was the final slide for monoclonal antibodies. Thank you, Umang. Marissa, can you review the PDL for us?

Marissa Tabile:

Hi. This is Marissa. So this is our AHPDL. These are the products that we have in our monoclonal antibodies class for asthma and COPD agents. So as you

can see -- and I'm just going to highlight it for my own reference -- our current preferred products in that class are Cinqair, Fasenra, Fasenra Pen, and Xolair are our preferred products. I will make a note, too, that Dupixent is actually in a different class. I believe it falls on our AHPDL as an atopic dermatitis class. That's why you won't see it listed here. And I believe also the Tezspire that Umang was talking about, I believe that falls in a class of its own, as well. The class name is here under monoclonal antibodies. But just to let you guys know, the reason why Dupixent is in Atopic Dermatitis in its own class, it's because when it first came out, I believe that was the first indication that it got FDA-approved for it, and that's the way it was kind of classified in our drug reference tables that we have, so that's the reason why. It's not included in the motions, so just a disclaimer there that you won't be making a motion on that particular class.

Jordan Storhaug: Thank you, Marissa. We do have a speaker stakeholder for this topic, as well. First up is Sunny Hirpara from AstraZeneca.

Sunny Hirpara: Hi. I just want to make sure you guys can hear me.

Jordan Storhaug: We can hear you fine.

Sunny Hirpara: Awesome. All right, I'm ready to go. [cross-talk]

Jordan Storhaug: All right. [cross-talk] you have three minutes.

Sunny Hirpara: Yep, sounds good. Thank you. Good afternoon. My name is Sunny Hirpara. I'm a pharmacist and a Regional Clinical Account Director with Medical Affairs representing AstraZeneca. Thank you for the opportunity to present some recently updated information on Fasenra for subcutaneous use. As a reminder, Fasenra is indicated for the add-on maintenance treatment with patients with severe asthma aged 12 years or older with an eosinophilic phenotype. The recommended dose of Fasenra is 30 mg once every four weeks for the first three doses, then 30 mg once every eight weeks thereafter by subcutaneous injection into the upper arm, thigh, or abdomen. Fasenra is not indicated for the treatment of other eosinophilic conditions. Fasenra is not indicated for the relief of acute bronchospasms or status asthmaticus. So today, we have two new real-world evidence studies to share, ZEPHYR 1 and ZEPHYR 2, to further help support the value of maintaining Fasenra on preferred status on the formulary. ZEPHYR 1 was a retrospective cohort study of patients 12 years or older with asthma in a real-world setting, taking

benralizumab to identify the impact on exacerbations. This study utilized data from a large medical and pharmacy claims data source between November 2016 and November 2019. A pre- and post-design was implemented to descriptively analyze and compare asthma exacerbations between 12-month pre-index and 12-month post-index periods. In the primary cohort, those with two or more records have been done on benralizumab, annual exacerbation rates decreased from 3.25 in the pre-index period to 1.47 in the post-index period, which is a 55% reduction, which was significant, and 41% were exacerbation free. In the persistent group, those with six or more records of benralizumab, annual exacerbation rates decreased from 3.23 in the pre-index period to 1.23 in the post-index period, a 62% reduction. Also significant, 43% were exacerbation free. For the additional switch cohorts, annual exacerbation rates decreased from 1.74 in the pre-index period to 0.79 in the post-index period, a 54% reduction from those that switched from omalizumab, and annual exacerbation rates decreased from 1.56 in the pre-index period to 1.02 in the post-index period, a 34% reduction for those switching from mepolizumab. Over half the patients were exacerbation free in the post-index period. ZEPHYR 2, a retrospective cohort study of patients on benralizumab using the US claims data between 2016 and 2018 evaluated the real-world effectiveness of benralizumab on asthma exacerbations and OCS use in patients with available blood eosinophilic blood levels and those who are switching from omalizumab mepolizumab. And in all cases, we saw a significant reduction in annual exacerbation rates per person. So AstraZeneca requests that Fasenra be maintained on the Preferred Drug List for the Washington Medicaid Program. I thank you for your time, and I'd be happy to answer any questions that you may have.

Jordan Storhaug: Thank you very much. I don't see that we have any other stakeholders who are raising their hands. So, Marissa, I will have you take us to a motion.

Kavita Chawla: This is Kavita Chawla. I move that all products in the Asthma and COPD Agents : Monoclonal Antibodies 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: This is Alex Park seconding that motion.
- Jordan Storhaug: All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay. So next, just keep on moving through. I will be doing our hemopoietic agents with Gaucher disease being first, and so we'll bring it back to Umang again.
- Umang Patel: Perfect. Thank you. So this is going to be very short on my end. There were no significant clinical updates for this disease state. So I'm going to pause right there and give it right back to you, sir.
- Jordan Storhaug: All right, and I'll pass it off to Marissa to review the PDL for us.
- Marissa Tabile: Hi, this is Marissa. So here I have displayed hematopoietic Gaucher disease. So right now, what we have preferred on our PDL is miglustat and Zavesca, and everything else is non-preferred.
- Jordan Storhaug: Thank you, Marissa. And I don't have a pre-approved stakeholder there, and I don't see any hands raised, so I think we're ready to go to the motion.
- Virginia Buccola: This is Ginni Buccola, and I move that all products in the Hematopoietic Agents : Gaucher Disease 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.
- Diane Schwilke This is Diane Schwilke. I second.
- Jordan Storhaug: All in favor, please say, Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay. Then we'll be on to sickle cell anemia, and back to Umang for that presentation.

Umang Patel:

Thank you. All righty, so moving right along with sickle cell anemia. It is an inherited red blood cell disorder caused by a single gene mutation in the beta-globin gene resulting in an abnormal hemoglobin. It affects approximately 100,000 patients in the US and is more common among African Americans, although it is seen in people with Hispanic ancestry, as well. About 1 in 365 African Americans are born with sickle cell disease, and 1 in 13 have the trait just as carriers. In Hispanic Americans, it occurs in 1 in 16,300 births. People with sickle cell disease have a reduced life expectancy by approximately 20 to 30 years. And people with sickle cell disease inherit two abnormal hemoglobin genes, one from each parent. It comprises several syndromes in which the sickle mutation is inherited along with a mutation at the other beta-globin allele that diminishes or eliminates the normal production of beta-globin. These include sickle cell anemia, which is homozygous sickle mutation, sickle beta-thalassemia, and hemoglobin sickle cell disease, among others. There are two types of beta-thalassemia: "0" (β^0) and "+" (β^+). HbS β^0 is usually a severe form of sickle cell disease, while HbS β^+ tends to be a milder form. Sickle cell anemia is the most common and severe form of sickle cell disease, and sickle cell trait is diagnosed when one normal gene and one abnormal gene are inherited. Patients with SCD do not have signs or symptoms of sickle cell disease, but they can pass the abnormal gene to their children. The treatment goals with sickle cell disease focus on the management of symptoms and disease complications. Strategies include management and prevention of disease sequelae, including VOC, chronic pain, chronic hemolytic anemia, organ damage, pulmonary hypertension, stroke, and infection. A hematopoietic cell transplant is the only cure for sickle cell disease, but its use is limited by associated risk and lack of match donors. HCT is typically performed in children with complications such as stroke. For treatment of acute VOC, IV hydration and analgesia are the mainstays of therapy. Blood transfusions are often used to treat and prevent complications of sickle cell disease, particularly in patients at risk for stroke. However, regular administration of transfusions is associated with iron overload and alloimmunization. Individuals with sickle cell disease are also at increased risk of bacterial and viral infections. Therefore, immunization and prophylactic penicillin are important aspects of care during early childhood defined as ages less than 5 years of age. Okay, now moving right along to the updated drug-specific clinical information. In December 2021, the FDA approved an expanded indication for Siklos for its use in adults to reduce the frequency of painful sickle cell crises and reduce the need for blood transfusions. Previously, it was only indicated in pediatric patients 2

years of age or older. No changes to any of the black box warnings, the dosing, or the availability here, as well. And on the next slide, here, we have Oxbryta. And in December of 2021, there were two significant updates. First, the FDA had granted accelerated approval to new a formulation. Tablets for oral suspension for the treatment of sickle cell disease in adults and pediatric patients 4 years of age or older. The accelerated approval is based on an increase in hemoglobin. Therefore, continued approval for this indication may require demonstration of benefit and confirmatory clinical trials. And second, the existing tablets also received a new indication via accelerated approval for the treatment of sickle cell disease in pediatric patients 4 years of age or older. Previously, the tablet formulation was only indicated for the treatment of sickle cell disease in adult and pediatric patients 12 years of age or older. And so as you can see here, the expanded indication and the availability of the tablets for oral suspension were the significant ones here. And the dosing for the expanded pediatric population is based on body weight, just like the adult one, as well. I'm going to pause right there. That's all the significant clinical updates for sickle cell agents.

Jordan Storhaug: Thank you, Umang. Next, we'll review the PDL, as well, and if our stakeholders want to raise their hands, we'll be onto that after the PDL.

Marissa Tabile: Hi, this is Marissa. So this is our PDL. This is for the sickle cell anemia class. So as you can see, we have Droxia as our preferred product in this class. And I will say a disclaimer, I believe we just recently actually split this class up. So this actually may not be currently up-to-date. We had to split it out because of some carve-outs we had to do for some of those products. So just a disclaimer. It's just for this particular class that we have right now.

Jordan Storhaug: Thank you, Marissa. And then for our stakeholders, our first one is Foxy Davison, who's a parent and represents the Metro Seattle Sickle Cell Task Force.

Leta Evaskus: This is Leta. I do not see Foxy on the list of participants. But John Dow has his hand raised.

Jordan Storhaug: All right, then we acknowledge John Dow.

John Dow: Hi, everyone. Can you guys hear me?

Jordan Storhaug: Yes, we can.

John Dow:

Perfect. I can go and get started. Hi everyone. My name is John Dow. I am a Physician Assistant as well as a Medical Science Liaison at Global Blood Therapeutics. Thank you for the opportunity to provide data on Oxbryta today. So sickle cell disease impacts 100,000 people in the United States, and its estimated economic burden is \$2.9 billion per year. The root cause of sickle cell disease pathology is the polymerization of hemoglobin S, which leads to sickled red blood cells, anemia, hemolysis, and vaso-occlusive crisis. Symptoms can appear as early as 5 months of age, and patients are at risk for stroke, kidney disease, and early mortality. While other therapies have focused on treating acute symptoms such as pain and VOCs, Oxbryta is the only drug that directly inhibits hemoglobin S polymerization. Oxbryta is indicated for the treatment of sickle cell disease in adult and pediatric patients 4 years of age and older. This indication is approved under accelerated approval based on increased hemoglobin levels. Continued approval for this indication may be contingent upon verification and description of clinical benefit and confirmatory trials. In an ongoing open-label study evaluating the safety and efficacy of Oxbryta in 45 patients aged 4 to 11 years old, 36% of the patients receiving at least one dose of Oxbryta achieved a hemoglobin increase of greater than 1 gram per deciliter at the 24-week mark, 47% of patients completing 24 weeks of therapy achieved a greater than 1 gram per deciliter with improvements seen as early as two weeks. The safety profile of voxelotor was similar to patients 12 and older, with the most common side effect being pyrexia, vomiting, and rash. In a qualitative study of sickle cell disease, patients aged 4 to 11 on voxelotor and their primary caregivers, 5 out of 8 reported improvements in severity and/or frequency of pain crises, 4 out of 5 reported improvements in fatigue and jaundice, 8 out of 10 reported improvement in health-related quality of life after starting voxelotor, and 5 out of 10 caregiver and patients report an improvement in patient's ability to engage in activities. In a retrospective claims review of 3120 patients greater than 12 years of age on Oxbryta comparing three months of pre- and post-initiation showed a 34% reduction in VOC hospitalization, a 37% reduction in all hospitalizations, a 52% reduction in transfusion, a 23% reduction in VOCs, and a 10% reduction in outpatient visits. Patients receiving voxelotor had a 46% reduction in iron chelation use and 13% fewer opiates prescribed. Sickle cell disease impacts communities that have been historically underserved. Other therapies have focused on acute symptoms, but having Oxbryta on the Preferred Drug List gives patients access to a drug with a novel mechanism that targeted the roots of sickle cell disease. We respectfully request that Oxbryta be listed as a

preferred agent to remove any potential barriers to access. Thank you for your time. And I would be willing to answer any questions if there are any.

Jordan Storhaug: Thank you very much. The next step, for stakeholders we have Stacey Beal.

Foxy Davison: Hi, this is actually not Stacy. This is Foxy Davison.

Jordan Storhaug: Thank you, Foxy Davison. You have three minutes.

Foxy Davison: Just wanted to say I had the privilege of being here a while ago when we talked about sickle cell. My name is Foxy. I am a parent of three children, two of who do have sickle cell disease. And that gets me the privilege of working for the task force, which is a group of people impacted by sickle cell throughout Washington State. My only thing is to say, please. Sickle cell -- it has taken so long for therapies to finally come on board. We are still facing so many barriers when it comes to actually utilizing these new therapies. And so whatever we can do to continue to push this forward, we're just asking that you do. My son currently, we are in the third denial of one of the actual therapies -- the drug is mentioned -- and it's just because of misunderstanding around sickle cell and access. And so we want to make sure that our families are getting absolute access to therapies that they have been waiting for years and years to access. So whatever we can do to keep moving these things forward, we're just asking that you do them. Thank you.

Jordan Storhaug: Thank you. I don't see that we have any other stakeholders, so I will have us move on to the motion.

Michael Corsilles: This is Michael Corsilles. I move that all products in the Hematopoietic Agents : Sickle Cell Anemia 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 with the same medication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Kavita Chawla: This is Kavita Chawla. I just want to -- sorry -- just to pause on the motion. And is there anything within this Committee's purview to help with the more novel agents being on the Preferred Drug List? Maybe a question for Donna?

- Donna Sullivan: I'm sorry, Kavita. I didn't quite hear what you asked.
- Kavita Chawla: My question was, is there anything within this Committee's purview that can help the newer agents that are not hydroxyurea help the newer agents be preferred on the PDL?
- Donna Sullivan: Marissa, are they not preferred, or do they just require prior authorization?
- Marissa Tabile: Let's see. So they are non-preferred with PA. You don't have any policies for them right now or created clinical criteria. But yes, they are non-preferred. And then I believe the Adakveo is in its own class. We just recently split that because of the carve-out status that we gave it, so that's why it's not listed. Yeah. But I can't remember the status of that one. It probably doesn't have one, actually, because it's a carve-out.
- Laura Beste: This is Laura Beste. I was a little confused, too, because it says you have to fail two preferred treatments, but if you just look at this view right here, there is only one preferred treatment [cough] [cross-talk] --
- Donna Sullivan: Yeah, we don't [cross-talk] require tried and failed on these, mostly because I believe they have different mechanisms of actions and indications. So that's why they're only on prior authorization for medical necessity.
- Laura Beste: But doesn't the motion say they have to -- can you bring the motion back up?
- Donna Sullivan: We might need to revisit the motion then.
- Alex Park: Yeah, it says two preferred.
- Donna Sullivan: Mm-hmm. I mean, that's just standard language that I think was an oversight, Marissa. We probably need to look to see what we're actually doing on the PDL because I didn't see a tried and failed two on the PDL document, which means we're not requiring tried and failed for these drugs.
- Jordan Storhaug: For the Committee, I'll point to that the last line of the standard language is the exception that if there's only one product preferred, then they only have to fail that one item.
- Donna Sullivan: Yeah. We don't even do that, though. And so, I'm confused why the individuals getting having difficulty. So whoever testified, if they could send

an email to our Apple Health Pharmacy Policy mailbox, which I'll put the email address in the chat, we can find out what's going on the health plans and why and what's being held up to make sure that they are reviewing these cases appropriately.

Laura Beste: Can we remove the line that says all non-preferred products require a trial of at least two preferred products?

Donna Sullivan: Yeah.

Jordan Storhaug: So I think the suggestion is to take out the last sentence in its entirety.

Laura Beste: Correct.

Kavita Chawla: Kavita Chawla here again. So if I may understand the prior authorization is to just show that the patient truly has sickle cell anemia? I'm just wondering why the additional step of the prior authorization if all of them are being granted.

Donna Sullivan: We are requiring prior authorization to make sure that they are being prescribed for their FDA-labeled indications and any other safety thing there might be, looking at any other contraindications that might be on the label.

Jordan Storhaug: So, Donna, what I'm understanding from you is that all medications in this category are currently preferred but behind prior authorization? Is that correct?

Donna Sullivan: I think except for -- can you bring that back up, Marissa? I believe except for the Droxia. Yes.

Jordan Storhaug: Which Droxia, you're saying all of them are preferred, but Droxia is available without prior authorization, and the rest of them would need prior authorization.

Donna Sullivan: Correct. I mean, they are essentially preferred because we don't require tried and failed, but we have them listed as non-preferred. But again, we're not requiring tried and failed. If anything, they just required prior authorizations. And we don't require tried and failed because Endari, Oxbryta, and Siklos all treat different aspects of the disease. One is treating pain, others are helping

treat the sickle blood cells and trying to focus on that. So that's why we removed the tried and failed on these.

Jon MacKay: This is Jon McKay. I would move to approve the amended motion.

Laura Beste: This is Laura Beste. I'll second that.

Jordan Storhaug: All in favor, please say Aye.

Multiple speakers: Aye. Aye. Aye. Aye. Aye.

Jordan Storhaug: Any opposed? Okay. Then back to Umang. It looks like Granulocyte Colony Stimulating Factors will be the next topic.

Umang Patel: Perfect. All right. So, this one will be specifically Granulocyte Colony Stimulating Factors (G-CSF). So myelosuppressive chemotherapy can induce neutropenia and a predicted decline to less than 500 microliters during the 48 hours after the dose and febrile neutropenia, which is a dose-limiting toxicity of chemotherapy. Febrile neutropenia can cause increased diagnostic and treatment costs, prolong hospitalization, and broad-spectrum antibiotic use, which may necessitate chemotherapy dose reductions, and treatment delays, and may ultimately compromise treatment outcomes. The risk of febrile neutropenia is dependent on treatment and dose intensity, which is often under-reported. CSF are hematopoietic growth factors that have been shown to decrease the likelihood of neutropenic complications resulting from chemotherapy and to improve relative chemotherapy dose intensity. Prophylactic CSF use can reduce the severity risk and duration of febrile neutropenia and decrease rates of infections and hospitalizations. Neupogen, Releuko, Nivestym, Zarxio, Neulasta, Nyvepria, Udenyca, Fulphila, Ziextenzo, and Granix are GCFs, whereas Leukine is a GM-CSF. On the next slide here, the NCCN in 2022 released practice guidelines for Hematopoietic Growth Factors in patients with solid tumors and lymphoid blood cancers. Due to recent approval, Nyvepria and Releuko are not currently addressed in the guidelines. Safety data appear similar between Neupogen, Neulasta, and the biosimilars, and the subcutaneous route is preferred for all agents. To date, there are insufficient head-to-head comparative studies on the clinical benefits of GSFs and GM-CSFs. Subcutaneous filgrastim, tbo-filgrastim, and pegfilgrastim have a Category 1 recommendation, stating there is high-level evidence from randomized controlled clinical trials. And there is a uniform NCCN consensus that they prophylactically reduce the risk of febrile

neutropenia. However, the guidelines advise caution should be used with prophylactic use of G-CSFs administered with chemotherapy and radiation concurrently. As I mentioned earlier, Releuko is a relatively new medication. In March 2022, the FDA approved this biosimilar to Amgen's Neupogen. The indications are, as you can see, it decreases the incidence of infection, as manifested by febrile neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever, to reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with AML. Third, to reduce the duration of neutropenia and neutropenia related to clinical sequelae. For example, febrile neutropenia in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplant. And lastly, to reduce the incidence and duration of sequelae of severe neutropenia in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia. There are some precautions. First, fatal sickle cell crisis. It is recommended to discontinue this medication if this occurs. And glomerulonephritis, they recommend evaluate and consider dose reduction or interruption of treatment if causality is likely. The dosage for this is stratified by indication and weight-based. There are two availabilities for this medication, first being a vial, and the second being a prefilled syringe. On the next slide here, there was an FDA communication in July of 2021 for Neulasta, the FDA issued an untitled letter notifying Amgen of misbranding of Neulasta due to false or misleading promotional communication regarding the benefits of its Onpro System compared to traditional administration of Neulasta formulations. Go ahead and pause right there.

Jordan Storhaug: Thank you, Umang. Marissa, do you have the PDL for us?

Marissa Tabile: Hi, this is Marissa. So this here displayed is our granulocyte colony stimulating factors drug class. So as you can see, our preferred products in this class are Granix, Neupogen, and it looks like those are the only two that we have preferred in that class.

Jordan Storhaug: Thank you. We don't have any stakeholders listed for this topic, and I don't see any hands raised. Excuse me, it looks like we do have a hand raised. Renee Curtis, go on and present for us.

Renee Curtis: Hi. I actually have two products in this category, and I was told that I would receive five minutes to do both products. Is that not correct?

Jordan Storhaug: [Cross-talk] I understand that to be incorrect but --

Renee Curtis: That's fine.

Jordan Storhaug: All right. Go ahead, Renee.

Renee Curtis: Thank you very much. My name is Renee Curtis. I'm a licensed pharmacist with Pfizer Oncology Medical Affairs. Thank you for the opportunity to address the Committee regarding Nyvepria, a biosimilar to Neulasta, and Nivestym, a biosimilar to Neupogen. Nyvepria is a leukocyte growth factor indicated to decrease the incidence of infection as manifested by febrile neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidents of febrile neutropenia. Nyvepria is not indicated for the mobilization of peripheral blood progenitor cells of hematopoietic stem cell transplantation. Patients with cancer receiving myelosuppressive chemotherapy should receive 6 mg administered subcutaneously once per chemotherapy cycle. Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy. Use weight-based dosing for pediatric patients less than 45 kg. See prescribing information for dose recommendation adjustments for pediatric patients. The most common adverse reactions are bone pain and pain in extremities. Nyvepria has warnings and precautions for the following: Fatal splenic rupture - Evaluate patients who report left upper abdominal or shoulder pain, or for an enlarged spleen or splenic rupture. ARDS - Evaluate patients who have a fever, lung infiltrates, or respiratory distress, and discontinue if they develop ARDS. Serious allergic reactions including anaphylaxis - Permanently discontinue Nyvepria. For patients who have serious allergic reactions, fatal sickle cell crisis, or glomerulonephritis - Evaluate and consider dose reductions or interruptions of Nyvepria if causality is likely. Leukocytosis - Monitor full CDC during Nyvepria therapy is recommended. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment. Potential for tumor growth stimulatory effects on malignant cells, the G-CSF receptor, through which pegfilgrastim and filgrastim products act has been found on tumor cell lines. The possibility that pegfilgrastim products act as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which pegfilgrastim products are not approved, cannot be excluded. Aortitis has been reported in patients receiving pegfilgrastim products, and it could

occur as early as the first week of therapy. Discontinue if aortitis is suspected. Nivestym is a leukocyte growth factor indicated to decrease the incidence of infection as manifested by febrile neutropenia and patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever. Reduce the time to neutrophil recovery and duration of fever following induction and consolidation of chemotherapy treatment in patients with AML. Reduce the duration of neutropenia and neutropenia-related clinical sequelae in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation. And mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis. And also reduce the incidence and duration of sequelae of severe neutropenia in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia. The dosing and administration are as follows: Patients with cancer receiving myelosuppressive chemotherapy or induction and/or consolidation chemotherapy for AML, the recommended starting dose is 5 mcg/kg/day subcutaneous, short IV infusion (15 or 30 minutes), or continuous IV infusion. Patients with cancer undergoing bone marrow transplantation to receive 10 mcg/kg/day given as an IV infusion no longer than 24 hours. For autologous peripheral blood progenitor cell collection therapy, 10 mcg/kg/day subcutaneous. Administrate for at least 4 days before the first leukapheresis and until the last leukapheresis. For congenital neutropenia, 6 mcg/kg subcutaneous twice daily for cyclic or idiopathic neutropenia 5 mcg/kg subcutaneous IV daily. Please see full prescribing information for dose adjustments. Most common adverse events for this drug are pyrexia, pain, rash, epistaxis, bone pain, anemia, diarrhea, hypoesthesia, alopecia, headache, cough, and dyspnea. Nivestym has warning precautions for fatal splenic rupture, acute respiratory distress syndrome, and serious allergic reactions, including anaphylaxis, fatal sickle cell crisis, and glomerulonephritis. Please see full prescribing information for a complete list of warnings. In conclusion, maintaining Nivestym, an FDA-approved biosimilar to Neupogen and Nyvepria. An FDA-approved biosimilar to Neulasta will offer an additional treatment option for patients requiring treatment with the leukocyte growth factor in the Washington State Medicaid population. I respectfully request the Committee to continue providing Nivestym and Nyvepria for your patients. Thank you for your time and attention.

- Jordan Storhaug: Thank you, Renee. I do not see any other stakeholders. And with that, then we will entertain a motion.
- Diane Schwilke: This is Diane Schwilke, and I move that all products and the Hematopoietic Agents : Granulocyte Colony-Stimulating Factors (G-CSF) 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.
- Susan Flatebo: This is Susan Flatebo. I second.
- Jordan Storhaug: Thank you. All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? All right. Thank you. Then the last presentation before the break. Umang will let us know about Erythropoiesis Stimulating Agents.
- Umang Patel: Okay. Again, this is a quick one. There were no significant clinical updates in the last 12 months for the ESAs. So I'll give it right back to you and Leta.
- Jordan Storhaug: And then off to Marissa to review the PDL.
- Marissa Tabile: Hi, this is Marissa. So in our Erythropoiesis Stimulating Agents class, the preferred products we have right now are Aranesp and Retacrit.
- Jordan Storhaug: Perfect. Moving right along. We don't have any scheduled stakeholders. I see Renee's hand is up. I don't know if that's older or if Renee wanted to present this category, as well.
- Renee Curtis: I would like to present on this category, as well, please. I just have one agent. Thank you.
- Jordan Storhaug: Okay. Sounds very good. Go ahead.

- Renee Curtis: Again, my name is Renee Curtis, and I'm a licensed pharmacist with Pfizer Oncology Medical Affairs. Thank you for the opportunity to address the Committee regarding Retacrit, a biosimilar to Neupogen. Retacrit is an erythropoiesis-stimulating agent (ESA) indicated for all the same indications as the branded reference product. The dosage administration and clinical safety profile including the box warning are all the same as the branded reference product. In conclusion, maintaining Retacrit, an FDA-approved biosimilar to Epogen on your PDL will offer an additional treatment option for patients requiring treatment with an erythropoiesis-stimulating agent in the Washington Medicaid population. Based on the efficacy and safety, I respectfully request the Committee to continue to provide availability of Retacrit for your patients. Thank you for your time and attention. I will return the remainder of my time back to the Committee for this. Thank you.
- Jordan Storhaug: Thank you, Renee. I do not see any other stakeholders. So we will look at a motion.
- Alex Park: This is Alex Park. I move that all products in the Hematopoietic Agents : Erythropoiesis Stimulating 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 with 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 that motion.
- Jordan Storhaug: All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? All right, very good. I think that brings us up to everything we're supposed to get covered before the break. I'll just check on timing. I know we're running about 10 minutes behind. I don't know if we want to come back at 2:40 or something along those lines?
- Leta Evaskus: That's what I was thinking. This is Leta. Why don't we come back? We'll take a 6-minute break if that's okay.

Jordan Storhaug: I'll see you guys at 240. Thank you.

Leta Evaskus: Great, thank you.

[break]

Jordan Storhaug: Perfect. Welcome back, everybody. I hope you had a very restful break. We will get back to another presentation from Umang. A number of agents in here, and our Oncology Agents leading the pack.

Umang Patel: Perfect, thank you. So the Oncology section gets a little bit tricky here. And how Magellan usually breaks these down is by cancer type. And for the review for Apple Health PDL will be going through mechanism of action, so I've kind of broken it down. On the next slide here you'll see the subclasses that fall under here. So we have the subclasses that fall under the HEME class, we have alkylating agents, anti-neoplastic miscellaneous, BCL-2 inhibitors, histone deacetylase inhibitors, immunomodulators, IDH1 and IDH2 inhibitors, JAK inhibitors, proteasome inhibitors, XPO1, and antimetabolites. Now, as you can see, there are a few that are bolded, Farydak and Zydelig. I have to apologize to the Committee for my pronunciation on these. And Vonjo and Tibsovo. So these are the ones with significant clinical updates here. [Cross-talk] --

Marissa Tabile: Sorry. This is Marissa. I just wanted to pause for a second and let the DUR Board know we'll do an overall motion at the very end for all of the oncology agents. You will notice that we have one class that's kind of differently named. It is Immune Modulators : Thalidomide Analogues. We did have to separate that on the AHPL so we could lump them all together. So that will be its own motion, and then all the oncology will be separately listed on one slide. But Umang has it split up in his presentation as hematological, and I believe breast. Correct me if I'm wrong, Umang.

Umang Patel: Correct.

Marissa Tabile: So after those two presentations, we'll just do stakeholder input altogether and then the motions for all of those at the end. So I just wanted to put that out there first. Sorry to interrupt, Umang. Go ahead.

Umang Patel: No problem. Thank you. So we'll move on right to the next slide. When I do present, some of these classes have a lot of different disease states or

different kinds of parallel therapeutic classes that kind of fall in there. I try to focus on the ones that correlate to the new updated clinical information and drug-specific information we'll be providing later. So the first here we have Graft versus Host Disease. And so this is an immune-mediated disease that can result following from hematopoietic stem cell transplant or transplanted cells the graft recognizes the recipient's body as foreign. Organ systems most commonly impacted by this include the skin, the GI tract, and the liver. Chronic GVHD is generally an extension of acute that often develops more than 100 days after transplant, but it can also occur in those without acute GVHD. Symptoms include ocular manifestations, oral and GI, respiratory, and neuromuscular manifestations. Now in terms of the guidelines here, as you can see, they are well over three years old, so I won't be going over these in detail. I did keep these here. The American Society of Bone Marrow Transplantation was renamed the American Society of Transplantation, so their therapy. The NCCN guidelines and the NIH are here again for the Committee's reference, but since they are over three years old, I tend to focus on the ones within the last year. On the next slide here, continuing the background, we have Waldenström macroglobulinemia. Now, this is a B-cell disorder presenting as bone marrow infiltration with lymphoplasmacytic cells that are CD19+, CD20+, and CD22+. The NCCN guidelines in 2022 state that these symptoms may include hyperviscosity, neuropathy, symptomatic adenopathy, organomegaly, amyloidosis, cryoglobulinemia, and cytopenia. Both zanubrutinib and ibrutinib with or without rituximab are listed as options for primary treatment, while ixazomib combined with rituximab and dexamethasone is category 2A and other recommended regimens for primary therapy. For patients who have received previous therapies, zanubrutinib and ibrutinib with or without rituximab are category 1 preferred regimens. Acalabrutinib is category 2A, other recommended treatment options. Up to 40% of Waldenström macroglobulinemia patients may have recurrent mutations in the CXCR4 gene, and certain CXCR4 mutations may confer resistance to ibrutinib. Therefore, the NCCN guidelines recommend consideration of CXCR4 gene mutation testing for patients being initiated on ibrutinib therapy as category 2A useful in certain circumstances recommendation. There are no current US guidelines that exist for the treatment of erythema nodosum leprosum, hypereosinophilic syndrome, or chronic eosinophilic leukemia. On the next slide, here we have the Philadelphia chromosome-positive or (Ph+) ALL. It is rare in pediatric cases of ALL, creating approximately 2% of cases. In contrast, approximately 25% of adult cases of ALL or Ph+. In terms of treatment, the NCCN guideline last year recommended incorporating a TKI in the frontline regimen for Ph+ ALL

as an established standard of care for adolescents and young adults, and adult patients. The TKI may be combined with either chemotherapy or corticosteroids depending on the patient's age and comorbidities. The options for induction therapy in adolescents, young adults, and adults include Gleevec, Sprycel, Tasigna, Bosulif, and Iclusig. They state that dasatinib and imatinib are preferred TKIs for induction therapy, while ponatinib is preferred as part of the hyper-CVAD chemotherapy regimen. In addition, the guidelines also state that Bosulif is an option but say there is limited data for that particular TKI and Ph+ ALL. Mutation testing for the ABL gene should be considered as this mutation can confer greater resistance or susceptibility to a particular TKI, and the choice of a specific TKI should also be based on disease-related features. Pediatric patients with Ph+ ALL are also candidates for TKI therapy. Additionally, the guidelines for pediatric ALL specifically list combined treatment option regimens containing imatinib or dasatinib. A study by the Children's Oncology Group utilizing imatinib for children with Ph+ ALL demonstrated a five-year event-free survival of 70%, which is superior to historical controls prior to the introduction of imatinib. On the next slide here, moving over to drug-specific, we have Tibsovo. So in August 2021, it was received an expanded indication for the treatment of adults with susceptible IDH1 mutations as detected by an FDA-approved test for patients with locally advanced or metastatic cholangiocarcinoma, who have been previously treated. It is also indicated for certain adults with susceptible IDH1 mutations as detected by an FDA-approved test with AML. Again, with just the secondary indication here, no changes to the Warnings and Precautions, as you can see dosing or availability here. Next, we have Jakafi. In September 2021, the FDA-approved oral Jakafi for chronic graft versus host disease after failure of one or two lines of systemic therapy in adults and pediatric patients 12 years of age or older. It is already indicated for steroid-refractory acute graft versus host disease in the same age group and for select patients with myelofibrosis or polycythemia vera. Again, no changes aside from the expanded indication here. No changes to the Warnings and Precautions. The dosing, as you can imagine, is stratified by set indication and possible baseline platelet count. And the availability here, you see are various tablet forms. On the next slide, we have Vonjo. In March 2022, the FDA approved Vonjo, a kinase inhibitor with specificity for JAK2 and IRAK1 without inhibiting JAK1 indicated for the treatment of adults with intermediate or high-risk primary or secondary post-polycythemia vera or post essential thrombocythemia, myelofibrosis with a platelet count of less than $50 \times 10^9/L$. This indication was approved under accelerated approval based on spleen volume reduction. And continued approval for this

indication rate may be contingent upon verification and description of clinical benefits in a confirmatory trial. This is a new medication. I just wanted to go over some of the Warnings and Precautions being thrombocytopenia, thrombosis, secondary malignancies, such as lymphoma and other malignancies may occur, and past or current smokers may be at an increased risk. And lastly risk of infection, as you can imagine with chemotherapy medications. The dosage here is 200 mg orally twice daily, and it comes in 100 mg capsule form here. Since this is a new medication, just an FYI for special populations, so patients who have hepatic impairment, it is recommended to avoid use in moderate hepatic impairment, which is defined as Child-Pugh B, as in beta. And it is also recommended to avoid in Child-Pugh C for severe hepatic impairment. And we'll move on to the next slide here. We have FDA communications. In October 2021, the FDA had granted recognition to a partial listing of the first Tumor Mutation Database that is part of the Public Human Genetic Variant Databases. And this was the Memorial Sloan Kettering Cancer Center's Oncology Knowledge Base or OncoKB. Now, lastly, we have some updates regarding withdrawals. First being Farydak. Secura Bio announced that they will withdraw this from the US market. The drug had received accelerated approval for use in combination with bortezomib and dexamethasone for the treatment of patients with multiple myeloma, who had received two or more prior regimens including bortezomib and an immunomodulator agent. Secura stated they are withdrawing the medication because it is not feasible to complete the required post-approval clinical studies to confirm clinical benefits. And the second is for Zydelig. In April 2022, Gilead announced the voluntary withdrawal of specific indications for the treatment of relapsed follicular B-cell non-Hodgkin lymphoma and relapsed small lymphocytic lymphoma, which were approved under accelerated approval based on objective responsive rates of 54% and 58%, respectively. The decision to withdraw these indications is based on an ongoing challenge of enrolling patients in the confirmatory trial. Zydelig's indication for relapsed chronic lymphocytic leukemia will still remain. Next will be breast cancer. And, Marissa, just to confirm, I'm just going to go right through this one, as well. Correct?

Marissa Tabile: Hi, this is Marissa. Yep. Umang can go ahead and just go into it.

Umang Patel: Perfect. Thank you. I'm just going to take a sip of water. I apologize.

Marissa Tabile: Yeah. Feel to take a breather if you need it.

Umang Patel:

These drug names can be a little bit intense. Going to the next slide, we'll go ahead and break down the subclasses that fall under Oncology : Breast Cancer. First one, we have are antimetabolites, and the second one we have are PI3K inhibitors here. Now, as you can see, Vioice is bolded here, so I will be reviewing that momentarily. Moving right along to a little bit of background. Breast cancer is the most common type of cancer for women in the US, accounting for 30% of all cancer diagnoses, and is second only to lung cancer as a cause of cancer death in American women. It's estimated there will be about 287,000 new cases of breast cancer diagnosed in the US in 2022, and there will be an estimated 43,000 deaths. The incidence of breast cancer in US women continues to increase by about 0.5% per year. Known risk factors that may be contributing to this increased incidence include a decline in fertility rate and an increase in body weight. Despite this increasing incidence, death rates for breast cancer have declined by 42% since 1989, largely due to improvements in both early detection and treatment. The overall 5-year survival for women diagnosed with breast cancer is 90%. Patients who present with localized disease have a 99% 5-year survival rate. However, the prognosis for patients presenting with a distant metastatic disease is much poorer, with a 5-year survival rate of only 29%. Breast cancer is most frequently diagnosed in women between 55 to 74 years of age with a median age at diagnosis being 63 years. Rarely, breast cancer may be diagnosed in men. Other risk factors include various endocrine, genetic, environmental, and lifestyle factors, and some of these risk factors are modifiable, some are not, and the impact of these factors is variable. And the reason there are no guidelines posted here, they are found in the TCR for the Committee, as they are all greater than one year since published. So I didn't feel the urgency to review them, but again, they are found in the TCR. So for the medication here, we have Vioice. In April 2022, the FDA approved this medication, which is a kinase inhibitor indicated for the treatment of adult and pediatric patients 2 years of age or older with severe manifestations of PIK3CA-related overgrowth spectrum who require systemic therapy. It is approved under accelerated approval based on response rates and duration of response, and continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial. Warnings and Precautions here. Diarrhea and embryo-fetal toxicity, as one can imagine. The dosing is stratified by age. And for pediatric patients, it's 50 mg once daily with food, adults 250 mg once daily with food. The availabilities are various dosage strengths of tablets here. Okay. In October 2021, the FDA did release a communication. They had

granted recognition again to the first tumor mutation database. I mentioned that previously, and I wanted to put it back in here, as well, because it does encompass all of the cancer subgroups that we would be reviewing. And I'm going to pause right there. And so that is the end of the Oncology section, I believe.

Jordan Storhaug: Thank you, Umang. That was a lot you got through. Thank you for all those efforts. Marissa, do you want to review the PDL for us?

Marissa Tabile: Yeah. Hi, this is Marissa. Apologies. They are doing yard work right outside of my house. So if you can hear it, I apologize in advance. So to go through the PDL, here are the Immune Modulators Thalidomide Analogues class. We have lenalidomide, Pomalyst, Thalomid, and Vyvgart as our preferred products in that class. And then for the Oncology agents, a general rule of thumb that we do is we typically prefer pretty much everything unless a product has a generic on the market. So like a capecitabine product, the brand name of that is probably non-preferred. So really, you'll see we have a lot of preferred products in our Oncology Agents class, and the only reason why it would be non-preferred is because there is already a generic on the market. So I'll be happy to answer any questions. But if not, we can go ahead and move on over to stakeholder input.

Jordan Storhaug: All right, yeah. Thank you. We do have two stakeholders who [cross-talk] --

Susan Flatebo: Excuse me. This is Susan Flatebo. I just wanted to question. I noticed under the immune modulators tab in this PDL that you have Vyvgart listed. I don't think Vyvgart belongs there. I think that's for myasthenia gravis. So I don't know if that needs to be removed. At least I don't think it's a thalidomide analogue. I'm not familiar with it.

Marissa Tabile: Hi, this is Marissa. I can definitely take that back. Susan [cross-talk] will be evaluated [audio cuts out] to be put out to another class. But thank you for bringing that to my attention. Honestly, off the top of my head, I'm not too familiar with that either. So I will re-evaluate that product for sure and see if I need to split that into a different class.

Susan Flatebo: Okay, thank you.

Jordan Storhaug: Thank you, Susan. The first stakeholder we have is Patrick Tamburro of CTI BioPharma. I think he's listed, however, under William Dozier.

- Leta Evaskus: Hi, this is Leta. And I see there are two names for William Dozier, so did we unmute the correct one?
- Patrick Tamburro: Yeah. Can everyone hear me?
- Jordan Storhaug: We can hear you.
- Patrick Tamburro: Awesome.
- Jordan Storhaug: Go ahead.
- Patrick Tamburro: All right. Cool. We'll get right into it then. So, yeah, my name is Patrick Tamburro. I'm an MSL with CTI BioPharma. I'm just covering pacritinib today. So on February 28, 2022, Vonjo or pacritinib, a kinase inhibitor with high specificity for JAK2 and IRAK1 was approved for the treatment of adults with intermediate or high-risk primary or secondary myelofibrosis with platelet counts below 50,000. This indication is approved under accelerated approval based on spleen volume reduction, and continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Pacritinib was approved based on PERSIST-2, a Phase 3 study evaluating pacritinib 200 mg twice daily compared with the best available therapy including ruxolitinib in patients with platelet counts below 100,000. In the ITT efficacy group, 22% of patients treated with pacritinib 200 mg twice daily versus 3% of patients in the best available therapy arm achieved significantly greater than or equal to 35% spleen volume reduction. Similarly, 32% of patients treated with pacritinib achieved greater than or equal to 50% reduction in total symptom scores compared to 14% in the best available therapy arm. Additionally, 57% of patients treated with pacritinib 200 mg twice daily reported much improved or very much improved patient global impression of change scores compared to only 20% in the best available therapy arm, who reported much improved with no [audio cuts out] [indistinct] much improved. The most common side effects are diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema. There is no black box warning for pacritinib; however, it is contraindicated with coadministration of strong CYP3A4 inhibitors or inducers. Diarrhea of any grade occurred in about 48% of patients, and the best available therapy arm versus 15% on the best available therapy arm and persists to less than 4% of those were Grade 3 to 4 diarrhea with none in the best available therapy arm. And it usually occurs within the first eight weeks and subsides

one to two weeks after onset and is easily managed with OTC antidiarrheals. Cytopenia was commonly reported overall, but there is a stabilization of platelets and hemoglobin that was observed in the pacritinib arm. And in addition, patients who were red blood cell transfusion-dependent at baseline experienced transfusion burden decline over time with pacritinib and were able to maintain full dose at week 24 with a median daily dose of 400 mg. I'm going as our Phase 3 PACIFICA trial or confirmatory trial looking at PAC versus Physician's Choice therapy in patients with MF and severe thrombocytopenia. And PAC was added to the NCCN guidelines in April as first-line therapy in patients with severe thrombocytopenia and second-line for patients with platelet counts above 50,000. So based on that, along with the treatment guideline recommendations, we respectfully ask that pacritinib be added to the formulary as a preferred agent for patients with myelofibrosis and platelet counts less than 50,000 and considered as second-line for patients who have platelet counts greater than 50,000, who lack response or are intolerant to other prior JAK inhibitor therapy. Thank you.

Jordan Storhaug: Thank you so very much. Next, we'll be hearing from Nathan Blake again from AbbVie.

Nathan Blake: Hi. Good afternoon. One final time, my name is Nathan Blake with AbbVie Medical Affairs. And I really just wanted to make myself available to Committee if there are any questions regarding venetoclax with the brand name Venclyxto, which is an oral BCL-2 inhibitor. Otherwise, I'd like to give my time back to the Committee.

Jordan Storhaug: Thank you. Would we be able to see the motion?

Leta Evaskus: Jordan, this is Leta. I see one question from Andrew Yu in the Q&A box. He said on the PDL I see Piqray listed under P13K inhibitors, but why isn't Vijojeice?

Marissa Tabile: Hi, this is Marissa. Andrew, off the top of my head, I'm not quite sure. It could be what I'm thinking because it's probably in a class of its own, and the list that we were using as we were creating the agenda is actually updated. So I'll have to double-check and research, but I have a feeling that is what is occurring. So that might be why. But I can research that. If you want to send that inquiry into the Apple Health Pharmacy Policy mailbox, I can get a definite answer over to you.

- Susan Flatebo: This is Susan Flatebo. I move that all products in the Immune Modulators : Thalidomide Analogues 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 with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- Diane Schwilke: Diane Schwilke. I second.
- Jordan Storhaug: All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay, and then I think we have one more motion.
- Marissa Tabile: This is Marissa. And I just wanted to verify the reason why the Vioice is not in the PI3K inhibitors class is because it does, indeed, live in a different drug class at the moment right now. So Vioice is in the Miscellaneous Therapeutic classes, a PIK3CA-related agents class that is not being reviewed at this meeting. So it's not listed here, but it will be added for review eventually to one of the meetings in the future.
- Diane Schwilke: This is Diane Schwilke, and I move that all products in the drug classes listed on slides 20 and 21 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.
- Laura Beste: This is Laura Beste. I second the motion.
- Jordan Storhaug: All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.

- Jordan Storhaug: Are there any opposed? Okay. On to our next presentation from Umang. The next one is Thrombopoiesis-Stimulating Proteins.
- Umang Patel: Perfect, thank you. So the next one is one of those classes where there were no significant clinical updates in the last 12 months. So volleying it right back to you, sir.
- Jordan Storhaug: All right. And Marissa, do you want to review the PDF for us?
- Marissa Tabile: Hi, this is Marissa. So these are the products that we have currently in our thrombopoiesis-stimulating agents class. So the preferred product we have right now is Promacta tablet.
- Jordan Storhaug: Thank you. We don't have any previous stakeholders noted I don't see any hands raised, but if you want to get that up, I'll keep on looking. Otherwise, Marissa, I think we can look at a motion.
- Virginia Buccola: This is Ginni Buccola. I move that all products in the Hematopoietic Agents : Thrombopoiesis-Stimulating Protein drug class are considered safe and efficacious for their medically-indicated 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: This is Alex Park. I second the motion.
- Jordan Storhaug: All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Are there any opposed? Okay. Back to Umang again, this time on the Growth Hormone-Releasing Hormones category.
- Umang Patel: Perfect. So the next slide here we have our growth hormone-releasing hormones. So we'll move right to the background. So achondroplasia is a genetic bone growth disorder that prevents cartilage from converting to bone and is the most common form of dwarfism. It is rare, occurring in 1 in every 15,000 to 40,000 live births. The condition is caused by a mutation of

the fibroblast growth factor receptor 3 gene, which leads to the prevention of normal bone growth. The average height of an adult with achondroplasia is approximately 4 feet, and other characteristics include macrocephaly, bowing of the legs, thoracolumbar kyphosis, small fingers, frontal bossing, and mid-face hypoplasia. Patients with achondroplasia have an increased risk of death in infancy, hypotonia, apnea, obesity, and difficulty walking. Voxzogo is the first FDA-approved therapy for this disease state in patients 5 years of age or older with open epiphyses. It is a human C-type natriuretic peptide (CNP) analog, and it binds to a specific receptor called the natriuretic peptide receptor and antagonizes the FGFR3 gene downstream signaling, which results in a positive endochondral bone growth while promoting chondrocyte proliferation and differentiation. On the next slide here, as I mentioned, the medication specifically is Voxzogo. And in December 2021, the FDA granted accelerated approval to this medication for the indication to increase linear growth in pediatric patients with achondroplasia who are 5 years of age or older with open epiphyses. Again with any accelerated approval, it is based on improvement in annual growth velocity; therefore, continued approval may require demonstration of benefit in confirmatory clinical trials. There are some precautions here, the first being renal impairment. It is not recommended in patients with a GFR of less than 60 mL/minute. And the risk of low blood pressure and transient decreases in blood pressure have been reported. In terms of dosing, it is based on the patient's weight. It is administered subcutaneously once daily, and it is recommended that the healthcare practitioner monitor growth and adjust dosage according to body weight. Permanently discontinue upon closure of epiphyses. In terms of formulations, for the subcutaneous injections, there is lyophilized powder in a single-dose vial for reconstitution here. And now since this is a new medication, I did just want to say for special populations, for patients who have hepatic or renal impairment, the effect is unknown. And for hepatic impairment, the effect is unknown for renal impairment we had discussed GFR of less than 60 should not be used. And in patients who are pregnant, there are no available data for this medication use in pregnant women to evaluate a drug-associated risk. I'll pause right there for the committee.

Jordan Storhaug: Thank you, Umang. Now, let's review the PDL.

Marissa Tabile: Hi, this is Marissa. So it looks like we only have one product that is in the GHRH endocrine and metabolic agents class. So we have Egrifta, and it is preferred.

- Jordan Storhaug: We don't have anybody listed for previous stakeholders, and I don't see any hand raised, so we can look at the motion.
- Leta Evaskus: Hi, Jordan. This is Leta. I do have one question from China [indistinct] with Takeda Oncology. I just want to confirm that the pages referenced in the prior oncology motion were accurate. The slide deck I have from the meeting materials shows the oral oncology therapies on slide 28, while the motion reference slides 20 to 21.
- Marissa Tabile: This is Marissa. I think, China, the slides that we're referencing in the motions are specifically the slides that are in the motions slide deck itself. So if it was looking at oncology therapies listed on slide 28 then, I don't know if that's referencing the slides that Umang is going through. That is actually separate. I can actually verify that right now. Yeah. So just to verify that the slides that we're referencing in the motion in is referencing the slides in the motion slide deck itself, not necessarily to the presentation that Umang is giving. So it's still accurate the way that we have it in the motions, but that's the difference between the two slide decks.
- Jordan Storhaug: Thank you, Marissa, for explaining that.
- Michael Corsilles: This is Michael Corsilles. I move that all products in the Endocrine and Metabolic Agents : Growth Hormone Releasing Hormones 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.
- Diane Schwilke: Diane Schwilke. I second.
- Jordan Storhaug: All in favor, please say Aye.
- Multiple speakers: Aye. Aye. Aye. Aye. Aye.
- Jordan Storhaug: Any opposed? Okay. On to the next presentation, Growth Hormones with Umang.

Umang Patel:

Perfect. Thank you. All right. The next and final class we have here are the Endocrine and Metabolic Agents : Growth Hormones. So growth hormone deficiency (GHD) results from inadequate production of growth hormone and can produce various medical conditions dependent on age. Adults with GHD may have diminished lean body mass, poor bone density, and a number of physical and physiological manifestations. It can be congenital or acquired in childhood or adult life in addition to being partial or complete. The condition is usually permanent and may be an isolated deficiency or occur in association with deficiencies of other pituitary hormones. In most cases, the diagnosis of GHD should be based on results from two provocative tests as recommended by the Pediatric Endocrine Society. The 2009 American Association of Clinical Endocrinologists Guideline for Clinical Practice indicates no evidence exists to support any specific growth hormone product over another. I did want to just let the Committee know, please note there are multiple disease states that kind of fall under growth hormone: Prader-Willi syndrome, idiopathic short stature, etc., but we are not reviewing those just because there were no correlated clinical updates for those just specifically GHD here. So the first medication we have is Skytrofa. In August 2021, the FDA approved this medication for pediatric patients one year of age or older who weigh 11.5 kg or greater and have growth failure due to inadequate secretion of endogenous growth hormone. That's because this is a new medication. Some of the precautions here are increased risks of neoplasm, glucose intolerance and diabetes mellitus, possible hypothyroidism, and pancreatitis here. The dosing should be administered subcutaneously, again in the abdomen, buttock, or thigh with regular rotation of the injection site, and the dosing is 0.24 mg/kg body weight once weekly. And for the formulation, there are various strengths of the injection. Since this is a new medication, for patients who are pregnant, there are no available data. And patients with hepatic or renal impairment, no specific data studies have been performed with Skytrofa here. On the next final slide here, just a little bit of an update. There was a drug shortage for Zomacton in May 2021. Ferring notified healthcare practitioners of a supply shortage of Zomacton 10 mg due to COVID-19 travel restrictions, causing delays in qualifying new filling lines. The recommended healthcare practitioners stop prescribing to new patients and transition current patients and future patients to Zomacton 5 mg. They also requested that healthcare practitioners and patients contact their support services. Again, this was about 12 months ago and has since resolved. But just for transparency's sake for the Committee, this was just added in here. And I'll go ahead and pause there for the Committee.

- Jordan Storhaug: Thank you, Umang, for all those presentations. Let's look at the PDL.
- Marissa Tabile: This is Marissa. So for our AHPDL, for growth hormones, our preferred products that we have at this moment are Genotropin, looks like Norditropin, and it just looks like those two are the only two preferred products at this time.
- Jordan Storhaug: Okay. Thank you. I do have a listed stakeholder for this one, Tracey Maravilla at Ascendis Pharma.
- Tracey Maravilla: Can you hear me okay?
- Jordan Storhaug: Yes, Tracy. We can hear you. Go ahead. You have three minutes.
- Tracey Maravilla: Thank you. Sorry for my voice. I got COVID this morning. Hi, everyone. I'm Tracy Maravilla. I'm a pharmacist with Ascendis Pharma in the Health Economics Outcomes in Research on the medical care side. As we already stated with Skytrofa the indication, I will just kind of follow along with that and just remind you that it is the only once weekly product currently approved in the United States for pediatric growth hormone deficiency. It addresses an unmet need providing an alternative to daily somatropin injections that are associated with significant treatment burden. And what I mean by that is it is a very intrusive therapy for these patients to receive daily injections, especially children, and it can be very challenging. And this is where we see that value in long-acting growth hormone being less intrusive for these patients and improving adherence to their therapy. Skytrofa is administered using an auto-injector This is provided free to the patients. It has the benefits of a low-volume injection, small needles, room temperature storage, no refrigeration required, preservative-free, no waste [indistinct] design with a long lifespan, and it gives patient feedback on the automatic reconstitution progress. The efficacy and safety were established through our global Phase 3 Clinical Development Program, which includes three trials. The first is the height trial with a 52-week head-to-head study with treatment-naive patients compared 0.24 mg/kg per week of Skytrofa to the equivalent daily Genotropin given per week. The primary analysis of the height trial showed a 0.86 cm/year difference with a P-value statistically significant at point 0.0088 for Skytrofa over the daily Genotropin. Importantly, medication adherence was controlled for the daily injections in order to create ideal conditions, most notably for the daily injections with the

Genotropin. As you all know, adherence is a well-known issue impacting patient outcomes with regard to daily injections. The flight trial is our 26-week switch study, which is designed to assess safety and patient and parent experience with Skytrofa among treatment-experience patients. So these patients were on daily injections prior to coming on to the trial, their dose averaged about 2.29 mg/kg per week prior to coming on to Skytrofa. We did include three treatment-naive patients under the age of 3. And treatment adverse events were generally mild and equivalent between those two groups and very similar, and there were no neutralizing antibodies seen in the Skytrofa group. I'm happy to take any questions.

Jordan Storhaug: Thank you, Tracy, for the presentation. And sorry about your illness. I don't see that we have any other stakeholders, so we can look at the motion.

Jon MacKay: [Cross-talk] This is Jon MacKay. I move that all products in the Endocrine and Metabolic Agents : Growth Hormone drug classes 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 the 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.

Kavita Chawla This is Kavita Chawla. I second the motion.

Jordan Storhaug: All who approve, please say Aye.

Multiple speakers: Aye. Aye. Aye. Aye.

Jordan Storhaug: Anybody opposed? Okay. Thank you. I think that is our agenda. I think we made it through. Thank you, everybody for helping out with the presentations today and getting everything on the screen while we do it this way. Maybe I'll just point to Leta first to see if we have got anything else to do today.

Leta Evaskus: No, that's it. Thank you all and, thank you, Jordan. You did a great job as Chair today. And we'll see you guys in August.

Jordan Storhaug: Sounds good. Thank you, all.

Leta Evaskus: All right. [cross-talk]

Multiple speakers: [Cross-talk] Thank you, Bye. Bye.

[end of audio]