Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
Meeting Transcription
April 17, 2024

Nonye Connor: Okay, Kavita.

Kavita Chawla: All right. Are we ready?

Nonye Connor: Yes.

Kavita Chawla: All right. Today is April 17, 2024. We will now convene the P and T Committee meeting. I am Kavita Chawla, the Chair of the P and T Committee. I will read off the names of the participating attendees, so please say "here" when I call your name. We'll start with the P&T Committee Members. Peter Barkett.

Peter Barkett: Here.

Kavita Chawla: Hi. Laura Beste.

Laura Beste: Here. Good morning.

Kavita Chawla: Good morning. Michael Corsilles.

Michael Corsilles: Here. Good morning.

Kavita Chawla: Good morning, Michael. Kevin Flynn.

Kevin Flynn: Here. Good morning.

Kavita Chawla: Morning, Kevin. Jon MacKay.

Jon MacKay: Here. Good morning.

Kavita Chawla: Good morning, Jon. Christy Weiland.

Christy Weiland: Good morning.

Kavita Chawla: Good morning, Christy. Zoe Taylor.

Zoe Taylor: Hello.

Kavita Chawla: Hey. And Greg Hudson.

Greg Hudson: Here.

Kavita Chawla: Here. Do you prefer Greg or Gregory?

Greg Hudson: Greg is fine. Thank you.

Kavita Chawla: Okay. All right. And then our HCA Members, Nonye Connor.

Nonye Connor: Hello. Hi. Here.

Kavita Chawla: And Luke Dearden.

Leta Evaskus: Luke won't be here today.

Kavita Chawla: Okay. Got it. Leta Evaskus.

Leta Evaskus: Here.

Kavita Chawla: Amy Irwin.

Nonye Connor: She might be joining later.

Kavita Chawla: Okay. Ryan Pistoresi.

Ryan Pistoresi: Morning.

Kavita Chawla: Morning. Donna Sullivan.

Donna Sullivan: Hi, it's Donna. Amy won't be coming.

Nonye Connor: Oh, okay.

Kavita Chawla: Okay. Marissa Tabile.

Marissa Tabile: Here. Good morning.

Kavita Chawla: Morning. Ryan Taketomo.

Ryan Taketomo: Hello. Good morning.

Kavita Chawla: Good morning, Ryan. Joey Zarate.

Joey Zarate: Here.

Kavita Chawla: Hi. Our Labor and Industry Members, Jaymie Mai.

Jaymie Mai: Here.

Kavita Chawla: Great. And then our DERP presenters, Shannon Kugley.

Shannon Kugley: I am here, thank you.

Kavita Chawla: Hello. Wesley Lindsey. Okay. Rachel McCauslin and Courtney Cooper.

Rachel McCauslin: [Cross-talk] I am here. Good morning.

Leta Evaskus: [Cross-talk] They might be coming on closer to their presentation time.

Kavita Chawla: Okay, got it. All right. And then our Magellan Medicaid Administration presenter, Umang Patel.

Umang Patel: Hi. Good morning.

Kavita Chawla: Good morning. And then our Managed Care Organization Representatives are Greg Simas from Molina Healthcare, Heidi Goodrich from Molina, Petra Eichelsdoerfer with United Healthcare, Omar Daoud with Community Health Plan of Washington, and Jeffrey Natividad with Community Health Plan of Washington. Now, Nonye will go over our meeting logistics.

Umang Patel: Sorry. Dr. Chawla, can I just ask for one thing?

Kavita Chawla: Please.

Umang Patel: I just wanted to quickly introduce Nina Wynn. She is my colleague here at Prime Therapeutics. Just to let the Committee know that I will be slowly phasing off of the Washington account, and Nina will be slowly taking over as well, and so this is their first meeting. I will still be presenting, and she is just kind of observing to get a lay of the land.

Kavita Chawla: All right. Hi, Nina. Welcome.

Nina Wynn: Hello. I look forward to working closely with you all.

Kavita Chawla: Thank you. Thanks for that, Umang. All right, Nonye, go ahead.

Nonye Connor: Yes. Hi. Good morning, everyone. The Committee and Presenters can mute and unmute themselves at any time, but please mute yourself when not speaking so as to limit background noise. Presenters, please share your webcams while presenting, and also, Committee Members, please share your webcams during discussions and motion consideration. For stakeholder participation, we read the list of stakeholder names who pre-registered to speak. We will unmute you. After the share, we ask if there are any other stakeholders. If they are, please raise your hands, and we can call upon you and unmute you. You can also use the Q&A box. We will address your questions during the stakeholder time. If you do not fill out the stakeholder conflict of interest form, please answer the questions we will post on the screen. Your three minutes will start after you answer the questions. Thank you.

Kavita Chawla: Thank you, Nonye. Any other logistics or operational updates from Leta? I will take that as a no. All right. With that, let's get started. So I see Shannon, you are up for us from DERP. Take it away.

Shannon Kugley: Okay, great. Hear me okay? Great. Okay. I will go ahead and share my screen. Okay. Can you see the presentation?

Kavita Chawla: Yes, we can.

Shannon Kugley: Great. Okay. I will get started. Hi, everyone. So I will be talking to you about Targeted Immune Modulators for Plaque Psoriasis, Psoriatic Arthritis, and Generalized Pustular Psoriasis. This is an update of a systematic review. My name is Shannon Kugley, and I am from the RTI-UNC Evidence-Based Practice Center. So here is an overview of today is presentation, and here we

have a list of the abbreviations that are used in the presentation. And as you know, this report covers plaque psoriasis and psoriatic arthritis. New to this report is generalized pustular psoriasis (GPP), and TIMS are drugs that selectively block the immune response. These drugs were initially FDA approved for use in these conditions in 2002. In 2022, the FDA approved spesolimab for treatment of generalized pustular psoriasis. Here in this figure are the drugs that are included in the review. We have them organized according to their mechanism of action. So the mechanism of action is listed in the dark green box, and the drugs in the gray blue boxes are approved for both plaque psoriasis and psoriatic arthritis. Those drugs in the light green boxes are approved for plaque psoriasis only, and those in the yellow boxes are approved for psoriatic arthritis only. There is just one agent in a peach shaded textbox, which is approved for patients with GPP. An asterisk indicates that biosimilars are available and approved for use. So new drugs with this update include the IL-36 inhibitor, spesolimab, which was approved by the FDA in September of 2022 for treatment of GPP, as well a new topical PDE4 inhibitor, roflumilast, was approved by the FDA in July of 2022; however, the oral Formulation is not yet FDA approved. Since the prior report, the tyrosine kinase 2 inhibitor, deucravacitinib. And the IL-17A inhibitor, bimekizumab, was approved for plaque psoriasis. And here are the PICOS for this updated review. The criteria were similar to the prior report, except that we added GPP, and we excluded cohort studies. Our Key Question for the update was #1 on the comparative effectiveness and the second on comparative Harms, the third on variation and effectiveness or Harms by subgroup, and the fourth on ongoing studies. Our updated search was conducted to cover the literature that was available through the end of August 2023, with active surveillance through November of 2023. We conducted individual study risk of bias assessment, and we calculated risk ratios and confidence intervals where possible. We applied the GRADE methodology to rate the overall certainty of evidence. Lastly, we searched ClinicalTrials.gov to identify ongoing studies. Here is the DERP approach to risk of bias. So low risk of bias indicates clear reporting and mitigation of any potential bias due to conflicts. Moderate indicates some incomplete information on methods or that unmitigated meaningful conflicts of interest exist. High is for studies with flaws that introduce serious bias. And here is a brief overdue overview of the great certainty of evidence. We Graded disease remission, clinical improvement, quality of life, adverse events, and serious adverse events outcomes for this review. As a reminder, RCT bodies of evidence start at high certainty of evidence and can be downgraded for problems of consistency, precision, risk of bias, and reporting bias. On this

slide is our study flow diagram. We screened just over 1450 citations, and we assessed 82 full text articles. We identified 11 new articles of which 6 were new studies. We carried forward 34 studies that were reported in 55 publications from the prior report, thus, the total for the current review is 66 articles representing 40 studies. The report included data from 30 studies of TIMS for plaque psoriasis, 10 for psoriatic arthritis. We found no eligible studies of TIMS for treating GPP. That is because studies had to be head-to-head comparisons to be included, and the studies of spesolimab were not eligible because they were placebo-controlled. This figure depicts selected study characteristics. Of the total 40 studies, 6 are new to this update, and 34 were included in the prior report. 36 are moderate risk of bias and 4 were high risk of bias. 30 were conducted among participants with plaque psoriasis, 10 among individuals with psoriatic arthritis, 37 studies were head-to-head comparisons of FDA approved TIMS, and three were comparisons of a pipeline TIMS to an FDA-approved TIM or placebo. As a reminder, this figure characterizes the unique studies included in the report. We refer to publications that report additional outcomes or longer term follow up for an included study as a companion. In the subsequent slides, I will present the review findings first for plaque psoriasis and then for psoriatic arthritis. Within each condition, I will describe findings for the comparative benefits including variation by subgroups, followed by comparative Harms, and lastly briefly report on the comparative benefit and Harms of pipeline drugs. On this slide, we list the most common outcomes used in the studies. ACR is a measure of arthritis clinical improvement and disease remission. DLQI is a quality of life measure specific to dermatologic conditions, where a score of 0 or 1 indicates remission. PASI is a measure of clinical improvement and disease remission for psoriasis, and the PGA/IGA/PTGA are global assessment items to measure clinical improvement and disease remission. I will now share the findings for the comparative effectiveness of RCTs for plaque psoriasis. Here is an overview of the studies we identified addressing the comparative effectiveness of TIMS for plaque psoriasis. As I noted, we included 30 RCTs representing 23 unique head-to-head comparisons. Nearly all studies enrolled participants with moderate-to-severe psoriasis based on at least a 10% BSA, a PASI score, or both for at least 3 to 6 months' duration. Some, but not all, studies required participants to be naive to biological agents. Four RCTs are new to this update, including two RCTs of deucravacitinib versus apremilast, one of guselkumab versus secukinumab, and one RCT of risankizumab versus apremilast. In addition, we identified one new publication associated with the previously-included RCT of guselkumab versus adalimumab, and one

companion study reporting results of subgroup analyses from a previously-included RCT of risankizumab versus secukinumab. Regarding the risk of bias ratings across the entire body of evidence, all the include RCTs are sponsored by industry and have extensive industry involvement in study design, execution, and reporting and were, therefore, downgraded from low to moderate. Furthermore, we assessed two RCTs as high risk of bias, one due to insufficient blinding and switching of treatments during the study, and a second because it was open label. Over the next series of slides, I will share evidence for each comparison. Here we see an example of the summary of the findings for Key Question 1. The comparison and the number of studies and participants are in the green textbox. We found one RCT, including 166 individuals comparing apremilast with etanercept. The outcome category and GRADE assessment are in bold text. In this example, clinical improvement and quality of life were reported. The findings are noted along with a specific measure that was used to obtain the result and the time point of follow up. This study reported no difference in clinical improvement or in quality of life, as measured by the PASI 75 and the DLQI respectively at 16 weeks. We GRADED each outcome as low certainty. For this presentation, we include only the outcomes that we GRADED. Other outcomes are described in the full report. For previously included comparisons without new data, I will summarize the findings, but I will provide more details on outcomes for new comparisons or companion papers with new data. In the interest of time, I will not discuss the rationale for individual GRADE assessments, but I can tell you that across the evidence, imprecision accounted for most of the downgrades of one to two levels. Downgrading for other reasons was less frequent. For details on the great assessment, please refer to the full report. We did not Identify any new studies or data bimekizumab versus adalimumab or versus secukinumab. Of note, bimekizumab was a pipeline in the prior report. Bimekizumab was more effective than adalimumab for disease remission and for quality of life. We assessed outcomes as moderate certainty. Bimekizumab was also more effective than secukinumab for disease remission and quality of life, also assessed as moderate certainty. We did not find any new studies or data for bimekizumab versus ustekinumab. Bimekizumab was more effective than ustekinumab or disease remission and quality of life. We assessed the certainty of evidence as moderate for both outcomes. We did not identify any new studies or data for the comparisons on this slide. Brodalumab was more effective than ustekinumab for disease remission and quality of life. We assessed the evidence as high for both outcomes. The higher dosage of certolizumab-pegol 400 mg was more effective than etanercept for clinical improvement. There were no differences

in clinical improvement between the lower dosage that is 200 mg and etanercept. The certainty of evidence was moderate. Deucravacitinib versus apremilast is a new comparison for this update. We included two RCTs comprised of more than 1200 participants. Deucravacitinib was more effective than apremilast for clinical improvement at 16 weeks, as measured by the PASI 75. The relative risk was 1.7, with a 95% confidence interval of 1.3 to 2.1 in one study and 1.3 with a 95% confidence interval of 1.1 to 1.6 in the second study, favoring deucravacitinib for clinical improvement. We assessed the certainty of evidence as high. Deucravacitinib was more effective than apremilast for quality of life as measured by achievement of a 0 or 1 score on the DLQI. At 16 weeks, the relative risk was 1.4 with a 95% confidence interval of 1.1 to 1.9, and it was 1.6 with a 95% confidence interval of 1.3 to 2.1 in the second study. At 24 weeks, the relative risk was 2.0 with a 95% confidence interval of 1.5 to 2.7 in one of the studies and was 1.9 with a confidence interval of 1.5 to 2.5 in the second study. We did not identify any new data or studies for etanercept versus infliximab or etanercept versus ixekizumab. For both comparisons, etanercept was less effective for disease remission as measured by PASI 75 and was less effective than ixekizumab for improving quality of life. Certainty was very low for the outcomes in the first comparison and high for etanercept versus ixekizumab. We did not identify any new studies or data for etanercept versus secukinumab. Etanercept was less effective than secukinumab for achieving disease remission and improving quality of life. Certainty was high and moderate for those two outcomes respectively. We did not identify any new studies or data for etanercept versus tildrakizumab. Etanercept was less effective for disease remission at 12 and 28 weeks. We rated certainty of evidence as high. Etanercept was also less effective than tildrakizumab for improving quality of life, and we assessed certainty of evidence as moderate. This comparison also had a subgroup analysis, which showed no difference based on having or not having metabolic syndrome. We did not identify any new data or studies comparing etanercept with tofacitinib. We identified one RCT that compared etanercept with two doses of tofacitinib either 5 mg or 10 mg twice daily. Of note, tofacitinib is not approved for plaque psoriasis, and there is no Indication that it will be resubmitted for consideration for plaque psoriasis. Etanercept was more effective than a 5 mg dose of tofacitinib for disease remission, clinical improvement, and quality of life outcomes. There was no difference in outcomes for etanercept versus tofacitinib 10 mg. Certainty of evidence was moderate for all outcomes, except for quality of life for the 10 mg tofacitinib comparison. We did not identify any new studies or new data for etanercept versus ustekinumab. Etanercept was less effective

than ustekinumab for disease remission. We assessed the certainty of evidence as low. 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 of evidence, respectively. We included one new companion paper with data from this previously included RCT of guselkumab versus adalimumab. The new companion paper reported that guselkumab was superior to adalimumab for improvement and work productivity loss. However, work productivity loss was not an outcome for which we assessed certainty of evidence. We identified one new high risk of bias RCT for this comparison. Based on the one previously reported RCT that reported disease remission, guselkumab was more effective than secukinumab at 48 weeks. Guselkumab was not inferior to secukinumab for the combined endpoint of 12 and 48 weeks. The response for guselkumab was numerically lower than secukinumab for disease remission response at 12 weeks. We assessed certainty of evidence as moderate. In a separate article, authors reported on this comparison by subgroups based on age, weight, BMI, severity of disease, body area affected, and prior medication use. Guselkumab remained more effective than secukinumab at 28 weeks in each stratum of every subgroup identified. The newly identified RCT compared guselkumab with secukinumab and 40 participants with a PASI score less than 10, which is not moderate nor severe disease, and with a single treatment refractory plaque. Guselkumab was less effective than secukinumab at 16 weeks for clinical improvement. We rated this study as high risk of bias, and the certainty of evidence for clinical improvement was very low. No new studies were identified for ixekizumab map versus guselkumab or for ixekizumab versus secukinumab. Ixekizumab was more effective than guselkumab at 12 weeks for disease remission. There was no difference between the agents by 24 weeks. Findings were similar for quality of life. We assessed outcomes as moderate certainty of evidence. There was no difference between ixekizumab and secukinumab for disease remission or clinical improvement at 24 weeks in a study of individuals with genital psoriasis. Certainty of evidence was moderate for both outcomes. We found no new studies or new data for the comparison of ixekizumab versus ustekinumab. Ixekizumab was more effective at achieving disease remission and improvements in quality of life at 12, 24, and 52 weeks, and we rated this evidence as moderate certainty. We did not identify any new studies or data comparing risankizumab to adalimumab. Risankizumab was more effective at achieving disease remission and improving quality of life compared with adalimumab at 16 weeks. We assessed outcomes as moderate certainty of evidence. We identified one RCT of a new comparison of risankizumab

versus apremilast with 352 participants. Risankizumab was more effective than apremilast for disease permission as measured with the PASI 90 and for clinical improvement measured as PASI 75 at 16 weeks. We assessed the certainty of evidence as moderate for both outcomes. We did not identify any new studies of risankizumab versus secukinumab, but we did identify one new companion paper. Risankizumab was more effective than secukinumab for achieving disease remission at 16 and 52 weeks. We rated this evidence as moderate certainty. The newly identified companion paper reported results of subgroup analyses from the previously included RCT. There were no significant differences in outcomes based on post hoc subgroup analysis for age less than 40 years versus 40 years and older, male versus female, white versus non-white, BMI of less than 25 versus 25 to 30 versus 30 or higher, disease severity at baseline, prior biological use versus no use, presence versus absence of psoriatic arthritis, current versus former versus never a smoker, and disease duration of less than 15 years versus 15 years or more. We did not identify any new RCTs or data for risankizumab versus ustekinumab. Risankizumab was more effective than ustekinumab for disease remission and quality of life at 12 to 16 weeks. We assessed the certainty of evidence as high for both outcomes. We did not identify any new studies or data for the comparison of secukinumab with ustekinumab. Secukinumab was more effective than ustekinumab for disease remission and quality of life at 16 and 52 weeks. We rated both outcomes as high certainty of evidence. All RCTs included for KQ1 also reported Harms. On the next slide I will review these comparisons that had a significant difference in either the AEs or SAEs and with at least an evidence rating of low. In one RCT, apremilast was associated with a lower incidence of AEs than etanercept. We rated this evidence as low certainty, and there were no significant differences in the incidence of serious AEs. In one RCT comparing etanercept with 100 mg and 200 mg dose of tildrakizumab, AEs were reported in two separate time periods, weeks 1 through 12 and weeks 13 through 28. There was a higher incidence of AEs with etanercept versus the 100 mg dose of tildrakizumab for both time periods. However, compared with the higher dosage, the difference was significant in the second period only. Certainty of evidence was moderate. In a study new to this update, the incidence of overall AEs was lower for risankizumab versus apremilast, with a relative risk of 0.68 and a 95% confidence interval of 0.54 to 0.86. There was no significant difference in the incidence of AEs. We assessed the certainty of evidence as moderate. In one of the three studies comparing risankizumab to ustekinumab, AEs were reported in two time periods, weeks 1 through 16, and week 17 through 52. A lower incidence of AEs was

observed for risankizumab during week 17 to 52, and a lower incidence of SAEs was observed for risankizumab during weeks 1 to 16. No significant differences were observed for AEs or SAEs in the other two RCTs. We assessed certainty of evidence as low for AEs and low for SAEs. Next, we'll review the evidence for TIMS for plaque psoriasis. On this in the next two slides is a table that summarizes the evidence for clinical improvement, disease remission, and quality of life, as well as overall AEs and SAEs for the 23 comparisons for plaque psoriasis that were included in this update. The comparisons in blue text are either new to this update or have new data for this update. The certainty of evidence is indicated by the number of filled circles within each table cell. The direction of a fact is indicated by cell shading. Blue means that the first TIM of the comparison is more favorable, purple means no difference between the two agents, and red means that the second TIM listed was more favorable. The cells shaded in gray indicate unable to determine the direction of a fact. Because the table of comparators is long, this information is split across three slides. One pattern to observe in this table is that there are very few differences between agents with respect to Harms. Differences between agents are observed for clinical improvement, disease, remission or quality of life. However, with so many comparisons, it's difficult to identify clear patterns about effectiveness. We have the most evidence for etanercept, which was represented in eight comparisons and for ustekinumab, which was represented in six comparisons. Etanercept was inferior to certolizumab, infliximab, ixekizumab, secukinumab, tildrakizumab, and ustekinumab. Etanercept was more effective than the lower dose of tofacitinib and was similar to apremilast. Ustekinumab was less effective than all comparator agents it was assessed against, except for etanercept. This includes bimekizumab, brodalumab, ixekizumab, risankizumab, and second. Agents other than etanercept and ustekinumab are represented in fewer comparisons, so identifying patterns or any given agent is challenging and requires a more complex analysis than what we can do in this present update. We found no eligible studies of pipeline agents for plaque psoriasis. Next, we will move on to psoriatic arthritis. We identified a total of seven RCTs. As you can see from this evidence map, six of them compare a TIMS agent to adalimumab. The seven study compares ustekinumab to the TNF-alpha inhibitors. However, the specific one was selected by the participants and their providers, so the study was not blinded, and this was the reason that it was assessed as high risk of bias. The other study that we assessed as high risk of bias compared adalimumab to etanercept and infliximab. It was not well described and allowed for dose adjustments of infliximab during the trial. We identified three companion

publications reporting data from previously included RCTs. One new companion publication reported a subgroup analysis, and two reported additional outcomes. We did not identify any new studies or data for this comparison. Clinical response was similar across agents. No statistically significant testing was done. We assessed the evidence as low certainty -- I am sorry -- a very low certainty. We did not identify any new studies or new data for adalimumab versus tofacitinib. Adalimumab has had numerically lower response rates on ACR 20 compared with both doses of tofacitinib. Adalimumab had a numerically lower response from PASI 75 for skin disease compared with a higher dose of tofacitinib and a similar response to the lower dose of tofacitinib. Quality of life outcomes were roughly similar across the groups. The study did not conduct statistical testing. We assessed all outcomes as low certainty of evidence. We did identify one new companion paper reporting a subgroup analysis, but no new trials for ixekizumab compared with adalimumab for psoriatic arthritis. There were two RCTs of this comparison. In one study, no statistical testing was done for ixekizumab versus adalimumab, as the primary aim of the study was to compare ixekizumab to placebo. Ixekizumab every 2 weeks and every 4 weeks was slightly better than adalimumab for joint disease improvement at 24 weeks. We rated this evidence as moderate certainty. Ixekizumab was superior to adalimumab for skin disease improvement in both studies, with a moderate certainty of evidence. We assessed clinical improvement as high for a composite ACR 50 and PASI 100 response and for sustained PASI 75 response at 52 weeks for ixekizumab versus adalimumab. The newly identified companion paper reported a post hoc analysis of a subgroup of our participants with psoriatic arthritis and moderate-to-severe plaque psoriasis from one of the previously included trials. The subgroup included 100 of the 556 trial participants. Ixekizumab was more effective than adalimumab at 24 and 52 weeks for the primary endpoint, which was simultaneously achieving ACR 50 and PASI 100 and for most of the other outcomes. Findings were mixed for quality of life outcomes. We did not identify any new studies or data for secukinumab versus adalimumab. One RCT reported no difference in arthritis clinical improvement at 52 weeks. Secukinumab was more effective than adalimumab for clinical improvement in skin disease. We assessed the certainty of evidence as moderate for both outcomes. We identified new data for one study that was previously included for the comparison of upadacitinib versus adalimumab. A larger proportion of individuals taking upadacitinib 30 mg dosage showed improvement in arthritis at 12 weeks as measured by the ACR 20. Upadacitinib 30 mg remained more effective than adalimumab at 56 weeks. The relative risk was 1.1, with a 95% confidence

interval of 1.001 to 1.2. There was no difference in clinical improvement with the lower 15 mg dose of upadacitinib. We assessed the certainty of evidence for clinical improvement as moderate. For quality of life, the authors reported change in HAQ-DI at 12 weeks, upadacitinib for 15 mg and 30 mg were better than adalimumab. The newly included companion paper reported quality of life at 56 weeks, upadacitinib 30 mg was more effective than adalimumab for quality of life, with a relative risk of 1.2 and a 95% confidence interval of 1.01 to 1.3 and was measured as the proportion of participants who achieved a change in HAQ-DI score of 0.35 or higher. There was no significant difference for the 15 mg dose. We assessed the certainty of evidence as moderate for quality of life. We did not identify any new studies for this comparison. A small RCT with 47 participants with active enthesitis, a narrow subset of overall psoriatic arthritis, compared ustekinumab with various TNF-alpha inhibitors. We GRADED the evidence as very low certainty for ustekinumab being more effective for enthesitis and skin disease remission but no difference in arthritis remission. Six of the seven studies that were included for KQ1 for psoriatic arthritis also reported Harms. As before for Harms, we are only presenting comparisons where significant difference in AEs or SAEs was reported and when the certainty of evidence was at least low. We identified one new companion paper with data from a previously included study that compared either 30 mg or 15 mg of upadacitinib versus adalimumab. More AEs were found with upadacitinib 30 mg, with a relative risk of 1.1 and a confidence interval of 1.02 to 1.20. We assessed this as moderate certainty of evidence at both the 12 and 56-week time points. The relative risks were 1.1 and 1.3, and both 95% confidence intervals exclude the null results. There were no differences in AES for the mg dosage for either timepoint. Furthermore, there were no differences in SAEs at 12 or 56 weeks for either dosage with low certainty of evidence. And here is a summary of the RCT evidence for benefits and Harms of TIMS for psoriatic arthritis. We did not identify any new comparisons of an FDA approved TIMS for psoriatic arthritis, but we did identify new companion studies with additional data for previously included studies. As you can see, the evidence is mixed. For the comparisons with at least low confidence of evidence -- low certainty of evidence, which is everything but the top and bottom row, you can see that compared to adalimumab, ixekizumab and secukinumab are more effective at improving skin disease, but there are no differences for arthritis symptoms and no differences in AEs. Upadacitinib is more effective than adalimumab at improving both skin disease and arthritis. However, it is associated with more AEs. On this slide, we summarize the pipeline treatments. As a reminder, bimekizumab has been approved for

plaque psoriasis, but it is not approved to treat psoriatic arthritis; thus, this is just listed as a pipeline agent. We identified two new RCTs reporting on bimekizumab. One new RCT was for a comparison that was included in the prior report bimekizumab versus placebo. This RCT also included a head-to-head comparison of bimekizumab with adalimumab. The other new RCT compared bimekizumab with placebo. Limitations of this evidence-based include for some comparisons that direct evidence is still lacking, so there are many possible comparisons for which we did not find any studies. There is limited long-term Efficacy and Safety data available. Also manufacturers sponsored nearly all RCTs. Studies were not powered for Harms outcomes. And our review did not include RCTs with a duration shorter than 12 weeks, nor did we include data from conference abstracts or press releases. We included studies published in the English language only and not in other languages. We identified 10 ongoing studies, two RCTs and participants with plaque psoriasis and eight RCTs in participants with psoriatic arthritis. Drug manufacturers are funding nine studies, and the university is funding one of these studies. We found no eligible ongoing studies of TIMS for individuals with GPP. In conclusion, for plaque psoriasis the largest body of comparative direct evidence is for etanercept and ustekinumab compared with other TIMS agents. For clinical improvement or disease remission outcomes, etanercept is less effective than the following comparators based on moderate or high certainty. Certolizumab, ixekizumab, secukinumab, tildrakizumab, ustekinumab. Ustekinumab is less effective than the following comparators based on moderate or high certainty: bimekizumab, brodalumab, ixekizumab, risankizumab, and secukinumab. Beyond the patterns we observed for etanercept and ustekinumab, several TIM agents demonstrated superior effectiveness in pairwise comparisons. You can refer to the heat map I showed earlier in the presentation for details. Lastly, few differences in Harms among TIMS agents were observed based on very low to moderate quality evidence. In the future, a network meta analysis or a review of such analyses may provide insights into patterns of effectiveness and Harms across the many available TIMS agents. For psoriatic arthritis, there are limited head-to-head comparisons. From the evidence we reviewed, we can conclude that upadacitinib may be more effective than adalimumab for improvement in arthritis and skin disease, and that ixekizumab and secukinumab are no different than adalimumab for improvement in arthritis but are more effective for improving skin disease. Any questions? And I thank you for your time.

Kavita Chawla: Thank you, Shannon. Any questions from Committee members? Okay. And then are there any stakeholders for this section while we are waiting? I don't see any hands raised, and I don't see any listed, Nonye. Sorry, you are muted.

Nonye Connor: [Laughter] I thought I unmuted myself, but, no, there is no one listed, and there are no hands raised.

Kavita Chawla: Excellent. Okay. I suppose then we could go ahead and review the motion.

Nonye Connor: And right, and I am just going to copy from the previous one, and I will make the edits while you guys discuss.

Kavita Chawla: I think the main sanity check would just be -- which I haven't been able to do from reviewing the motion is -- that all the drugs that were reviewed are actually on that list. Do you know? This is an updated left column for the drugs reviewed, Nonye.

Nonye Connor: Yes, they are updated.

Kavita Chawla: Oh. Mm-hmm, awesome. Okay, great. All right. I will invite the Committee members to come back on camera. Oh, I see most of you are. Yeah, Any comments, updates, or suggestions?

Nonye Connor: So are all the ones in the left column supposed to also be in the paragraph?

Ryan Pistoresi: This is Ryan. Yeah. We'll need to add in a few of them.

Nonye Connor: Yeah. They are not all in there and remove some. So the ones with the asterisks are the ones that they are drugs that were carried over from previous review, so I am just removing them right now.

Kavita Chawla: Okay.

Nonye Connor: Mm-hmm.

Ryan Pistoresi: So this is Ryan. So just to remind you that the TIMS class has more than just plaque psoriasis, psoriatic arthritis. It also has the rheumatoid arthritis report, which is a separate report, and then the Crohn's and Ulcerative Colitis report, which is a separate report. So depending on how these drugs are approved for the different Indications, the list on the left includes all of the

drugs within the TIMS class, and then for this, we were going to have it be the ones that were in this report. So if you recall, earlier on in the presentation, where they had that slide that had all the list of different drugs, and they were different colors, and they are kind of in the different columns for the IL-17s and the IL-23s, and the TNFs. Yeah. So we are just trying to make sure that what was presented today is what's here in the motion.

Kavita Chawla: As Nonye works on that, any comments from the Committee regarding the rest of the language? I think right now it says the PDL must include a drug approved for treatment of the following FDA Indications, so RA, Crohn's, ulcerative colitis, and I guess because psoriatic arthritis is at the very top in the title. Any amendments to the language?

Nonye Connor: So we copied this from a statement about a different disease, right? So we need to change out all those diseases, I think, to the ones that we are talking about now? [Cross-talk] --

Kavita Chawla: [Cross-talk] Ryan [cross-talk] --

Nonye Connor: [Cross-talk] and paste it from the paragraph below, which is about different diseases?

Kavita Chawla: Exactly, right. Yeah.

Ryan Pistoresi: Yeah. So this is Ryan. So the last time that we reviewed this drug class, we did rheumatoid arthritis, [cross-talk] ankylosing spondylitis [cross-talk] disease and UC, so we will want to [cross-talk] --

Nonye Connor: [Cross-talk] We'll replace all that parenthetical with what's in the title.

Ryan Pistoresi: Right. Plaque psoriasis [cross-talk] and psoriatic arthritis. Yep.

Nonye Connor: Just give them a second to get to that [cross-talk] --

Kavita Chawla: Yeah.

Nonye Connor: All the changes.

Laura Beste: Do we need to review which ones are preferred? Or since we are not saying you have to try two preferred agents within this text that doesn't apply?

Ryan Pistoresi: So this is Ryan. So this is for the Washington Preferred Drug List, not the Apple Health Preferred Drug List, and so when you move to the DUR Board in the latter half of today's meeting, you will be doing more of reviewing what's on the Apple Health Preferred Drug List and looking at the policies. For the Washington PDL, you are making the recommendations of how we should do our cost analyses and then select the preferred and non-preferred? So that happens later with a cost analysis.

Laura Beste: Thank you.

Ryan Pistoresi: And this is Ryan. And so if you would like to see it, we can pull up the Washington PDL, but I think we would just need a moment to get that brought up.

Nonye Connor: Okay, it looks like I have made the edits to the drug names, and so I am ready to slice and dice. [laughter]

Kavita Chawla: So the, Nonye, at the bottom where there are the conditions listed in the parentheses, the rheumatoid arthritis -- yeah. That whole section needs to be replaced by the conditions in the title.

Nonye Connor: Okay.

Kavita Chawla: And I think to Laura's point at the piece here is that they cannot be subject to therapeutic interchange on the PDL is probably, I think, the most relevant here. Washington PDL? I don't think we've done that previously to the best of my memory. Are any of the Committee members interested in reviewing that? And if not, if anybody wants to propose a motion.

Nonye Connor: Oh, sorry. Before you propose, do you want me to make this change here?

Kavita Chawla: No, no. That part is perfect. Yeah.

Nonye Connor: Okay.

Kavita Chawla: Yeah.

Nonye Connor: And you want to change it to this paragraph?

Kavita Chawla: Yeah.

Zoe Taylor: So this -- the list of drugs in the paragraph should match what was on the slide earlier.

Kavita Chawla: [Cross-talk] Yes.

Nonye Connor: Okay. And we are sure that does.

Shannon Kugley: [Cross-talk], and I think there might be some missing there. Do you want to see the slide? Would that help?

Nonye Connor: Yeah.

Shannon Kugley: I think guselkumab, for example, you will want to add.

Nonye Connor: Which one is missing?

Shannon Kugley: Guselkumab after golimumab.

Kavita Chawla: I almost wonder, like. do we need to -- anyway, yes, go ahead. I don't know if anybody has a clever idea of how to do a check of all of the names and whether they are comprehensively included or not. Kevin's got one.

Nonye Connor: Oh, sorry. You said -- am I missing in the paragraph, or am I missing it in here?

Kavita Chawla: In the paragraph. So the guselkumab is not in the paragraph [cross-talk] --

Nonye Connor: [Cross-talk] Oh, okay.

Kavita Chawla: -- in the left-hand column.

Nonye Connor: I see.

Ryan Pistoresi: This is Ryan. After the golimumab.

Nonye Connor: Yeah. [Cross-talk] --

Kavita Chawla: I suppose if we want the entire list, do we just like copy/paste that list in there and just remove the spaces after the drugs, would that go faster?

Donna Sullivan: You could.

Laura Beste: Could you also just refer to the medications listed in the table? I mean do you have to write them out all over again?

Kavita Chawla: That is a great point, too, yeah. Would that be okay, I guess, to Ryan, and Nonye asked a question. The drugs listed in the left column or something like that.

Zoe Taylor: But the drugs in the left column are all of the TIMs, we only want to list here the ones that are for the Indication at the top.

Donna Sullivan: Correct.

Zoe Taylor: So it can't just reference the column. So we have to double check from Shannon's slide that we have all the drugs listed that are for this Indication. And then also this paragraph still says at the top, rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, and ulcerative colitis, instead of saying the [cross-talk] --

Greg Hudson: [Cross-talk] Yeah.

Nonye Connor: The new Indications. Oh, I am sorry. On the top, where?

Greg Hudson: Before it lists, before we list the medications.

Nonye Connor: Oh, thank you for pointing that out. Let me --

Kavita Chawla: Okay. Shannon also makes a point that the drugs in the column are not the drugs reviewed. So, sorry, I misunderstood that earlier.

Zoe Taylor: We'll just want to highlight starting at rheumatoid arthritis, just from rheumatoid arthritis through to the period, and then replace that. Yeah. Perfect. And then, Shannon, do you want to just read out the drugs?

Shannon Kugley: Oh, yeah, that might be a good way to do it.

Zoe Taylor: Yeah. If you can read them in alphabetical order, too, then we can make sure that [cross-talk] --

Shannon Kugley: [Cross-talk] I will do my best, yes. [Cross-talk] --

Zoe Taylor: Okay, I'm easy.

Shannon Kugley: [Cross-talk] [laughter] I know we could do split screen. Those are [cross-talk] -- Let's see. Okay, I will try to do this. Okay, so adalimumab you have, abatacept I think you have.

Zoe Taylor: Mm-hmm, yep.

Shannon Kugley: Certolizumab. Sorry, that is out of order. We need [cross-talk] --

Zoe Taylor: [Cross-talk] No, that is fine.

Shannon Kugley: -- adalimumab and bimekizumab. The two B ones. [Cross-talk] --

Zoe Taylor: [Cross-talk] is the adalimumab.

Shannon Kugley: Yeah.

Nonye Connor: I'm sorry, which one am I missing?

Kavita Chawla: The brodalumab. B-R-O-D-A -- right where your cursor is. Oh, and --

Nonye Connor: Oh.

Donna Sullivan: Nonye, can you bring up the presentation again? The slides.

Nonye Connor: Yes.

Shannon Kugley: I think it might be best to [cross-talk] --

Donna Sullivan: [Cross-talk] And then will you [cross-talk] go to the beginning where it lists the drugs that were included in this report?

Shannon Kugley: So the list is that slide that you see. It's there order by mechanism of action. We don't -- I don't have right at that -- I can get you an alphabetical list if that

would help. Like, I can just go off mute and make a list and copy and paste it in the chat if that would help.

Donna Sullivan: No, that is fine. Can you just say in your motion, "the drugs listed on Slide 5 of the TIMS for plaque psoriasis presentation, and then we can fix the motion later.

Zoe Taylor: That sounds awesome.

Donna Sullivan: This is going to happen [cross-talk] probably for all of these, so we are sorry we did not get -- we were not prepared for breaking it out by Indication with the past motion.

Kavita Chawla: That sounds reasonable to me. And do the other Committee members agree? Can we use that? Yes? I see thumbs up. Okay. Nonye, does that sound good to update the motion [cross-talk] language? So I think after I move that, I would probably move the name of the drugs and just see.

Nonye Connor: All the drugs on Slide 5, and then I will update everything.

Kavita Chawla: Yes. So do you want to remove the drug names from the paragraph and [cross-talk] --

Donna Sullivan: Yeah, remove the drug names from the paragraph, insert the drugs listed in Slide 5 with the presentation name so we know which -- just the drug names.

Nonye Connor: Oh, sorry.

Kavita Chawla: Go ahead, Jon.

Jon MacKay: You need to call out anything in regard to biosimilars at all?

Donna Sullivan: We don't -- the way -- and I am speaking for the Center -- if it's a biosimilar, I don't think we consider that as a different drug. So if it's adalimumab, you know, X, Y, Z, we don't list them all individually.

Ryan Pistoresi: This is Ryan. That is correct. So we do have several of the adalimumab already on the Washington Preferred Drug List, so we don't break them all out here because, otherwise, that list would get much, much, much longer

than it already is. So if you see adalimumab, you can consider all seven or eight of those approved biosimilars to be with them then.

Jon MacKay: Great, thank you.

Laura Beste: This is Laura Beste. Along those lines, just for the sake of completeness, should it say the medications plus their biosimilars? Or is that not even an issue?

Ryan Pistoresi: So this is Ryan. In the past, we haven't considered that an issue. Like we don't do that for the generics. If there is an extended release of another drug, we don't necessarily have to then include that. So some of the older motions you may notice that we do have certain dosage forms, but we've tried to reduce that in these newer motions.

Kavita Chawla: All right, great. So I am just reading through here, and make sure we are not missing anything. So after considering the evidence of safety, Efficacy, effectiveness in special populations with the use of TIMS for their FDA approved Indications relative to the listed conditions, I move other drugs in Slide 5 of the TIMS for name of the slide deck are efficacious for their approved Indications, including their applicable biosimilars when available. The PDL must include a drug approved for the treatment of these FDA Indications and must include a self-administered agent if indicated. These medications cannot be subject to therapeutic interchange in the Washington PDL. Okay, so that is the language. Is that -- how does that sound to the Committee? I see some nods. Okay, then whenever we are ready to propose the motion.

Kevin Flynn: This is Kevin Flynn. So after considering the evidence of safety, Efficacy, and effectiveness in special populations for the use of targeted immune modulators for their FDA-approved Indications relative to plaque psoriasis, psoriatic arthritis, and generalized pustular psoriasis, I move that the drugs listed in Slide 5 of the targeted immune modulators for plaque psoriasis, psoriatic arthritis, and generalized pustular psoriasis update slide deck are efficacious for their approved Indications, including their applicable biosimilars when available. The PDL must include a drug approved for the treatment of the following FDA Indications: plaque psoriasis, psoriatic arthritis, and generalized pustular psoriasis. It must include a self-administered agent when 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.

Kavita Chawla: Thank you. All in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed? Okay. With that, the motion carries. Thank you. Okay. With that, I think we move on to Wesley Lindsey for the Atypical Antipsychotics session. Do we have Wesley online? Oh, I see, I see the name.

Wesley Lindsey: Good morning to all. Can you hear me?

Kavita Chawla: Yes, we can. Good morning, Wesley.

Wesley Lindsey: Ah, welcome from Alabama. How is everything in the State of Washington today?

Kavita Chawla: Sunshine, surprisingly.

Nonye Connor: Oh, I am so sorry. Wesley. Before you start -- I just noticed that there was a hand raised in the attendance list from the -- okay, it's down now. So never mind. Sorry. Go ahead.

Kavita Chawla: All right, Wesley, take it away.

Wesley Lindsey: All right. So am I driving the slides? Is that the preference here? Or do you have a designated driver on those?

Nonye Connor: You can drive the slide, no problem.

Wesley Lindsey: All right. So hopefully I am sharing my screen. Does everybody see the appropriate slides, please?

Multiple Speakers: [Cross-talk] Yes, yes [cross-talk] --

Wesley Lindsey: Okay, great. And is there a preference whether I stay on camera for the presentation or off camera? What's the typical process?

Kavita Chawla: Whatever you would prefer.

Wesley Lindsey: All right. Well, I am going to stay on just in case. So first of all, thank you so much for the opportunity to join you this morning, I had the opportunity to present this obviously, a couple of weeks ago to the full collective of DERP, and I am excited that you are interested in this topic. This obviously was a pretty large report and something that we put a lot of effort and energy into. I think we got some great information here, and I am excited to share it with you this morning or if you are in the Eastern Time Zones this afternoon. So today I am going to be talking about atypical antipsychotics and their use as adjuvant treatment for major depressive disorder. The clinical evidence, and this is a systematic review, we also performed a meta analysis with this, and you will see some of the results of that as we proceed. Our overview for today. So this is going to be the typical process that we follow for systematic reviews. So we'll talk a little bit about background and table setting just to kind of get us the context and the clinical importance of this particular topic. We'll go through our PICOS to assess or to report the populations involved and the other elements that we evaluated. We'll take a look at our Key Questions, so looking at the Efficacy and looking at the Harms and any specific parameters to that that you are interested in. We'll go through our methods, so that you can get a sense of how we performed this systematic review and meta analysis, probably what you are all here for, the findings. So we'll take some time to walk through the findings and what we saw with these particular agents and their Efficacy and their Harms in this particular clinical situation and then obviously get to our discussion and kind of how we pulled it all together and how we can take this information forward as an actionable item for you as a state. So for our background, major depressive disorder has a lifetime prevalence of about 21% in the US, and it is ranked as the leading cause of disability worldwide. Part of the reason that we took on this topic, 50% of those with depression will experience recurrent episodes. So we need something that is going to be effective for those who are treatment resistant or for potentially getting recurrent issues. It is the guideline-based strategies to achieve remission. They include lithium or an atypical second-generation antipsychotic, which is what we'll talk about today along with an antidepressant in those patients who demonstrate treatment-resistant depression, which we will abbreviate as TRD through the rest of the presentation today. SGAs appear to be a preferred treatment strategy, particularly when you compare it to first-generation antipsychotics, and we can probably imagine why with the side effect profile as first-generation antipsychotics and all of the risks and complications that come along with those agents. The populations we evaluated for this review: so we

assess adults with major depressive disorder. The interventions just for the early part of this presentation, we broke them up into two groups. We have a group who actually does have an FDA Indication for adjuvant therapy for major depressive disorder. So those five agents are aripiprazole, brexpiprazole, cariprazine, olanzapine and fluoxetine, and quetiapine. Interventions that do not have an FDA-approved Indication, we also assess those, but the agents that fall into that category are asenapine, clozapine, iloperidone, lumateperone, lurasidone, paliperidone, pimavanserin, risperidone, and ziprasidone. So it looks like I got the better end of the deal today instead of having to present all of the biologics that look like the two we are talking about in the previous report. So I know that that is always kind of an adventure working through all of those drug names. The comparators that we evaluated for this, we looked at another listed intervention, so this is the long way to say head-to-head studies. And we did actually find one of those, but I wouldn't get my hopes up. If you are really excited about a head-to-head study, you might be a little disappointed when we actually get to that study and discuss it. We also evaluated standard of care and placebo. But as of note, that is a little bit later in the presentation. All of the patients that were in these studies, were on some type of antidepressant therapy, so nobody was getting no treatment, they at least had some type of antidepressant monotherapy throughout. Outcomes that we evaluated: We wanted to look at depression severity, and there are obviously a number of different assessment tools that we can use for this particular outcome, and we'll talk about some of those as we go through. We wanted to assess quality of life. We assessed function, and that could either be social functions, sexual function, any kind of quality or live or issue of life to improve function, suicidal behavior or risk, adverse events and serious adverse events. And the study design that we evaluated for this review was a randomized controlled trial. What are our key questions? We obviously wanted to assess the effectiveness of these agents. We also wanted to take a look to see if there were any variations about patient characteristics, such as age, duration of major depressive disorder, severity, etc., that might impact the Efficacy of these agents. We did the same with Harms. So what are the global Harms? And then are there any patient characteristics that might make somebody more susceptible to a particular Harm, such as age, duration of major depressive disorder, etc. We also evaluated the characteristics of ongoing studies and selecting pipeline agents such as pimavanserin and lumateperone. So now to the Methods for our project. So if you are familiar with the DERP process, we evaluated using the DERP typical clinical evidence sources. So we searched Ovid MEDLINE as well as the Cochrane Library,

DuckDuckGo, Google Scholar, etc. For ongoing studies, once again, the usual sort of resources there for ClinicalTrials.gov, FDA resources, etc. And you can see the others there on the screen. For additional sources, we looked at review articles, so any review article that was included in our searches, we evaluated the reference list and bibliography to see if there were any additional studies that might not have been captured in those earlier evidence searches. So we searched the clinical evidence sources from inception to October 20, 2023, and that is when we began screening and moving through the rest of the process. As I mentioned, we examined the reference list for systematic reviews. Once we had all of our studies, we assessed the risk of bias for all of the included original trials. We then used the GRADE approach for the overall certainty of evidence for critical clinical outcomes that we'll talk about in a moment. And once again, ClinicalTrials.gov and those other resources for our ongoing studies related to this particular topic. So the risk of bias assessment scheme that we use, you, again, if you are familiar with the DERP process, there are three levels to the risk of bias assessment. A study can have a low risk of bias, a moderate risk of bias, or a high risk of bias, just depending on the criteria that we evaluate for each of these, and there is a rubric that we use to assess the risk of bias for the individual studies. In evaluating the GRADE of certainty of evidence, there are four levels to the GRADE. You can see high is, obviously, the highest GRADE that we can recommend or that we can evaluate the evidence with. We have moderate, low, and very low. The outcomes that we focused on for our GRADE ratings for this particular project, we looked at the Montgomery-Asberg Depression Rating Scale (MADRS) scale. That was one of the most common that was used to assess the depression severity throughout the studies. We also looked at the HAM-D17, the Hamilton Depression Rating Scale. This also is a common rating scale used in depression. We looked at CGII, which is the Clinical Global Impression Scale Improvement, so this is a clinician rated scale to evaluate patients as they progress through treatment. We assessed response, so response is typically going to be defined as a 50% reduction in symptoms from baseline. For Harm outcomes, we evaluated the BARS, which is the Barnes Akathisia Rating Scale. So this is something as the name implies, assesses akathisia and looking for unwanted movement disorder, unwanted movement, adverse events for a patient. And lastly, change in body weight, because that can be one of the more significant quality of life or patient acceptance issues whenever they are started on therapy. This can be something that can be a barrier to therapy. So we wanted to make sure that we address that as part of this project. As mentioned, we also performed a meta analysis on the valuable

studies, and so these were assessed with RevMan 5.4. It does also need to be noted that not all study results could be reported and incorporated into the meta analysis. So on the GRADE rating, you might see a larger number of studies than what you might see in the meta analysis graphic that we'll talk about as we move through the presentation today. For the meta analysis, we focused on those outcomes that were assessed rating -- that was assessed using the GRADE rating. And if you would like to spend a little more quality time with those meta analysis figures, those are available in Appendix C. That is part of the report that is available to you from DERP. So now the good stuff. This is what you came for. So we are actually going to approach the Findings, and we are going to look at all of these agents, and we are going to use them or just approach them alphabetically. So -- oh, I'm sorry, not yet, but we'll get there. And so for the study flow diagram we wanted to give you an idea of sort of the project flow. So, initially, we had about 1402 documents screened. Once we went through the process, we ended up with 96 publications that were eligible for this particular project. And so we had 47 of these that were original studies, and then 49, which were additional analyses, so these might be post hoc or secondary analyses, or it might be a pooled analyses of similar things within a particular subject, or particular agent. Measured in the ones that we'll talk about today, I mentioned the MADRS and the HAM-D scale, the ones that we'll look at for depression severity. For overall improvement, we'll look at clinical global impressions, response, and remission. Although admittedly, we didn't spend a lot of time particularly at least on our presentation talking about remission, that is a pretty difficult benchmark to meet, especially with as short as many of these studies are that we'll talk about. So there is additional information in the report on remission, but we are not going to talk about remission very much today. And then for adverse events, again, we'll look at the Barnes Akathisia Rating Scale, and also another movement adverse event scale called the AIMS or the Abnormal Involuntary Movement Scale. So some overall context for the findings that we have. So in total, as I mentioned, we have had 47 original studies and 96 publications. Looking at those that have an FDA approval versus those that don't, we had 38 studies that were performed, and those that do have an FDA Indication for adjunct therapy and major depressive disorder, and nine of those studies were performed in agents that don't have an FDA approved Indication. The population. So we were looking at adults in general but wanted to note that we actually had two studies that looked at older adults, so one study will be 55 and older, and the other 60 and over. The rest of the studies, the other 45 just looked at 18 and over as adults. The comparators that were assessed. So 46 of these studies looked at placebo or monotherapy.

And as I mentioned, we had one head-to-head study that evaluated multiple agents within the class. So again, giving kind of a high-level overview of the number of studies and publications. So for those that are FDA approved, for aripiprazole there were 12 randomized controlled trials. Study sizes range from 52 to 1522, and you can see a total in just under 5000 total participants for these studies. On the right-hand column, you can see study durations, and it range from 6 to 12 weeks. Brexpiprazole had five randomized controlled trials. You can see the study size ranges there with a total of just under 3000 total participants in the studies in study durations 6 to 26 weeks. Cariprazine had five total RCTs with just over 3000 participants with study durations of 6 to 8 weeks. The olanzapine/fluoxetine combination product had five RCTs with just over 2000 total participants. And quetiapine had 10 total studies, and you can see again just over 2100 total participants for quetiapine XR, and study durations of 6 to 12 weeks. So for those that have an FDA-approved Indication, we had 37 total studies in this case and a total of 78 publications, just under 15,000 total participants, and relatively short study durations, and you are going to see that is a theme and a limitation we come back to 6 weeks for most of them but up to 26 weeks. So I know some of you are saying, well, wait a minute, you said in the previous slide, there were 38 publications in those that were FDA approved. So here is that one lone head-to-head study that we have. So we have aripiprazole versus olanzapine versus lithium. So we have one study in one publication. A grand total of 30 participants in this study and it's total study duration of 4 weeks. So I hope that I lowered your expectations earlier efficiently so that you weren't terribly excited about what we are going to learn from this particular study. The study characteristics for those that did not have an FDA approved Indication, we had two RCTs for a pimavanserin, and you can see 501 total participants with study durations of 6 to 10 weeks. Risperidone, we have five RCTs with just under 1000 participants with studies in 4 to 24 weeks. And for ziprasidone we had two RCTs, a total of 203 participants, and these studies both lasted for 8 weeks. So as noted here, we didn't find any study --published studies for the use the asenapine, clozapine, iloperidone, lumateperone, lurasidone, or paliperidone as adjuvant treatment for major depressive disorder. All right. Now, as promised, I mentioned that we would get to these alphabetically. So just like Alabama is the first state in the United States alphabetically, we are going to start in the As with aripiprazole. So just some overall study characteristics. We had 12 RCTs and 23 additional publications with aripiprazole, so eight of those were secondary or post hoc analyses, and 15 of those publications were pooled analyses. And again, this had the two RCTs that were performed in older adults. And most of the studies did have a

running period to confirm that the participant did have treatment-resistant depression. Looking at the GRADE ratings for the outcomes associated with this particular agent with aripiprazole, this is going to be a comparison to placebo or to ADT monotherapy (ADT standing for antidepressant therapy). So for our Efficacy outcomes, we had for MADRS, the Montgomery-Asberg Depression Rating Scale, we had nine RCTs with just under 2800 participants. We assessed this as a GRADE of high. And we saw that MADRS scores typically improved 2 to 3 points during initial treatment. And to give that a little bit of additional context, for most of the studies that for aripiprazole and that we'll talk about for almost all the agents, baseline MADRS scores were somewhere between 25 to 30. So a 2- to 3-point improvement is fitting in that context of 25 to 30 at baseline, so roughly 10% improvement from baseline score. For the CGI-I scores, we had eight randomized controlled trials reporting this outcome, and we assessed this as having a GRADE of high. And so we did see some modest improvement and CGI-I scores typically about 1 point throughout the course of treatment. For Response, so that is a 50% improvement in symptom score from baseline for a participant. Nine RCTs evaluated that outcome. We assessed this as having a GRADE of moderate, and so we did see that aripiprazole showed higher rates of response, and that was about a 10% to 28% absolute change from baseline. And typically, you will see anywhere from 20% to 40% of total participants in the aripiprazole achieving response as an outcome. So giving a little bit of visual to what I have just mentioned, this is the meta analysis plot. And so you can see on the left-hand side you have the different studies. You have the differences seen within the individual study. And then on the right-hand side you can kind of see this plot and the visual, so the top of the plot with the green boxes and lines are the results of that individual study. And then at the bottom you will see the black diamond, which indicates the cumulative effect of the pooled -- the meta analysis for those evaluable studies. So you can see in this particular finding for MADRS, one of the studies didn't achieve significance, but when you pooled all of the studies together, you did see an improvement overall in participants that were assigned to aripiprazole. For CGI-I scores, again, you can see the individual studies and their contribution to the meta analysis. You can see at the bottom the black diamond isn't particularly prominent down there. It's actually pretty, pretty narrow, but it does again indicate improvement overall with those taking aripiprazole, but you can see from the individual studies several of them didn't achieve significance on their own. And finally, for MADRS Response, once again, you can see the individual study contributions and where they fell in terms of their statistical significance. And once again, you

can see when combined that we did see some overall improvement with aripiprazole as part of the meta analysis. Harms findings. So looking at the BARS, that akathisia rating scale, seven RCTs evaluated that, and we saw a GRADE -- or we assessed it as having a GRADE of moderate, and we saw the aripiprazole showed modestly higher scores, which means they had a slight increase in akathisia. For change in body weight, 11 RCTs assess this outcome, and we had a GRADE rating of high, and aripiprazole typically showed between 1 kg to 1.5 kg increase in body weight within the first 6 weeks of therapy. A couple of subpopulations that we wanted to note. So factors that were noted in some of the secondary and post hoc analyses, so factors that improved the rate of response or remission for individuals, but it was noted that they were employed or if they had less severe symptoms at enrollment, that those tended to have higher rates of remission and response. A couple of factors that didn't seem to impact response or remission were age or baseline anger or hostility scores. Moving to our next agent, brexpiprazole. So we had five RCTs as part of this particular agent and had 12 additional publications, all of those being pooled analyses. And again, most of the studies had a run-in period to confirm that these participants did indeed have treatment-resistant depression. Looking at MADRS scores for brexpiprazole. So we had five RCTs evaluating this outcome. We assessed this as having a GRADE or certainty of evidence of high, and MADRS scores typically improved 1.5 to 3 points during treatment. And again, same sort of baseline typical profile of MADRS score of 25 to 30 at baseline. For the CGI-I score, as you can see, four RCTs assess this outcome. We had this as a GRADE of moderate, and we did see some modest improvement in CGI-I scores. However, there were inconsistent results between the four studies. For response, we noted five RCTs evaluated this outcome. We assessed this as having a GRADE of moderate, and we did see that brexpiprazole showed higher rates of response, though we had 4% to 12% absolute change within the agent. Once again, assessing the meta analysis, so giving a visual to what we just noted. For change in MADRS scores, we did have two evaluable studies for this outcome, and you can see that they are when combined that they did show an improvement towards brexpiprazole. Looking at Response, so again, that 50 [audio cuts out] improvement from baseline. You can see, once again, we go to inconsistent results, and you can see that sort of visually on the top four studies. Only one of those achieved significance. But once again, when combined all together, you can see a tendency toward an improvement with brexpiprazole in that combined analysis. Brexpiprazole versus placebo in our Harms. For the BARS Assessment, we had three randomized controlled trials, and we assessed this as having a GRADE of

high. We saw that brexpiprazole, again, had modestly higher scores, so an increase in akathisia. And for change in body weight, five RCTs noted this. Again, we had a GRADE of high on this. And brexpiprazole typically showed a 1 kg to 1.6 kg increase in body weight through the first 6 weeks of therapy. Moving along to cariprazine. Looking at the Efficacy outcomes with cariprazine, we had five RCTs evaluating the MADRS score. So we assessed this outcome with assertive evidence of high, and MADRS scores typically improved 1 to 3 points during initial treatment. Once again, typically having a 25 to 30 MADRS score at baseline. For CGI-I, five RCTs assessed this outcome. We had this as a GRADE of moderate, and so we did see maybe some modest improvement in CGI scores, but they typically weren't significant within the individual studies for this agent. For Response, we saw again five RCTs. We assessed this with a certainty of evidence of high. Cariprazine showed response rates of 1% to 10% absolute change, but they were typically not significant within the individual studies. So looking at the meta analysis for these outcomes. So cariprazine versus placebo and change of MADRS. Once again, you can see that most of the individual studies didn't achieve statistical significance as the bar crosses that point of no difference of zero, but when combined all together, you can see some improvement in the total combined analysis. For CGI-I, you can see that none of the studies achieved significance. And I know whenever I pull up this slide, for those of you that are reading this and seeing it, you are probably a bit skeptical that this slide is correct, but we triple checked it, and yes, just based on the variances and sample sizes, this is how this particular analysis shook out. So kind of just some interesting viewing there, saw a bit of an anomaly with this slide, but yes, this is correct. Once again, you can see that there was improvement when combining all of the studies together with cariprazine. Looking at Response. Once again, you can see most of the studies didn't achieve statistical significance on their own, but when combined we do see some favor toward and rates of response. Looking at Harms and the BARS assessment, we had five RCTs assessing this, and we assessed this with a certainty of evidence of high. And once again, cariprazine showed modestly higher scores, so an increase in akathisia. And for the change in body weight, we assessed this as having a GRADE or certainty of evidence of high, and cariprazine showed typically 0.4 kg to 0.9 kg increase in body weight through the first 6 weeks of therapy, so less weight gain than what we have seen in the previous set of agents. Moving along to olanzapine and fluoxetine, so a combination product. You are probably kind of getting into the rhythm now. So for our MADRS scores, we had five RCTs evaluating this outcome. We assessed it as having a GRADE of high, with olanzapine/fluoxetine improving scores typically 3 to 5

points throughout the studies. For response, we have four RCTs reporting this result with a GRADE of moderate, and olanzapine/fluoxetine combination showed inconsistent results ranging from 1% to 18% absolute difference. You can see from the meta analysis here, so looking at the change in MADRS scores, we had two evaluable studies, and when combined you can see that there is some favor towards olanzapine/fluoxetine combination. Looking at Response, you can once again see that most of the individual studies did not achieve statistical significance, but the overall combined analysis did achieve statistical significance just by the barest of margins, but it is significant. Looking at the Harms for olanzapine and fluoxetine. Looking at the BARS Assessment, we had four randomized controlled trials, but assessed as this having a GRADE of low, and we didn't really see much increase in the scores during treatment for this particular assessment. For change in body weight, this was one that was kind of notable. So we actually had this as a GRADE of high, but olanzapine and fluoxetine actually showed up to a 6 kg increase in body weight at the start of therapy, so this was the one obviously associated with the most weight gain among the class that we are talking about today. So our head-to-head study. Olanzapine versus aripiprazole versus lithium. So as noted, we only had one head-to-head study and a grand total of 30 participants. They were divided evenly, so 10 in each of the treatment arms for olanzapine, aripiprazole, and lithium, and there was no significant difference between the therapies at week 4, and so a very, very short study for this particular trial. So for quetiapine versus placebo, looking at the MADRS score, so we had five RCTs, assessing this and so we had this as a certainty of evidence or GRADE of moderate, and MADRS scores were typically improved around 3 points during initial treatment and significance was inconsistent. So you are probably seeing the theme now for these. Second-generation antipsychotics, we are seeing roughly about a 3-point improvement in MADRS scores throughout the class. For CGI-I, we had six RCTs. We assessed this as having a GRADE of high, and we saw again a relatively modest 1-point improvement in the CGI-I scores. For Response, we evaluated this as having a certainty of evidence of high, and we did see that quetiapine showed consistently higher rates of response and a 10% to 13% absolute change. Looking at the combined analysis for quetiapine and change of MADRS, you can see that in the combined analysis this is one that did not achieve statistical significance even when combining the groups. In Response, you can see that the two individual studies both achieved significance as well as the combined analysis between them. For our Harms outcome for quetiapine versus placebo, for our BARS Assessment, we assessed this as having a GRADE of low and that there were no significant

differences reported. For change in body weight, we assessed this as having a GRADE of high, and quetiapine typically showed about a 1 kg increase in body weight in the first 6 weeks of therapy. So we do have an assessment or two here for quetiapine versus lithium as a different pharmacologic agent. So we had two RCTs that assess this particular matchup. And so for Efficacy, we saw in the MADRS score we have this as a GRADE of low. Quetiapine showed a significant improvement in MADRS in one study and no difference in one study. For CGI-I, we assessed this again as having a GRADE of low. Same thing, we saw a significant difference in one study but not the other. And for Response, we assessed this as having a very low, and there was no difference between the groups, with both groups reporting sort of unusually high response rates. So it seemed out of the norm from what we saw from the other studies. For Harms in quetiapine versus lithium, we had one RCT assessing change in body weight. They didn't actually report how much weight that the participants actually gained, but they just said that more participants reported weight gain as an adverse event in the quetiapine group, and we assess this as having a certainty of evidence of low. So moving along to risperidone. So risperidone versus placebo for our Efficacy outcomes for MADRS. We assessed this as having a GRADE of low, and that MADRS scores improved between 1 to 7 points during initial treatment. For HAM-D scores, they actually reported those for these agents. We assessed this with a GRADE of low, and we saw inconsistent improvements in the HAM-D17 scores. For Response, we had two RCTs that assessed this. For GRADE, we had it as moderate, and we did see risperidone showing high rates of response with 15% to 22% absolute difference between risperidone and placebo. Again, putting the visual to our findings, you can see here for change in MADRS scores when we assessed -- or we combined all of these, the assessment was that there was no significant difference between risperidone and placebo. For change in HAM-D, same finding that we didn't see a significant difference within the pool or, excuse me, the combined analysis for this particular outcome. Harm outcomes for risperidone. For BARS, we had two randomized controlled trials but assessed this as a certainty of evidence of high, and risperidone did not significantly worsen BARS scores. So we didn't see an increase in akathisia. In change in body weight, once again, we GRADED this as high, but they didn't report the amount of weight gain. They simply reported that participants in the risperidone reported weight gain as an adverse event, but again, didn't specify how much weight was gained. All right. So for today's presentation, everybody's favorite drug was ziprasidone. So why is it everyone's favorite drug? Because it's the last one. It starts with Z. So our final drug we will talk about today, ziprasidone

versus placebo. So for our MADRS, we had one RCT with 64 participants, and we assessed this as having a certainty of evidence or GRADE of very low, and so MADRS scores improved by 4 points, but this was not significant. For CGI-I, we had two RCTs and a GRADE of moderate, and we saw that ziprasidone didn't show an improvement in one study and no improvement in the other. And for the HAM-D, we assessed this as having a GRADE of moderate. Once again ziprasidone showing significant improvement in one study and no improvement in the other. Due to the low number of studies, we weren't able to perform a meta analysis on those outcomes. And for BARS, the akathisia rating scale, one study, a GRADE a very low, and there were no clinically relevant changes that were reported in this particular study. For the ongoing studies that are relevant to this particular topic, we actually identified 13 ongoing studies evaluating SGAs as adjuvant therapy for MDD. So we can see through here we have two studies of aripiprazole. Comparators of relevance are bupropion, venlafaxine, and escitalopram, and completion dates anywhere from April 2021 -- so the results haven't been posted yet -- to December of 2025. We have five studies with brexpiprazole compared as a relevance for placebo, citalopram, and escitalopram. Once again, we have estimated completions where some of these studies may already have been completed but haven't reported results all the way through April 28 and 29. We have two studies with cariprazine comparing placebo -- compared to placebo, with a completion date of September 2021. Again, results haven't been posted for that one yet. Additional studies: three will lumateperone, comparing it to placebo. Estimated completion is February of 2024 through May of 2024. And one study with quetiapine evaluating it against amantadine and pramipexole, sample size of 150, and it is estimated to be completed in September of 2024. So now to our discussion and bringing all of this information together. So to kind of tie it all up, SGAs are a guideline-recommended addition to ADT in patients that have treatment-resistant depression. As noted, most agents we saw typically a 2- to 3-point improvement in MADRS scores during the first 6 to 8 weeks of therapy. Response rates were somewhat inconsistent overall between this group of therapies we have talked about today. Movement adverse events were typically slightly higher, as noted by the BARS and AIMS scores, but it is not really known if these would improve with continued therapy. So you see an initial worsening, but as the patient continues therapy, they adapt, and this is something that resolves with continued treatment. Weight gain is a significant concern, and it was consistently reported We saw usually about a 1 kg increase, although we did see a much larger increase with the olanzapine/fluoxetine combination of up to 6 kg, so something that we need

to be mindful of if we want to start patients on these particular agents so that we can counsel them appropriately, so they have appropriate expectations. GRADE ratings were generally high to moderate and consistent results between the study groups with aripiprazole and brexpiprazole. But I think one of the things that consistently came up throughout the project was the clinical Efficacy. I am going to come back to that in just a moment. GRADE ratings were a bit more variable with other therapies within this class, and I think you noted that particularly with those that had fewer numbers of studies and smaller studies. A consistent limitation that we encountered evaluating these studies was the short duration. Most of them were 5 to 8 weeks, so assessing initial response, we got some information there, but assessing long-term therapy in terms of both Harms and Efficacy, we really just didn't get a great sense of that throughout the studies. A lack of head-to-head studies. Again, we only had one, and it wasn't particularly impressive, and a lack of long-term follow up. So once again, seeing if Efficacy is maintained for the long-term or if adverse events or Harms stay, resolve, or even get worse with continued therapy. So in the clinical efficacy debatable part, one thing that one of our clinicians here at Auburn University who does specialize in psychiatry, so talking about when we see about a 3-point we will say on average for improvement in these patients. She said that while you are still looking for response, so cutting in half those improvements -- or cutting in half the symptoms from baseline, a lot of times what they see clinically in their practice is that even though the rating scales don't improve a whole lot, a patient will just sort of holistically say, "Well, I feel better." And so clinicians tend to -- if the patient is reporting that they feel better, even though they can't necessarily quantify, the clinicians are somewhat hesitant then to remove the agent from the patient. So the clinical Efficacy part, again, depending on practice, might have some variation there. So with that, I will be happy to take any questions from the panel.

Kavita Chawla: Thanks so much, Wesley. That was an excellent comprehensive review. Committee -- oh, I guess I will ask for stakeholder input first. I don't see any listed. [Cross-talk] --

Greg Hudson: [Cross-talk] I'm sorry, this is Greg. Real quick for Wesley, a quick question. I didn't see any noted on your slide deck, but I was just wondering if you saw any up and coming comparative studies?

Wesley Lindsey: When you say comparative studies, are you talking about like head-to-head?

Greg Hudson: Yes -- excuse me -- head-to-head studies between different agents such as aripiprazole versus lithium. Anything like that coming up.

Wesley Lindsey: And I do try to note that in the comparators. Uh, no. Mostly [cross-talk] well, there was only the one with the amantadine and pramipexol comparing the quetiapine. That is the only head-to-head study that was currently in the pipeline based on our searches.

Greg Hudson: Okay, thank you. I am just trying to note those as you are.

Kavita Chawla: Other questions from Committee members? No? Okay. And I don't see any hands raised from stakeholders. I guess, Nonye, if you can take us to the motion.

Nonye Connor: Mm-hmm. Okay. I kind of started copying this in here, and I am going to make an update on the lists of drugs and then slice and dice.

Kavita Chawla: So yeah, I guess the older ones, the clozapine, iloperidone will need to be removed. The lurasidone, yeah. Thank you.

Nonye Connor: The top that has different Indications just like the last one.

Kavita Chawla: Okay. [Cross-talk] --

Ryan Pistoresi: So you know where it says Autism Spectrum Disorder, we'll say treatment for MDD.

Nonye Connor: Yeah.

Zoe Taylor: Oh, yeah.

Nonye Connor: Let me.

Kavita Chawla: I think she is still cleaning up the [laughter] list of meds on the paragraph. But yes, thank you for calling that out.

Nonye Connor: Mm-hmm, thank you. [Indistinct] Okay.

Wesley Lindsey: Not to interrupt, but this is noted in the report, but I didn't mention it today. I noticed that you had pimavanserin off to the side, so makers of pimavanserin

actually abandoned their effort to get an Indication in this particular space due to lack of efficacy. Again, that is in the report, but I didn't mention that as part of the presentation today.

Kavita Chawla: Appreciate that, Wesley, thank you. So maybe we can just remove it from the list altogether on the left. Yeah, perfect. We can remove that. Oh, no. We can leave the major depressive disorder.

Zoe Taylor: I would just keep going and remove all the way through disruptive behavior disorders and then [cross-talk] --

Kavita Chawla: [Cross-talk] Oh, yeah. There is [cross-talk] --

Zoe Taylor: [Cross-talk] they set with the -- what it says on the top -- as adjuvant therapy for the treatment of MDD -- is what it probably should say.

Nonye Connor: So right there? [Cross-talk] --

Kavita Chawla: [Cross-talk] Yeah.

Nonye Connor: Okay. [Cross-talk] --

Zoe Taylor: [Cross-talk] Um, no.

Nonye Connor: Oops.

Zoe Taylor: All the way. No, that is fine. Just also keep going with erasing.

Nonye Connor: Hm, um, all the way.

Zoe Taylor: Keep going all the way through disruptive behavior disorders. Perfect.

Nonye Connor: Oh, thank you.

Zoe Taylor: And then we could say for treatment as adjuvant therapy for the treatment of MDD. [Cross-talk] Well, I don't know if that is redundant.

Nonye Connor: This?

Kavita Chawla: Um, as a part as adjuvant therapy for the treatment of MDD. Yes, please. We'll see how that rolls. Okay. After considering the evidence of Safety and Efficacy for the treatment -- for the adjuvant treatment, so I guess you would remove the treatment? Um, no, no. Sorry. [laugh] The treatment comes up twice, so if you can just remove --

Ryan Pistoresi: Yeah.

Kavita Chawla: Yeah, For the adjuvant treatment therapy of the MDD.

Jon MacKay: We need to call out that olanzapine wasn't used in isolation in terms of like with fluoxetine. Or can we just leave that out?

Ryan Pistoresi: This is Ryan, and typically when we see drugs with combinations from two different Washington PDL drug classes, we tend to not use them within the motion. So if you think about the asthma, COPD, we do have a lot of those combinations there for other drug classes like with diabetes drug classes. For some of the statins, we typically don't have those combinations listed in the motion. Also, one of the ways that those studies were done is it was olanzapine and fluoxetine versus placebo or fluoxetine monotherapy. So essentially, a lot of those studies are looking at the effect of adding in olanzapine. So we opted to just leave it as olanzapine here in the motion, knowing that it was studied in association with fluoxetine.

Jon MacKay: Thank you.

Kavita Chawla: Go ahead, Peter.

Peter Barkett: Thanks. I am trying to recall the language that we typically use, but just past halfway in the motion that is showing on the screen, and there is a sentence that says something like these medicines should be on the Washington State Preferred Drug List, and I thought we usually used the language "are eligible" to be on the Preferred Drug List. And I am wondering if maybe I have got that wrong, or maybe this class is being treated differently as, like, a protected drug class? And so [cross-talk] --

Ryan Pistoresi: This is Ryan. Yes. Yeah, for most drug classes we typically have language that says, "and are eligible to be preferred." I believe years ago the P&T Committee made the recommendation to the agency to try to have as many of these drugs be preferred, so that way when a patient is starting therapy

that the providers do have the option. In fact, looking at the current Washington Preferred Drug List, all of these drugs are listed as preferred, and so that is typically how we've reviewed this class, in particular, as a protected class for antipsychotics.

Donna Sullivan: This is Donna. But we do require generics first. And this is old language taken from a different motion from a different review, so I think it is due time to update the language to refer how these drugs are -- that they are all eligible.

Peter Barkett: Yeah, I mean, I think it's reasonable to copy the language that we have for other motions about eligibility, and then it leaves a little bit more flexibility. I don't feel super strongly about it, but I think for consistency's sake, I think it would make sense. Curious to hear if other Members of the Committee feel strongly one way or another.

Kavita Chawla: Other comments from the Committee Members? I think that is a great point. And I assume, like, the [cross-talk] --

Donna Sullivan: Hey.

Kavita Chawla: Yeah, go ahead.

Donna Sullivan: This is Donna. I mean all of these drugs are already on the PDL in the antipsychotic class. I don't think it's -- to be honest with you, I don't even think it's necessary unless you feel strongly about using these in major depression disorder, depressive disorder. We don't usually prefer drugs based on Indication, so I mean [cross-talk] --

Kavita Chawla: [Cross-talk] I see.

Donna Sullivan: -- these drugs are already preferred on the PDL, so I don't know what this motion is going to do to the status of these drugs on our PDL.

Kavita Chawla: Okay. That is helpful. And that is a good point that these medications are preferred and non-preferred, period, not really by Indication. Other comments?

Laura Beste: So this is Laura Beste. Donna, are you recommending then that the line that says "should be preferred on the Washington Preferred Drug List" just be removed?

Donna Sullivan: I'm -- this is Donna -- I'm questioning whether we even need to make a motion and just take the presentation that we saw as information only because unless you are going to say that these need to be preferred for major depressive disorder, there is no policy, and we don't require diagnosis for these. If they are being used for depression, then they are on label, then they are just approved based on their preferred status as they are today.

Kavita Chawla: Okay. So I am hearing that maybe we don't even need a motion. We can move forward? Unless there are questions.

Donna Sullivan: I think you need to have a motion of whether or not you need a motion. [laughter]

Zoe Taylor: Why don't we just do the motion because we already wrote it, and it seems fine. It's basically just certifying that we agree that all of these are still effective. I don't know if there is any use to having this sentence about pregnancy, too, but if that is sort of like what is usually written, I feel like we might as well just keep it.

Laura Beste: This is Laura Beste. Did we want to remove the -- pimavanserin from the side?

Kavita Chawla: Yes.

Laura Beste: On the left column?

Kavita Chawla: Yeah, great point. Let's do that. Nonye, if we can remove the grayed out medication on the left column, the pimavanserin.

Christy Weiland: This is Christy Weiland. Donna, I am curious. If we choose to move towards a motion, but it's not necessary, is it more work on the back end for you guys if we don't actually need this?

Ryan Pistoresi: This is Ryan. You know, this could be similar to how we do some of the other surveillance reports, where we just present here is the update in the class, here is the evidence, and then we can do a cost analysis on the back end and update the PDL as needed.

Kavita Chawla: Okay. So with that, Ryan, do we need to change the language at all? Or should we move forward with the motion as written, if other if the Committee members agree?

Laura Beste: This is Laura Beste. Or do we just update the surveillance accepted as adequate column?

Ryan Pistoresi: Yeah. We could update that to say the report accepted as adequate and reiterate in the prior motion.

Kavita Chawla: Yeah. Kavita here. I think the difference in the language is, like -- what was it? -- a systematic review versus a surveillance because this was not just a surveillance report. So I don't know if we'll have to then change all of that, too. So thoughts about moving forward with the motion as is, and then that way we can just approve the systematic review as well.

Peter Barkett: Probably going to spend more time just talking about whether or not we need a motion than [cross-talk] a motion, so I would say let's just make the motion and continue on.

Kavita Chawla: All right. Who would like to go for it?

Laura Beste; This is Laura Beste. I make a motion that after considering the evidence of safety, efficacy, and special populations for the adjuvant therapy of the treatment of MDD, I move that aripiprazole, brexpiprazole, cariprazine, olanzapine, quetiapine, risperidone, and ziprasidone are efficacious for their approved FDA Indications and should be preferred on the Washington Preferred Drug List. Second-generation antipsychotics cannot be subject to therapeutic interchange in the Washington Preferred Drug List. The Preferred Drug List should include at least one medication as considered safe in pregnancy.

Peter Barkett: This is Peter Barkett. I will second the motion.

Kavita Chawla: All in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed? And the motion carries. Thank you, all. And great, we are not only on schedule but a touch ahead of schedule. Do we want to keep going or should we take a break?

Nonye Connor: Um, we can go ahead [cross-talk] --

Kavita Chawla: [Cross-talk] All in favor for a break. [Cross-talk]

Nonye Connor: [Laugh]

Kavita Chawla: Go ahead.

Nonye Connor: I was going to say we can go ahead and take a break.

Kavita Chawla: Okay, sounds good. So we'll be back in 15 minutes, so 10 past 11:00?

Nonye Connor: Sounds good.

Kavita Chawla: All right. Thank you. Thank you, Wesley.

[break]

Kavita Chawla: We can make sure we have quorum. It looks like we do. All right. So going into the next part of our morning is the Multiple Sclerosis report by Rachel McCausland and Courtney Cooper. Are you on?

Rachel McCausland: Hi, yes. Good morning.

Kavita Chawla: Hello. Good morning.

Courtney Cooper: Hi, good morning.

Kavita Chawla: The floor is yours.

Rachel McCausland: Great. Thank you. name is Rachel McCausland. I am one of the researchers from the center and I will be presenting this update along with my colleague, Courtney. We are presenting on disease-modifying therapies for multiple sclerosis, and this is an update of prior reports. Next slide. This briefly an overview. We'll start with the background of MS and disease-modifying therapies. We'll go through our PICO criteria, the Key Questions that we were

looking to answer, our Methods for this review, Findings, and finally a discussion of those findings. Next slide. We have a pretty extensive list of abbreviations that are used throughout this presentation. A lot of these are standard for reviews and statistics, and I won't go over them. But there are a few that are specific to this topic that I want to touch on starting with DMT, that is for disease-modifying therapy. And then we have MS, which is multiple sclerosis. We have four types of MS. There is CIS, clinically isolated syndrome. RRRMS, which is relapsing-remitting MS. SPMS is secondary progressive MS and PPMS is primary progressive MS. We will go over those in further detail later. These are just the acronyms. And then we have two outcomes measures, EDSS, which is the Expanded Disability Scale Score, and MSFC, which is the Multiple Sclerosis Functional Composite Score. Next slide. As I mentioned, this is an update. This report was -- the prior report was completed in 2020. But as you can see here, the topic has been reviewed and updated many times in the past. The original report dates back from 2007, and that report and all subsequent updates are archived in the DERP clearing house. Next slide. So now I am going to go into a little bit of the background of multiple sclerosis and disease-modifying therapies. Next slide. Myelin surrounds and insulates neurons and allows efficient transmission of nerve impulses. In multiple sclerosis, the body's immune system attacks the myelin. This leads to neurologic dysfunction. Symptoms of MS include sensory issues, such as numbness, muscle weakness or spasms, vision problems, dizziness, and trouble walking or speaking. Next slide. Multiple Sclerosis is the most common and unmediated inflammatory demyelinating disease of the central nervous system. The prevalence of MS has been increasing over the past five decades. A 2019 population-based estimate found that one million adults were estimated to be living with MS in the US alone. MS is the most common disabling neurological disease of young adults with symptom onset, typically occurring between the ages of 20 and 40 years. Next slide. MS is currently categorized into four main types, although the pattern and course of MS is unpredictable and can vary substantially from person to person. First, we have clinically isolated syndrome, or CIS, and that is the first episode of neurologic symptoms caused by inflammation and demyelination in the central nervous system. Then there is relapsing-remitting MS, or RRRMS, and RRRMS is characterized with clearly defined attacks of new or increasing neurologic symptoms followed by periods of partial or complete recovery, also known as remission. RRRMS can be further characterized as either active with relapses, evidence of new MRI activity over a specified period of time, or both, or it can be not active. Then we have SPMS, or secondary progressive MS, and that is progressive worsening of neurological function or

disability accumulation from RRMS with or without occasional relapses, minor remissions, and plateaus and severity. Finally, we have primary progressive MS, or PPMS, and that is characterized by neurological function worsening or disability accumulating from disease onset, with occasional plateaus and severity, temporary minor improvements, or acute relapses. Progressive relapsing MS was an older term that has now been eliminated. People who were previously diagnosed with progressive relapsing MS would now be considered to have primary progressive MS, and so that is not listed here in our types of MS. Next slide. For some people a visual helps to understand, so that is what we have here. And starting on the left you see RRRMS, which is clearly defined attacks. Those are the relapses of new or increasing neurologic symptoms. In remissions, all symptoms may disappear, or some symptoms may continue and become permanent. However, during those periods the disease does not seem to progress. And then the middle you see SPMS, the secondary progressive MS, and some people diagnosed with RRRMS eventually go on to have a secondary progressive course in which neurologic function worsens progressively or disability accumulates over time. In SPMS the person may have occasional relapses as well as periods of stability. There on the right you see PPMS. That is a primary progressive MS, and that is the neurologic function worsening or disability accumulating as soon as symptoms first appear. PPMS can have those brief periods of stability and periods of increasing disability with or without a relapse or new MRI activity. CIS, a clinically isolated syndrome, is not pictured here because it is just the first case of neurologic symptoms. MS is unpredictable. It can vary substantially from person to person. These are the descriptors that are currently in use, but an international committee organized by the National MS Society and the European Committee for Treatment and Research in Multiple Sclerosis have posed a new way of classifying MS as a continuous disease process. A change in classification will take years, however. So this report uses the current system of dividing MS into different disease types, since that is what is currently used in the available research. Next slide. At the time of this report, the FDA has approved 19 disease-modifying therapies for multiple sclerosis and clinically isolated syndrome. The aim of these DMTs is to reduce the number of relapses, delay progression of disability, and limit new MS disease activity as seen on MRI. Next slide. Over the next three slides, we have a table with the disease-modifying therapies that are included in this report. There are 17 DMTs that are indicated for people with relapsing forms of MS, which includes clinically isolated syndrome, relapsing-remitting MS, and active secondary progressive MS. DMTs that are prescribed for people diagnosed

with CIS. Those that are experiencing the first episode of neurological symptoms have the goal of preventing or delaying a second attack. That second attack is also known as conversion to MS. Next slide. The second line down you see siponimod. In March 2019, the siponimod labeling was the first to explicitly describe that relapsing forms of MS include CIS, RRMS, and active SPMS. All sponsors of other DMTs approved for the treatment of relapsing forms of MS have since updated their Indication statements to conform with this contemporary nomenclature. It is important to note though that DMTs approved for relapsing forms of MS are not indicated for people with non-active secondary progressive MS. There are two DMTs, cladribine and alemtuzumab -- you can see those here on the screen -- that are indicated for people with relapsing-remitting MS and active SPMS, who have had an inadequate response to other DMTs. Unlike the other DMTs that are approved for all relapsing forms of MS, cladribine and alemtuzumab are not approved for people diagnosis with CIS. And then one of these DMTs, siponimod, the third one down on the screen, is also indicated for primary progressive MS. This is the only DMT currently FDA approved for PPMS. Next screen. This is just the final listing from that table. Of note, there are 19 FDA-approved DMTs for MS, but two of those, the mitoxantrone and [indistinct] are not included in this table because they were excluded from the prior DERP reports on DMTs for MS and have remained excluded from this review. This table is also included in the complete report, and you can look over it in detail there if you need to. Next slide. Our PICO criteria. Population that we focused on was adult outpatients aged 18 years and older with multiple sclerosis including relapsing-remitting, secondary progressive, and primary progressive. We also looked at adult outpatients with clinically isolated syndrome, those having the first demyelinating event or symptoms. The interventions that we looked at were those listed DMTs in the previous table with FDA approval for the treatment of multiple sclerosis in clinically isolated syndrome. Next slide. Our comparators that we looked at were any other listed intervention. We only looked at head-to-head comparisons. The landscape of DMTS for multiple sclerosis has rapidly evolved over the past 20 years. The previous report did look at placebo-controlled. However, because there are so many different FDA approved DMTs as treatment options, we wanted to limit this evidence review to the comparative effectiveness and Harms of DMTs for MS. So placebo-controlled comparisons were excluded, except for RCTs evaluating DMTs for clinically isolated syndrome, placebos were included as a comparator. Outcomes that we looked at were relapse, disability, quality of life, functional outcomes, persistence, or for those with CIS conversion to MS diagnosis, which is the second instance of an attack or

the first relapse. We also looked for adverse events, overall adverse events, serious adverse events, withdrawals due to adverse events, and specific adverse events such as hepatotoxicity. Next slide. Study designs. We looked at randomized controlled trials, placebo-controlled trials for CIS only, and retrospective and prospective cohort non-randomized studies comparing an intervention type with another for outcomes on Harms only. We did not look at Efficacy in those cohort studies. We required a 12-week study duration or longer for all included studies, and for those prospective cohorts reporting on Harms, we also required a minimum total sample size of 1000. Next slide. Key questions that we answered. KQ1: What is the effectiveness of DMTs for multiple sclerosis? KQ2: What is the effectiveness of DMTs for people with clinically isolated syndrome? KQ3: Do DMTs differ in Harms by Indication meaning those with MS or CIS. Did the effectiveness and Harms vary by subgroup? was KQ4. The subgroups, for example, would be participant characteristics, use of prior DMTs for MS subtype of MS, presence of comorbidities, or antibody status. And finally, KQ5, what are the characteristics of ongoing studies of DMTs for MS? Next slide. Our Methods. Next slide. We limited searches of evidence sources -- sorry -- we searched for clinical evidence sources. We limited the searches of those evidence sources to citations published after the previous DERP report searches, which were done on October 15, 2019, with an updated Ovid MEDLINE search on February 3, 2020. For newly approved DMTs that were not included in the previous DERP reports we searched from database inception. We checked all of the studies from previous reports against our inclusion criteria. So specifically, we looked for those placebo-controlled trials that were previously included, and we excluded them from this updated report. We assessed the risk of bias of individual studies. We combined the studies using review manager for major outcomes. We use the GRADE approach for major outcomes, and finally research clinicaltrials.gov for ongoing studies through the end of 2023. Next slide. As I mentioned, the risk of bias of individual studies was assessed. We use the standard DERP risk of bias assessment for low, moderate, or high, low being clear reporting methods and mitigation of potential bias and conflict of interest, up through high with clear flaws that might introduce serious bias. Next slide. We use the GRADE approach for certainty of evidence across the key outcomes, which were relapse, disability progression, change in disability as assessed using the EDSS, change in function assessed using MSFC, persistence, and serious adverse events. Just as a little reminder GRADE approach to rating the certainty of evidence is based on a four-level system. There is high, moderate, low, or very low. The GRADE approach classifies randomized controlled trials

as initially starting at high certainty and observational as initially starting out low certainty. By assessing the five domains, which are risk for bias, inconsistency, indirectness, insufficient precision, and publication bias, that certainty can be rated down, or in the case of large effects, existing dose response relationships or plausible compounders, they can be rated up. Next slide. Our findings, excellent. So as I have mentioned, this was an update, we brought forward 109 studies that were included in the previous report. Combined with data based searches, this resulted in 3614 unique records. We screened 741 at the full text stage, of which 612 were excluded. If you want to see exclusion reasons by studies, those are included in Appendix D of the full report. If you direct your eye down to the bottom left in the green square, for this update, we included a total of 38 RCTs, 45 cohort studies, and 39 sister publications. This includes newly identified studies and the studies that were pulled forward from the previous report. Next slide. So here we can see another breakdown of those final inclusions. There were 122 total inclusions. 98 were previous inclusions, and 24 were new studies. Of those 24 new studies, we had 6 RCTs, 15 cohort studies, and three sister publication or ancillary studies. Of the 6 RCTs that we included, all six included populations with MS. We did not identify any new studies looking at clinically isolated syndrome. And for those 6 RCTs, there were four different head-to-head comparisons. Next slide. Now we'll go into those Findings in a little bit more detail on the -- starting with the comparative effectiveness and Harms for multiple sclerosis. Now, next slide. So this is a diagrammatic representation of the RCT evidence that was eligible for this report for the MS population. I realized that there is a lot of information on one page, so on the next slides we'll zoom in on some important parts in just a moment, but I wanted to give you a high-level overview of all of the evidence. You will see here that the newly-approved DMTs are in green. The four new head-to-head comparisons are shown with both connections, and the other evidence shown here was identified in the 2020 report. Next slide. So here zoomed in we are focusing on the four new head-to-head comparisons. There were three newly-approved DMTs: ofatumumab, ponesimod, ublituximab, and they were each compared with teriflunomide. We also identified a comparison of glatiramer acetate with fingolimod, although fingolimod and glatiramer acetate were included in the previous report, this specific head-to-head comparison is new. Next slide. If you will direct your attention to the right you will see that there are five FDA-approved DMTs, diroximel fumarate, cladribine, monomethyl fumarate, siponimod, and peginterferon beta-1a that we did not identify any eligible RCTs for. Next slide. And here we see the portion of the diagrammatic representation that focuses on the

previously reviewed head-to-head comparisons and different dosing schedules comparisons that we did not find any new evidence for. Next slide. The previous report that we just saw in that diagram included 11 head-to-head comparisons. There were 23 RCTs, and four different dosing schedule comparisons. We did not identify any new evidence for these previously reviewed head-to-head comparisons. The findings from the 11 previously reviewed head-to-head comparisons have not changed since the previous report, and because of that, we will not be discussing those specific studies in this presentation. The Findings from specific studies remain included in the report, and the slides from the 2020 presentation with the findings from those specific studies can be found at the end of this presentation. Next slide. As previously mentioned, for patients with MS. We identified four new head-to-head comparisons evaluating the Efficacy and Harms of DMTs in patients with MS. Three new DMTs, ofatumumab, ponesimod, ublituximab were each compared with teriflunomide. And we also identified a new head-to-head comparison of fingolimod with glatiramer acetate. Three of the studies included participants with both relapsing-remitting MS and secondary progressive MS. One trial was limited to only relapsing-remitting MS, in two trials included relapsing forms of MS. The studies ranged in length from 12 to 30 months. Next slide. The first comparison that we'll be discussing was the ofatumumab 20 mg versus teriflunomide 14 mg. We identified two RCTs with a total sample size of 1882, evaluating the Efficacy and Safety of subcutaneous ofatumumab compared with teriflunomide in patients with RRMS or SPMs. So as the ASCLEPIOS I AND ASCLEPIOS II trials, they were identically designed, conducted concurrently, and reported together in one publication. Each trial was powered for the primary endpoint of the annualized relapse rate, and the combined trials provided the sample size and power for the pre-planned meta analysis of disability worsening. Participants in the subcutaneous ofatumumab group also receive oral placebo, and participants in the oral teriflunomide groups also received subcutaneous placebo corresponding to the active drug in the other group. We assessed this ASCLEPIOS trials to both be at moderate risk of bias because of concerns around author conflicts of interest and sponsor involvement in the study design and analysis. Next screen. A meta analysis of the two ASCLEPIOS trials found that ofatumumab significantly reduced annualized relapse rates at 30 months. The pooled analysis of the two trials found that ofatumumab significantly reduced the risk of disability worsening at 6 months, but there was no significant difference in confirmed disability improvement at 6 months. There is a moderate certainty of evidence for both of these Findings. Next slide. Study completion, which is an indirect measure

of persistence, was found to be significantly higher for participants in the ofatumumab group, also moderate certainty of evidence there. There is no significant difference in the rate of serious adverse events; however, this was rated with a low certainty of evidence. Disability progression and changes in function with the MSFC were not evaluated in the ASCLEPIOS trials. Next slide. We identified one RCT with a total sample size of 1133 participants evaluating the Safety and Efficacy of oral ponesimod compared with oral teriflunomide in patients with relapsing-remitting MS or SPMS. This was the OPTIMUM trial, and we rated it at moderate risk of bias because of concerns around attrition, author conflict of interest, and sponsor involvement all aspects of the study. Next slide. In the OPTIMUM trial it was found that ponesimod significantly reduced relapse rates at 108 weeks, so right at two years, with a moderate certainty of evidence. Changes in disability. There was no significant difference between ponesimod and teriflunomide at 12 weeks, but there was a very low certainty of evidence. Next slide. Similarly, there was no significant difference in study completion, which is that indirect measure of persistence, and no significant difference in rates of serious adverse events. These are both rated at a low certainty of evidence. Disability progression and changes in function were not evaluated in the OPTIMUM trial. Next slide. We identified two RCTs with a total sample size of 1094, evaluating the Efficacy and Safety of intravenous infusions of ublituximab compared with oral teriflunomide in patients with relapsing MS. This was the ULTIMATE I and ULTIMATE II trials, and similar to our previous discussion, these ones were identically designed, conducted concurrently, and reported together in one publication. The authors analyzed results separately for primary outcomes in the two trials, but they conducted a pre-specified pooled analysis for selected secondary and tertiary outcomes. Participants in the intravenous ublituximab group did receive an oral placebo, and participants in the oral teriflunomide group received an IV placebo corresponding to the active drug in the other group. We assess the ULTIMATE trials both at high risk of bias because of author financial conflicts of interest, and a high level of sponsor involvement in study design, analysis, and publication. Next slide. A meta analysis of the ULTIMATE I and ULTIMATE II trials found that ublituximab significantly reduced relapse rates at 96 weeks, with a moderate certainty of evidence. The pooled analysis of the two ULTIMATE trials found that there was no significant difference between ublituximab and teriflunomide for changes in disability at 12 weeks. Next slide. There was no significant difference in study completion, and no significant difference in rates of serious adverse events. The persistence was rated with a very low certainty of evidence in this year's adverse events with

a low certainty of evidence. Change in function as measured by the MSFC was reported in the ULTIMATE trials. However, it was reported as a tertiary endpoint from which no conclusions could be made. Disability progression was not evaluated. Next slide. Finally, we identified one RCT with a total sample size of 1064. Evaluating the Safety and Efficacy of oral fingolimod 0.25 mg and/oral fingolimod 0.5 mg, each compared with subcutaneous injections of glatiramer acetate in patients with relapsing-remitting MS. This was the ASSESS trial, and we evaluated it to be a moderate risk of bias because of concerns around the number of enrolled participants, lack of participant blinding, and author conflicts of interest. The ASSESS trial enrolled fewer than half the planned number of participants, which affected the power calculations, and randomization ratios that were requested by the FDA were not possible. Although the trial was rated blinded, a double-blind design was not used for this trial. Investigators stated that they did not use a double-blind design because it would have required double-dummy treatment and thus daily sham injections for the two fingolimod arms. Next slide. Fingolimod was found to significantly reduce relapse rates at -- sorry. That is the fingolimod 0.5 mg was found to significantly reduce relapse rates at 12 months. There was no significant difference with fingolimod 0.25 mg and glatiramer acetate at 12 months. This was a moderate certainty of evidence. For changes and functions, similarly, the fingolimod 0.5 mg significantly improved functional disability at 12 months, but there was no significant difference with fingolimod 0.25 mg and glatiramer acetate at 12 months, with moderate certainty of evidence as well. Next slide. Study completion, which is that indirect measure of persistence, was higher for both fingolimod groups, and of those participants who completed the study, higher proportions of the fingolimod groups received the study drug until completion. There was no significant difference in rates of serious adverse events. Low certainty of evidence there. And disability progression and changes in disability were not evaluated in the ASSESS trial. Next slide. KQ2 and KQ3, the comparative Effectiveness and Harms for clinically isolated syndrome. Next slide. So the previous report identified five placebo-controlled comparisons in eight RCTs and one dosing schedule comparison for people diagnosed with CIS. We did not identify any new evidence for those previously reviewed comparisons. So similar to what we discussed previously for the MS population. The findings from the previously viewed comparisons have not changed since the previous report, and we will not be discussing the specific studies in this presentation. Findings from those specific studies remain included in the report, and slides from the 2020 presentation with the findings from specific studies can be found at the end

of this presentation. Next slide. KQ4 was looking at variations by subgroup. Next slide. We looked for variation by subgroup across all 43 RCTs reviewed, including the six new for this report. Participant factors such as age and prior treatment may change the effectiveness of treatment, but subgroup analyses are not reported consistently across studies which limits our ability to draw robust conclusions. The presence of neutralizing antibodies does not appear to be associated with a reduction in the effectiveness of treatment. Next slide. And from here, I will be passing the mic over to my colleague, Courtney Cooper.

Courtney Cooper: Thank you, Rachel. We will revisit Key Question 3: Do DMTs different Harms by Indication when considering evidence on people with MS and CIS. And this time we'll be reviewing the eligible cohort studies. So in contrast to the RCT evidence identified for this updated report, we identified new cohort study evidence that evaluated some of the same comparators and outcomes as cohort study evidence identified in 2020. Therefore, we have integrated the newly identified evidence with findings that have remained unchanged from the 2020 report where applicable. So in summary, we identified 45 cohort studies, 15 of which are newly identified for this update. The majority of studies were assessed as moderate risk of bias because of concerns about author conflicts of interest and industry funding. The rest were assessed as high risk of bias due to additional concerns about adjustment for confounding 35 cohort studies, 11 of which are newly identified for this update reported on treatment discontinuation or switch. Twelve cohort studies, six of which are newly identified for this update, reported on serious adverse events. There is an overlap of two cohort studies which reported on both treatment discontinuation or switch and serious adverse events. And additionally, we did not identify any direct comparison of Harms by Indication. As mentioned on the previous slide, 35 cohort studies, 11 which are newly identified for this update reported on treatment discontinuation or switch. Overall, from the evidence reviewed treatment discontinuations for switches appear to be significantly lower with fingolimod and dimethyl fumarate. Notably, a number of cohort studies investigated treatment discontinuation or switch of oral DMTs compared with the injectable DMTs; however, not every FDA-approved DMT was included in the reviewed studies, and the reported outcomes are not generalizable to all categorically oral or injectable DMTs. Therefore, uncertainty does remain regarding the risks of treatment discontinuation or switch for oral DMTs compared with injectable DMTs. Additionally, 12 cohort studies, six of which are newly identified for this update, reported on serious adverse events. It is important

to note that serious adverse events are higher in some DMTs. Specifically, the risk of liver injury was higher for interferons, alemtuzumab, teriflunomide, and fingolimod. The risk of PML was higher with fingolimod and dimethyl fumarate. The risk of infection was lower with interferon beta and glatiramer acetate. And lastly, based on the evidence reviewed, uncertainty remains regarding the association of cancer risks and DMTs. Multiple cohort studies reported association among various DMTs and an increased risk of cancer. However, only one identified study reported a statistically significant association. In this study, interferon beta, dimethyl fumarate, and fingolimod were significantly associated with cancer reporting. Key Question 5: What are the characteristics of ongoing studies of DMTs for MS and CIS? We identified a total of 12 ongoing studies, and these ongoing studies have the potential to fill important evidence gaps, particularly where we did not identify published comparative RCT evidence for DMT. And this is specifically the case for cladribine, diroximel fumarate, monomethyl fumarate, peginterferon beta-1a, and siponimod. However, it is important to note that all the information about these ongoing studies is based on posted eligibility criteria and not on published results, so these findings represent our best estimation for current ongoing trial information of interest to DERP. Six ongoing studies are comparative RCTs. Notably, every single one of the DMTs eligible for inclusion in this DERP report have ongoing comparative RCT trials. Across these trials, there is a trend towards comparing it against groups of DMTs rather than one DMT against another DMT. For example, two of these trials are investigating ofatumumab versus first-line DMTs and other approved DMTs categories, which are published in the registry and defined by trial investigators. Two additional trials have grouped the DMTs as early aggressive therapy versus traditional therapy and early highly effective therapies versus escalation therapies. And these categories are once again defined by the trial investigators and are not necessarily reflective of the evidence we identified. Lastly, we identified two trials comparing several eligible DMTs of interest to DERP to a stem cell treatment that is not currently FDA approved. These trials were included given the possibility of subgroup analyses comparing DMTs of interests for this report. This table contains additional information for the six comparative RCTs that were discussed on the previous slide. So I will walk through this briefly. In terms of study populations. One trial includes individuals with relapsing MS, and the rest include individuals with relapsing-remitting MS. Estimated enrollment numbers range from 100 to 900 participants, and estimated completion dates range from March 2024 to April 2030. Finally, there was also an ongoing comparative RCT that was identified in the previous 2020 report. It

has been completed but has yet to publish results. This trial was completed almost three and a half years ago at this point and was investigating peginterferon beta-1a compared with interferon beta-1a or 1b and has a study population of 80 participants. The study is still of interest given that no comparative RCT evidence on peginterferon beta-1a was identified for this report. We also identified two ongoing placebo-controlled RCTs that include adults with primary progressive MS and relapsing MS. Both trials are comparing ocrelizumab against a placebo. One of them has the potential to investigate a population with CIS, which would meet eligibility criteria for this report. The other trial is looking at a population with primary progressive MS, which is a potential interest as ocrelizumab is the only DMT currently FDA-approved to treat individuals with PPMS, so there is a gap in terms of head-to-head RCT evidence currently available for this population. Lastly, we identified three ongoing prospective cohort studies in which we emphasize comparative evidence. As with the comparative RCTs, these cohort studies hold potential to provide evidence on all our DMTs of interest. However, we will not be able to notice with certainty until results are published. One trial that included any DMT was completed in September 2023, with 1250 total participants who either had relapsing-remitting MS or relapsing secondary progressive MS. Trial results have yet to be published at the time of our search. The other two trials, both of which are evaluating diroximel fumarate are only including pregnant women with MS. This table contains additional information for the two ongoing placebo-controlled RCTs and three ongoing prospective cohort studies. For the two placebo-controlled RCTs, estimated enrollment numbers are 175 and 1000, and estimated completion dates are December of 2027 and August 2028. We touched on the details of the completed prospective cohort study on the prior slide, so of the two prospective cohort studies that are not yet completed, estimated enrollment numbers are 908 and 1178, and estimated completion dates are January 2031 and July of 2032. And we'll conclude this presentation with a brief discussion and a summary of our findings. In total, we identified 38 RCTs, six of which are newly identified for this update, 15 of these are head-to-head comparisons in people with MS for which are newly identified for this update, and these were evaluated in 29 RCTs, six of which are newly identified for this update. We did not identify any new evidence for this update in terms of RCT evidence on comparisons of different dosing schedules for people with MS, comparison of different dosing schedules for people with CIS, and placebo control comparisons for people with CIS. All of the findings on this information remain unchanged from the 2020 report and entails four comparisons of different dosing schedules for people with MS

evaluated in nine RCTs, one comparison of different dosing schedules for people with CIS evaluated in one RCT, and five placebo-controlled comparisons for people with CIS evaluated in eight RCTs. Furthermore, we also identified 45 cohort studies, 15 of which are newly identified for this update. As a reminder, there are 17 total FDA approved DMTs included in this report, 13 of them received FDA approval prior to the publication of the 2020 DERP report on this topic, and four DMTs received FDA approval since the prior DERP report, and this topic was finalized in 2020. These approvals were made between April 2020 to December 2022. All four of these DMTs, which are ublituximab, ponesimod, ofatumumab, and monomethyl fumarate are approved for adults with relapsing forms of MS. These DMTs cover a variety of different routes of administration as well as administration frequencies. Notably, two ongoing comparative RCTs projected to complete by February 2026 are specifically interested in ofatumumab, and three of these new DMTs, ublituximab, ponesimod, and ofatumumab were evaluated against teriflunomide and five of our six newly identified comparative RCTs. We did not identify any RCT evidence in this report for monomethyl fumarate. Monomethyl fumarate was FDA approved based on bioequivalence with dimethyl fumarate, and notably it is the sole active metabolite detectable in the plasma of dimethyl fumarate. And we will briefly summarize findings for the 29 RCTs against six of which are newly identified for this update comparing DMTs for people with MS. As mentioned previously, we only found comparative RCT evidence for three of the four newly approved DMTs, ofatumumab, ponesimod, and ublituximab against teriflunomide. When compared against teriflunomide, the newer DMTs all significantly reduced relapses, and compared with teriflunomide, ublituximab was associated with increased serious adverse events. However, ofatumumab and ponesimod were not. In a newly identified comparison in which fingolimod was compared with glatiramer acetate, fingolimod significantly reduced relapses. And when comparing the older DMTs directly, alemtuzumab, fingolimod, ocrelizumab, and teriflunomide significantly reduced relapses and are not associated with increased serious adverse events compared with other DMTs. This finding remains unchanged from the 2020 report. Considering that same set of 29 RCTs, six of which are newly identified for this update, it is important to note that we did not identify head-to-head trials for every possible comparison of relevant interventions. so we are not able to state conclusively that other therapies are any more or less effective overall. We did, however, identify a recent and relevant network meta analysis drawing comparisons that is summarized in the full report. Furthermore, we did not identify any eligible RCTs for five FDA

approved DMT, and these are diroximel fumarate, cladribine, monomethyl fumarate, siponimod, and peginterferon beta-1a. Lastly, subgroup analyses are not consistently reported across studies, so we are limited in our ability to draw robust conclusions about these. From what was identified, the presence of neutralizing antibodies does not appear to reduce effectiveness in patient factors such as age and prior treatment may change effectiveness. Next, we'll briefly summarize findings for the five placebo-controlled comparisons in eight RCTs, none of which are newly identified for this update, for people with CIS. Findings, they again, remain unchanged from the 2020 report include that the following DMTs significantly reduced conversion to MS in individuals with CIS in comparison with placebo. Cladribine, glatiramer acetate, interferon beta-1b, interferon beta-1a, and teriflunomide. Additionally, when compared against placebo, the same group of DMTs did not appear to be associated with serious adverse effects. As with the therapies for people with MS subgroup analyses are not reported consistently across the studies, but there is some evidence that women may benefit more than men from glatiramer acetate and interferon beta-1a. As a reminder, further details are included in the report itself and in the 2020 slides with findings from individual studies, which are included at the end of this slide deck. In total, we identified 45 cohort studies, 15 of which are newly identified for this update. Evidence from the reviewed cohort studies indicates that treatment discontinuations and switches appear to be significantly lower with fingolimod and dimethyl fumarate, and uncertainty remains regarding the risks of treatment discontinuation or switch for oral DMTs compared with injectable DMTs. From this same group of cohort studies, we identified evidence on adverse events. It is important again to note that DMTs do have adverse events and differ in their safety profile. Specifically, the risk of liver injury was higher for interferons, alemtuzumab, teriflunomide, and fingolimod. The risk of PML was higher with fingolimod and dimethyl fumarate. The risk of infection was lower with interferon beta and glatiramer acetate, and uncertainty remains regarding the association of cancer risk and DMTs. Overall, evidence is not consistent in terms of which DMTs are compared, which does limit our ability to draw conclusions. Thank you.

Kavita Chawla: Thank you, Rachel and Courtney. That was a very comprehensive review. Committee Members, any questions for Courtney and Rachel? Okay. And I don't see any stakeholders that were signed up ahead of the meeting. Any online currently? Okay. I don't see that either. So with that, Nonye, if you can please pull up [cross-talk] --

Leta Evaskus: This is Leta. There is one hand raised [cross-talk] --

Nonye Connor: [Cross-talk] There is? [cross-talk]

Leta Evaskus: [Cross-talk] or two hands right now. Or one hand raised. Hang on just a second. We have Lisa Carman.

Nonye Connor: Lisa, you can unmute [cross-talk] --

Lisa Carman: Okay. Can you hear me?

Nonye Connor: Yes. And let me put the question here on the screen. Just give me a quick second and share my screen. Uh oh. Is it coming along? Can you see? Okay. [laugh] It looks like it was thinking about that. And I will pull up my [cross-talk] --

Kavita Chawla: [Cross-talk] All right, Lisa, and if you can please go ahead and answer the questions on here. And then get ready, Leta, we will start the timer.

Lisa Carman: Sure. Hi, I am Lisa Carman. I am representing on behalf of Genentech, and we make ocrelizumab or Ocrevus. I am not a provider or a patient, and the only conflicts of interest is as an employee of Genentech.

Nonye Connor: Okay.

Kavita Chawla: All right. Go ahead.

Lisa Carman: Okay. I wanted to talk briefly around the Key Question #5 from the DERP review, which really is the open-label extension data from our OPERA-I and OPERA-II are RCTs. We have been tracking outcomes for these patients. We are now about 10 years and have been doing regular updates through the ECTRIMS focusing on not just relapses but really impact to disability. So I just wanted to highlight some of those data that has read out. We are tracking 52% of patients who have completed the original RCT that completed out this far in the open-label extension. After 10 years, patients who have been continuously treated with Ocrevus, the annualized relapse rate is 0.017, which is equivalent to a relapse almost every 60 years. In addition, after 10 years, almost 8 out of 10 continuous-treated Ocrevus patients were progression free. I additionally wanted to point out because in this trial, it

was a head-to-head against Rebif at the time, and there is a significant difference in disability accumulation. So originally in the trial for two years they were treated on Rebif or Ocrevus, and later the Rebif arm was allowed to crossover and then continue an open-label receiving Ocrevus and starting Ocrevus two years earlier. So the patients who were not on Rebif, save 10 years of disease progression. And another way to say it, the years between progression events between the Rebif trial who crossed over to Ocrevus and Ocrevus is 9.5 years. In addition, after 10 years over 90% did not require a walking aid. I have additional wheelchair data as well. But back to the primary endpoints after 10 years, led to an almost complete suppression of MRI activity and these benefits were seen in patients once they switched from Rebif to Ocrevus in that arm. I just also wanted to mention those are kind of the highlights. I have some from PPMS open-label as well, but I don't have time to go into those today. A few other additional points, Ocrevus subcutaneous is we are hoping to hear from the FDA in September. Thought that might be important for you guys to know. In addition, in regard to special populations, we do have some employment data looking at it as a continuation of a trial. We have pregnancy data, we have lactation data, and we have newborns who we have tracked. And last, I will leave you with our two-year RWE, where we look at events associated with relapse use and costs and looking at first-line versus second-line Ocrevus at all medical costs in patients who were on the first-line Ocrevus were less, and that was attributed to lower inpatient stays on Ocrevus compared to other medications. So thank you.

Kavita Chawla: Thank you, Lisa. Any questions for Lisa from the Committee members? Okay. Any other stakeholders signed in? And Leta and [cross-talk] --

Nonye Connor: [Cross-talk] No. [cross-talk] --

Kavita Chawla: -- Nonye to let me know.

Nonye Connor: No, I don't see any more.

Kavita Chawla: All right. Okay. Then with that we can move on to the motion.

Nonye Connor: Can you guys see the motion?

Kavita Chawla: Yes, we can. Thank you, Nonye.

Nonye Connor: Mm-hmm. So I have already copied and pasted the previous motions and have updated with the lists of drugs that were brought up -- that were presented today.

Kavita Chawla: Great. Thank you so much.

Nonye Connor: Mm-hmm.

Kavita Chawla: Okay. Comments from the Committee? You know, one of my main points was the oral agents, so I am glad to see that that is already called out. Any language that is up for debate? Otherwise, we can move forward with proposing the motion.

Michael Corsilles: This is Michael Corsilles. I think it looks good for me. I would like to make a motion and pronounce all these names. After considering the evidence of safety, efficacy, and special populations for the treatment of multiple sclerosis, I move that alemtuzumab, cladribine, dimethyl fumarate, diroximel fumarate, fingolimod, glatiramer acetate, interferon B-1a IM, interferon B-1a SC, interferon B-1b SC, monomethyl fumarate, peginterferon B-1a SC, ocrelizumab, ofatumumab, ozanimod, ponesimod, siponimod, teriflunomide, and ublituximab are safe and efficacious. A product that is safe for use during pretty should be made available. The MS drugs cannot be subject to therapeutic interchange in the Washington Preferred Drug List for the treatment of multiple sclerosis. An oral agent should be included in the list of preferred drugs on the PDL.

Greg Hudson: This is Greg, and I second.

Kavita Chawla: Thank you. All in favor, please say aye.

Multiple Speakers: Aye. Aye.

Kavita Chawla: All right. Any opposed? And the motion carries. Michael, great job with those drug names. All right. By our schedule, we are scheduled for lunch next. Does that sound good to everybody? Yes? [cross-talk] --

Nonye Connor: Yes, it does.

Kavita Chawla: All right. So 12:07, should we say we'll be back by 12:40 for lunch?

Nonye Connor: Yes, that works. Does that work for everyone?

Kavita Chawla: Great. Wonderful. [Cross-talk] --

Nonye Connor: Okay.

Kavita Chawla: We'll see you in a bit.

[lunch break]

Kavita Chawla: All right. I think we have quorum. All right. So now -- I guess I didn't officially say P&T Committee adjourns after the last session, and the DUR Board now convenes. And the first item on the agenda is with Marissa, who will be taking us through the Apple Health Policy for Movement Disorder Agents. Marissa, do we have you online?

Marissa Tabile: This is Marissa. Yes, I am ready. So let me go ahead and just tee up my policy, and then we should be able to get started. Sorry, I am trying to do some reshuffling of some screens here. Okay. I have what I need. Let's share. Okay. Okay. You should be able to see the policy that is displayed.

Kavita Chawla: Yes.

Marissa Tabile: Oh, okay. Perfect. So good afternoon, DUR Board. My name is Marissa. I will be going through the Movement Disorders Agents, particularly, this is a policy around valbenazine or Ingrezza. This is a brand new policy that we are creating, so it's not something that we currently have implemented, it would be implemented, if approved, after this meeting -- a couple of months after this meeting, I will go over some very high-level background information just on the disease state, and then a little bit about the drugs or drug types themselves, just because I don't believe we are going through any kind of clinical review on them in the review of the classes. So just to kind of give you some Background. Tardive dyskinesia, or TDs, are involuntary movements of the tongue, lips, face, trunk, and extremities that occur in patients treated with long-term dopaminergic antagonist medications. They are most common, TDs are most common in patients with schizophrenia, schizoaffective disorder, or bipolar disorder, who have been treated with an antipsychotic medication for long periods. However, tardive dyskinesia can occur in other patients as well. So people that have fetal alcohol syndrome, other developmental disabilities, and other brain disorders make these

particular patients vulnerable to TD. Huntington's disease, on the other hand, is a hereditary disorder that causes nerve cells in the brain to gradually break down, so chorea or uncontrollable movements is the defining symptom of Huntington's disease. Huntington's Disease chorea is progressive and can affect finger and hand coordination, walking, mouth movements, and swallowing. The current treatments available to treat tardive dyskinesia and chorea associated with Huntington's disease are vesicular monoamine transporter 2 or (VMAT) inhibitors, which are the products that I will be going through in the policy. Those are the products in question today. How VMAT2 inhibitors work is they deplete the transport of dopamine, thus decreasing the release of dopamine and its breakdown by monoamine oxidase, so very high-level overview on the drugs and the disease state. So I will just go ahead and jump right into the clinical criteria. So the first criteria that we have is -- well, let me go through it box by box. So the first one is really our blanket statements that we have at the top of our policies just saying that this policy applies. This drug may be considered medically necessary in patients who meet the criteria below, which we'll get into shortly, and then we have at the top, here, our blanket statement of if all the criteria are not met, but the clinical reviewer determines that it's a medically necessary medication for this patient, it can be approved on a case-by case-basis. And then also the clinical reviewer can choose to use the reauthorization criteria if a patient has been previously established on therapy or is a new client to Apple Health. So that just kind of encapsulates that. For the first Indication, I will be going through the chorea associated with Huntington's disease. And actually, let me just give a little background. In this class currently -- and it's not on your PDL publication that you were given -- but the drugs that are in this class are Austedo, Austedo XR, and Ingrezza, and currently they live in what is called our Movement Disorders Apple Health PDL drug class. And currently, the two preferred products that we have in that class -- well, three actually -- the three preferred products are, we have tetrabenazine, which is generic, we have brand name Austedo, and then brand name Austedo XR, so all three of those products are preferred without PA on our AHPDL, so this policy that I will be presenting today applies to this nonpreferred Ingrezza, and patients that do -- patients that are requesting this medication would have to meet all of this criteria in order to get it with the intention of really having to step through the preferred Austedo, Austedo XR, or generic tetrabenazine. So that is just some background on what is going on in that drug class and what that looks like. So for this first Indication, the clinical criteria are just as follows: We would require the patient to be 18 years of age and older, and that is just following

labeling for these products for this product specifically. It is prescribed by or in consultation with a neurologist or psychiatrist. The third, the patient should have a diagnosis of Huntington's disease. Four, we would require at least some type of baseline assessment, and what we found was it would be probably using the unified Huntington's Disease Rating Scale or UHDRS. And this particular assessment is, from what I have gathered, it's a very big assessment, and it's broken up into parts, so whichever part, I guess, either of these, whether that be motor, cognitive, behavioral, functional independence, or total functional capacity, if any of those particular assessments were submitted, then we would accept them. But, you know, I understand that it's a big test, but even if they submit parts of it, that is really what that is really getting to. For five, the medication will not be used in combination with another VMAT inhibitor or monoamine oxidase inhibitor, and that is just per labeling as a contraindication, particularly the MAOIs. And six, this is what I was alluding to as far as stepping through our preferred product. So treatment with deutetrabenazine or deutetrabenazine ER, which is Austedo or Austedo XR is contraindicated or has been ineffective or not tolerated for a minimum of 12 weeks. So if they meet all those criteria, we will authorize it for 12 months or one year. And then for the reauthorization criteria, it would just be for number one, they would just need to meet Criteria 5, so really just stating that the patient won't be using this in combination with another VMAT2 or MAOI. And then 2, documentation is submitted demonstrating disease stability or positive clinical response. So some examples of that would be a reduction in involuntary movements, a decrease in total maximal chorea score, and that is the decrease in total maximal chorea score is actually measured in these, and these functional assessments are part of the UHDRS scale. If they meet both of those reauthorization criteria we will authorize it for another year. Getting into the tardive dyskinesia Indication. It's pretty similar to above with a little bit of changes. So the first two are relatively the same as above. Age Indication 18 or older, prescribed in consultation with a neurologist or psychiatrist. Three, they would need a diagnosis of tardive dyskinesia. Four, this is where it's a little bit different just for the baseline assessments. So we would want baseline assessments using one of the following tests: so an AIM score, so the Abnormal Involuntary Movement scale or Clinical Global Impression of Change Tardive Dyskinesia. So at least one of those would need to be submitted. Same as above, it is not used in combination with a VMAT or MAOI. And then six, at least one of the following treatment approaches was ineffective, unless all are contraindicated, not tolerated, or put psychiatric stability at risk. So if the provider switched from a first-generation to second-generation

antipsychotic, and that wasn't effective, or b. the patient has a history of discontinuation or dose modification of the offending medication. So they have tried to either discontinue the medication or tried to change the dose and it wasn't effective, so either of those two. And then seven, kind of same as above, just stepping through our preferred agents. So if they have tried Austedo or Austedo XR and it wasn't effective, or it's contraindicated, and the trial was at least for a minimum of 12 weeks. So if they meet all the criteria, it will be authorized for one year. And then for the reauthorization criteria, it is pretty much the same as the other one. We would just require that they are not using it in combination with a VMAT or MAOI, which is number five, here. And then we would just need documentation that there is disease stability or positive clinical response. So things we would be looking for would be reduction in involuntary movements, improvement in the AIM score, and improvement in the CGI-TD score. If they meet all of those criteria, the request will be authorized for another year. And then here, these are just the dosage and quantity limits for those, and then it's broken up based off of the Indication. I will go ahead and stop there for a little bit and let you look over that. And then scrolling down a little bit more to the bottom, it's just the background and the references. And then I will go ahead and get into the form that supports this. So this is the prior authorization form that helps guide the provider if they are requesting this medication or putting in the PA request. So let me actually zoom out a little bit. This up here at the top is just basic demographic information, patient information, prescriber information, medication information and direction. Here are the kind of checklist items that we would be looking for. So I will go ahead and pause. Let me see if there is another page. Okay. I will pause here, and then I can take any questions from the Board.

Ryan Taketomo: Hi, Marissa. This is Ryan Taketomo. When I am looking at the scan, I don't know if other people see it, but it looks like the policy is still up.

Marissa Tabile: Yeah, I need to switch it. Hold on one second. Thanks, Ryan. Let me do my screen. Okay. Can you see the form now?

Kavita Chawla: Yes, we can.

Marissa Tabile: Okay, perfect. Sorry about that.

Kavita Chawla: That's okay.

Jon MacKay: Marissa, this is Jon MacKay. I had a quick question for you. So in terms of tardive dyskinesia and treatment failure moving from a first-generation to a second-generation antipsychotic, what about in terms of failure two second-generation antipsychotics versus going from a first-generation to a second-generation? Is there any need for maybe just a failure of one second-generation to another second-generation?

Marissa Tabile: The way that the clinical policy is written right now is that it would just -- sorry, I apologize for the scrolling -- we would just require the way that I wrote it was just one second-generation antipsychotic. I didn't put switching from like one second to another second. Yeah. So I could consider that if you feel very strongly about adding that type of language in, then I can definitely do that.

Jon MacKay: I am just wondering from like a treatment perspective if they have never tried a first-generation, and they are on a second-generation but stable otherwise moving forward.

Marissa Tabile: Yeah. I see what you are saying. I think that is a good call out though, so I could, yeah, consider taking that back.

Greg Hudson: Yeah. I would just second Jon's statement there to simplify that.

Zoe Taylor: Yeah, the term switching I think is just confusing. Like, what are you needing to prove that they failed? Is it the first? Is it the second? Is it both? So I think maybe you just want to say -- because it says, at least one of the following treatment approaches was ineffective. Maybe a is just like one second-generation anti psychotic is actually what you are getting at?

Marissa Tabile: This is Marissa. So the way that it is written is the intent would be that they would have tried a first-generation antipsychotic and then switch to a second one. But I didn't think about it in the way that they would be they could have not taken the first and started with the second-generation and then switch to like another second-generation, I think, Jon, is what you were getting to. So it is not written in the way that I believe I am understanding Jon is saying, so they would -- I could incorporate some type of language into the policy because that is not what is taken into account. So it is not necessarily that they are failing -- I'm trying to think of the best way to say this. [Cross-talk] --

Kavita Chawla: It looks like Donna has a comment.

Donna Sullivan: Yeah, Marissa, I think if you think of it from a standpoint where they have tried two different second-generation antipsychotics, and they are still experiencing movement disorder symptoms.

Marissa Tabile: Yeah.

Donna Sullivan: [Cross-talk] So they are not really failing a second-generation antipsychotic. It's just they have tried two and they are still experiencing abnormal movements.

Kavita Chawla: Yeah. And that would kind of be consistent with the language we have had in other policies, which is a trial of two agents.

Laura Beste: This is Laura Beste. Would you want to state at least one of the following treatment options caused movement disorders as an adverse effect? So because like you have was ineffective. It wasn't really the question whether it was ineffective, it is whether it caused the movement disorder as an adverse effect.

Kevin Flynn: Could you just state like continue to experience tardive dyskinesia despite trialing two different?

Laura Beste: There you go?

Kevin Flynn: Because that is kind of what we are getting at. Right?

Kavita Chawla: Exactly.

Laura Beste: Yeah.

Greg Hudson: Yeah, I think that is accurate.

Marissa Tabile: This is Marissa. Sorry. Can you point me to where you would like me to change it? And then I can start typing.

Kavita Chawla: Go ahead, Kevin.

Kevin Flynn: I think you could just because the whole point is not switching, so you just -- so instead of you just say, continue to experience tardive dyskinesia --

Kavita Chawla: [Cross-talk] -- Or persistent tardive dyskinesia despite trialing [cross-talk] --

Kevin Flynn: Of two second-generation --

Zoe Taylor: Making it be two is stricter than what she had originally put, though. Like she only put that had to be one.

Kavita Chawla: I think the original language was indicating that they have done at least a first-generation and a second-generation.

Laura Beste: Isn't this -- [cross-talk] also this is Laura [cross-talk] --

Zoe Taylor: [Cross-talk] You said the first-generation like, made -- caused it though, and then switching to a second-generation didn't fix the problem? Right?

Donna Sullivan: This is Donna. You could have abnormal movements on a second-generation antipsychotic. Most people don't -- aren't started on a first-generation anymore, or very seldom, so they are more likely to have started on a second-generation, experienced a movement disorder, and then -- or switched to a different second-generation to see if that would resolve the issue. So I think just having that they tried to second-generation antipsychotics, and they still are experiencing abnormal movements.

Kavita Chawla: Go ahead, Peter.

Peter Barkett: It might be helpful to split these criteria into two separate elements, one an exclusion criterion because the first-generation antipsychotics are more likely to cause this, we would want to say, if you are taking the first -- if you are still taking a first-generation antipsychotic, then that would exclude you from getting this therapy because you should have switched. But then just say that you've tried switch -- you've tried changing at least once from, say, one second-generation to a second pill and a second-generation antipsychotic. So it might make sense to just try to do this in two criteria elements.

Kavita Chawla: So would that be as she has listed, so she left a. as is, which is first gen to second general, and then this [cross-talk] --

Peter Barkett: I would make it more generic than that and just say, patient has tried changing their antipsychotic, and then I would have another point somewhere below this that would be an exclusion continued use of a first-generation antipsychotic medication is an exclusion to this use.

Laura Beste: Rather than making it wordier, though, could you just reword the whole question or the whole number six as far as, patient continues to experience tardive dyskinesia after the following approaches: a.) switch from first-generation, second generation, b.) after a trial of two -- so then you are just combining [cross-talk] --

Zoe Taylor: [Cross-talk] That's smart.

Laura Beste: -- the top piece to make it less verbiage. [Cross-talk] So patient continues to experience persistent tardive dyskinesia after the following -- what's the word? -- approaches, I guess [cross-talk] --

Zoe Taylor: [Cross-talk] after at least one of the following --

Kavita Chawla: Yeah, after the following treatment approaches, and then the unless all are contraindicated or not tolerated. That whole sentence.

Zoe Taylor: And just make sure you put at least one in there so that it's not stricter than before.

Marissa Tabile: This is Marissa. Sorry. I can't -- I'm trying to type and spell at the same time, so I apologize -- then experience it after -- so this would be -- it would be switching. I think, Laura, what I understand it would still be like these. It's just I'm like rewording and switching.

Laura Beste: Correct. And then b.) would just be trial of two second-generation, or -- I mean, shouldn't a.) always be the first thing they try, though? I don't know how to put that in there. If they are on a first-generation, that brings up, I think Peter mentioned it, that [cross-talk] but that should be always included. So it would almost be like a.) plus one of the b.) and c.)? I don't know how to verbiage that.

Kavita Chawla: I think if I understood Peter correctly, it's like we just skip on the a.) because being on a first-generation will be an exclusionary criterion separately in the policy, and so we will just start with b.). Is that right, Peter? I don't want to speak for you.

Peter Barkett: There. Now I'm off mute. Yeah, yeah, that's what I was thinking.

Kavita Chawla: Yeah. I'm good with that. Do we have a section, Marissa, for exclusion criteria?

Marissa Tabile: Um, no. This is Marissa. Sorry. No, I don't -- we don't have like a section where we include that.

Donna Sullivan: So are you trying to say if they are on a first-generation, you would not allow them to be on?

Peter Barkett: Right? Yeah. Because the risk for these movement disorders is so much higher on a first-generation, and there are so many choices for second-generation medications that if you are still choosing to use a first-generation. I mean, you shouldn't. It's bad, its bad clinical medicine, but it would be an exclusion to using one of these meds.

Donna Sullivan: Is there a reason? I don't know, like a first-generation will be giving better other symptom control, like, psychoses, delusions, hallucinations? [Cross-talk] --

Peter Barkett: [Cross-talk] I can't think of one. [cross-talk] --

Greg Hudson: [Cross-talk] I didn't hear your comment. [cross-talk] --

Donna Sullivan: [Cross-talk] If you feel like if you have b.) you don't need a.).

Greg Hudson: This is Greg Hudson. I mean, look, I agree with Peter in general that in the vast -- in general clinical practice, it's not preferred to use a first-generation antipsychotic. However, I can think of specific cases where first-generations might be -- again, these are specific cases -- might be preferred or necessary for continued use and continued stabilization of some persistent mental illness, and I wouldn't want to exclude the use of this medication in those populations, so I would not recommend that -- the exclusionary criteria.

Jon MacKay: This is Jon, I would kind of second Greg's concerns. They are just terms of usually we would see it in like treatment resistant, like, schizophrenia and in the cases like use of Clozaril or some of those other first-generation antipsychotics that might be more resistant and not amenable to use of the second-generation antipsychotics. Yeah, I think like, this is a case in which this is, like, an expert who is making this decision, right? And so I don't think we should, like, make it so that like a for some reason somebody does have one of these reasons to take this medicine, and then they can't get it, I guess, like, the whole need for six when we have seven, I don't understand because, like, they are only getting this nonpreferred med if they have tried deutetrabenazine anyway. So then, in order to get deutetrabenazine, didn't they already have to trial this other stuff? So why are we even making them prove all this stuff in six if they can only get this med if they have tried seven in the first place? Does that make sense? [Cross-talk] Why do you need to prove that you did all the stuff in six if you already tried seven?

Kavita Chawla: Marissa, is there intent behind this?

Marissa Tabile: This is Marissa. Um, I mean it was just to really follow, like, clinical practice of, like, what you would expect to see. So like if someone was going -- did experience tardive dyskinesia, I mean, clinically, you would expect -- if they are on an antipsychotic, you probably would expect to see them either switching from something or discontinuing the medication, so it was really just to go along with the clinical guidelines. But I could see where Dr. Taylor is coming from, but it is just to be inclusive and really be specific, as specific as we could be in the criteria.

Donna Sullivan: Marissa, this is Donna, do we require -- and maybe I missed it -- do we require a PA for deutetrabenazine that they have tried and failed -- or that they have tried to different second-generation antipsychotics?

Marissa Tabile: This is Marissa. No, we don't have any. That is just preferred without PA, Donna, so [cross-talk] --

Donna Sullivan: [Cross-talk] Okay.

Marissa Tabile: So I could [cross-talk] see where [cross-talk] -- I could see where Dr. Taylor is going because we wouldn't if there was a, like, if we got a claim for it, particularly, like, we wouldn't be able to see that info. I mean you could from

a claims information, but it's not like we would be looking for the trial and the failure of the antipsychotics in order for them to get the Austedo.

Peter Barkett: So yeah, then I would be in favor of leaving six in and like even sometimes when there is that other prior auth criteria, it's helpful to put it in because you can imagine if you get a denial letter, and it says you have to try this other medication. Then they try that medication, and then they get another denial letter that says you have to try these other things first. So it's important in those because usually those denial letters include the criteria, the policy, and laying out all those steps is helpful so that people don't get trapped in a cycle of denial letters, and they kind of work their way back through all of the criteria. So that would be my two cents.

Kavita Chawla: Um, it's a really good discussion. I can see different points of view here. I guess, why don't we take maybe a vote on that first. So if I may summarize, the question is, like, do we leave the motion as is now like with those changes that Marissa has noted in the comments, but leave six in there versus remove six altogether because [cross-talk] --

Zoe Taylor: [Cross-talk] I don't think -- actually I like withdraw that proposal now that I understand that the other one doesn't require a PA. I thought the other one also required a PA. I am fine with leaving six with our rewrites. We don't need to vote on it.

Kavita Chawla: Awesome. Great.

Zoe Taylor: I still don't understand the c.) part though. Which offending medication are you talking about?

Marissa Tabile: It could be whichever, so you will probably be looking for, like, an antipsychotic, even though that is addressed up here, but I guess whichever other medications could cause tardive dyskinesia besides the antipsychotics, too, would fall under that umbrella. Or if they have had issues with dosing the antipsychotic that it would fall under that as well.

Zoe Taylor: Okay.

Marissa Tabile: Yep.

Zoe Taylor: So basically, if you are a patient who is on Haldol, and you have a history of discontinuing Haldol, then you are good on six. You don't need to try a second-generation, and you don't need to try to second-generations because it's just one of the three that you need. That is why I am not sure if that is really what we -- or I am reading it wrong.

Laura Beste: Can we just say and -- this is Laura Beste -- under age, and say this and one of those two following b.) and c.)? Or is that, like, getting too confusing instead of [cross-talk] --

Zoe Taylor: I mean [cross-talk] is included in a.), right? It's like switching from the first-gen is the same as discontinuing the first-gen.

Laura Beste: Well, but this just said you are just discontinuing it, and it doesn't say you are switching to a second-generation [cross-talk] under c.).

Zoe Taylor: [Cross-talk] Right. Yeah, true. I guess you need -- I guess you need to have -- you have persistent tardive dyskinesia after trying and stopping the offending agent, which is, I guess, what c.) is getting at? [cross-talk] --

Marissa Tabile: Yeah. Yep, that is what that is getting at.

Zoe Taylor: Okay.

Marissa Tabile: Yeah.

Kavita Chawla: This is Kavita here. Is c.) trying to be a catch-all for things not covered in a.) and b.), like offending agents that are not covered in a.) and b.)?

Marissa Tabile: This is Marissa. Yeah, it can be, but really, I think the essence of how it is like if a patient was on an antipsychotic, stopped, was experiencing tardive dyskinesia, stopped the antipsychotic, but even after stopping they were still experiencing the tardive dyskinesia, that is really [cross-talk] that was how it [cross-talk] --

Zoe Taylor: [Cross-talk] [indistinct] got it.

Marissa Tabile: Yeah.

Zoe Taylor: Okay. It's probably fine. I think it's a little bit hard to parse, but I think it's going to probably be no matter how we word it, so --

Christy Weiland: This is Christy Weiland. Marissa, I just appreciate that last phrase you said because if we add it at the end offending agent with continued symptoms, which might provide some clarity because I don't know that I fully understood that until you added that.

Marissa Tabile: This is Marissa. Yeah. I can add that. Let me see. You said with continued symptoms? Did I read that? Did I hear that right?

Kavita Chawla: Yeah.

Marissa Tabile: Correct. Okay. [Laugh]

Kavita Chawla: Okay. So we have focused nicely on points 6. and 7. Do we want to look at the remaining policy? I guess I will let you finish there, Marissa. Sorry.

Kevin Flynn: Do we need to update the actual what you have written there? Continues to experience persistent tardive dyskinesia because it's not in the actual text.

Marissa Tabile: This is Marissa. So what I have in the note here is what I would be switching number six to completely if I captured that correctly. I just didn't want to do it, like, all at once and then lose kind of some of the [cross-talk], but the intent is what is in here is exactly what would be translated over to the policy for the new version.

Kevin Flynn: Sure [cross-talk] --

Marissa Tabile: [Cross-talk] Let me know if I missed anything. Yeah, I think I got the persistent tardive dyskinesia part, Kevin.

Kevin Flynn: Perfect. Thank you.

Marissa Tabile: Okay. [laugh] Let me know if I missed anything, please.

Kavita Chawla: No, I think you got it, Marissa. You did a great job there. Okay. So maybe looking at -- was there any other part of the policy? Should we scroll down further if there is anything else in there? Criteria 5. Okay.

Marissa Tabile: This is Marissa. And I can also go back to the prior authorization form, as well, if you all didn't get a chance to look at that either. I know we might have skimmed over that pretty quickly.

Laura Beste: This is Laura. Can we go back to the prior authorization form so we can make sure that the decision we just made on the verbiage is --

Marissa Tabile: Yeah.

Laura Beste: -- copied over.

Marissa Tabile: I'm trying to get -- this is Marissa -- I'm trying to get seven in there. It's a little hard.

Kavita Chawla: Okay. So yeah, so seven will need to be reworded a little bit.

Marissa Tabile: It doesn't like when I do that, so apologies. [Cross-talk] If you were looking it, scroll down.

Kavita Chawla: I think this is minor -- Kavita here -- but would seven come before six in terms of just chronologically? Is that the series of events the physician would go through?

Marissa Tabile: Oh, this is Marissa. Sorry. For this, I was just referring back to the criteria in the policy. I believe it was number six. That is why I [cross-talk] there. Yeah. But it does look like the way that this form is written, this is specifically for the tardive dyskinesia, and it doesn't look like we have -- Yeah, it looks like that is what is specifying this a little different. I apologize. [Cross-talk] My dog is getting [cross-talk] a little angry. [laugh]

Greg Hudson: And [cross-talk] --

Kavita Chawla: Okay, I see that.

Greg Hudson: And this is Greg Hudson. Marissa, if I can ask a question. I just want to make sure I clarify. So for the form with deutetrabenazine or Austedo, is question seven a part of that requirement for this to be covered as well? I guess I am wondering if our criteria for covering both of these medications if they are the same, or if we are adding sort of extra criteria for Ingrezza that is not reflected in Austedo.

Marissa Tabile: This is Marissa. So currently how it would work is Austedo really doesn't have any clinical criteria that like a provider would need to fill out because, right now, the way it is on our PDL, it is preferred without any PA.

Greg Hudson: [Cross-talk] Gotcha. Okay, thank you for clarifying.

Marissa Tabile: [Cross-talk] So if the pharmacy were to fill it, it would hit with no PA required. For this policy, really, only applies to Ingrezza. If I could just be -- I guess that is really [cross-talk] the underlying theme. Yeah. So these criteria that you are looking for are really only for Ingrezza.

Greg Hudson: Thank you.

Marissa Tabile: Yep, mm-hmm.

Kavita Chawla: All right, Board, other comments on the policy or the form?

Zoe Taylor: I know some forms like this have, like, if yes, go to question blank, if no, go to question blank, and I just want to make sure it's clear that you only have to answer question seven if the patient has tardive dyskinesia. If maybe there is a way to do something like that or reorder them so that, like, if you could say like chorea, answer questions 3.) to 6.). Tardive dyskinesia, answer questions 3.) to 7.). It's not elegant but just something because I wonder if it's clear enough that you only have to answer seven. Maybe you could just put it in the body of the question itself. Like, instead of just at the top, like, for patients with -- or only answer if -- I don't know. I filled out a lot of these for imaging, and sometimes you feel like you are in like a video game where you don't know which way to go next.

Laura Beste: This is Laura Beste. Can you just say, if tardive dyskinesia, please check boxes for diagnosis or --? So then it's just in that box on the very end before question seven.

Marissa Tabile: This is Marissa. So we have just this statement [cross-talk] right here. We haven't traditionally done it on these forms. I believe where it's like, oh, if you don't meet -- if it's not for this diagnosis, skip to question [cross-talk] --

Zoe Taylor: [Cross-talk] Oh, okay.

Marissa Tabile: -- or what have you, I think that might be a good takeaway, though, for us as far as the form. So I can take that back and see if maybe we can make it in a way where, like, for these particular diagnoses, you would fill out questions, like, three, five, and seven, for example. I totally made that up. [cross-talk] Yeah. But I can take that back to our team and see if we can make some types of updates for that, just so that then it's a little bit clearer as far as, like, which questions you actually have to answer. Because I can see the providers getting confused as far as, like, which questions they do answer, which ones they don't answer, or you get, as a reviewer myself, usually we get questions I get answered that are completely not relevant to what you are even looking at. You know? Because it's just confusing. So I think that is a great call. I will go ahead and add that note, and we'll take that back.

Kavita Chawla: Kavita here. I think along the lines of what Laura was saying to support Zoe's comment was just for question 7 or for point 7, the question could just begin with, "If [cross-talk] the patient has started dyskinesia, so that way it is very clear that you don't need to answer the question if they don't have tardive dyskinesia.

Zoe Taylor: I agree. I think that would be simple enough for this example.

Laura Beste: [Cross-talk] also have [cross-talk] --

Zoe Taylor: I'm sorry.

Laura Beste: There is the Huntington's Disease section, too. So maybe you just have a box that is not applicable that they can check [cross-talk] --

Kavita Chawla: [Cross-talk] Yeah.

Zoe Taylor: Okay. And then I guess, just like, as a person who, like, in our system, like, somebody would put this form in my box, right? And I wouldn't necessarily have read the policy. I mean I guess if I was a neurologist I probably would have, but just like the big picture, it's a little bit frustrating when you don't know which is the right answer to get the drug approved because if you didn't know which one was the right answer, then you wouldn't even fill out the form if you were going to put in the wrong answer. You would be, like, Oh, whoops, we need to try this instead. So just the reality being that the provider won't always get the policy and the form both. I wonder if you could either link to the policy or have some things on the -- I mean I think it would

be a lot more work to put something on the form. Like, if no, like, this might get rejected, but on a lot of the, like, imaging ones, they do put stuff like that, and it's really helpful. [Cross-talk]

Kavita Chawla: [Cross-talk] I think you [cross-talk] --

Zoe Taylor: [Cross-talk] to the policy.

Kavita Chawla: Yeah. Is that on the top of the form, Marissa? I feel like we made this adjustment early on that there would be a reference website for the referring [cross-talk] --

Zoe Taylor: [Cross-talk] It says the Preferred Drug List. I don't know if that is the same [cross-talk] --

Kavita Chawla: [Cross-talk] Yeah.

Zoe Taylor: -- site or not.

Donna Sullivan: [Cross-talk] So --

Marissa Tabile: [Cross-talk] This is Marissa. Yeah. It just is [cross-talk] --

Donna Sullivan: [Cross-talk] This is [cross-talk] --

Marissa Tabile: The PDL. Go ahead, Donna.

Donna Sullivan: This is Donna. I understand what you are saying, but the policies are posted online. We can try to get there. You need to answer the question truthfully [cross-talk] not just mark the box that's going to [cross-talk] --

Zoe Taylor: [Cross-talk] I'm not saying that it [cross-talk] would be truthful. I am saying I wouldn't bother submitting it in the first place [cross-talk] --

Donna Sullivan: [Cross-talk] Okay.

Zoe Taylor: That's the thing that wastes people's time is submitting things that are going to get denied. Right? So it's helpful to have a clue, like, this is probably going to get denied if you haven't tried this yet. So that's all moot [cross-talk] --

Donna Sullivan: Maybe Marissa and we can go back with the OP staff and reword some of the questions to say, must have tried two of these. You know? What have you tried?

Kavita Chawla: I think the 30,000-foot view question, though, that Zoey, I think, is proposing is with each of these policies -- or each of these forms, rather, is there a way to include which policy would be linked to it?

Donna Sullivan: This is Donna. If it is specific to a policy, yes, we could include the policy number, I think, in the title of the form.

Kavita Chawla: Okay.

Zoe Taylor: [Cross-talk] That would be helpful. [cross-talk] --

Donna Sullivan: [Cross-talk] But if it doesn't get you to the website, we could probably put -- Marissa, we need to add a link to the actual policy page, and that way they can at least copy and paste [cross-talk] --

Zoe Taylor: [Cross-talk] That would be super helpful.

Donna Sullivan: Yeah and get to the policy page. You will have to then navigate to the individual policy itself. I think it will be too difficult to try to give you a specific [cross-talk] link directly to the policy.

Kavita Chawla: And that is reasonable.

Zoe Taylor: Yeah. I think that is pretty simple, too.

Donna Sullivan: It will be, and that is a lot of work for us to do, so it won't happen overnight, just to give you some [cross-talk] --

Zoe Taylor: [Cross-talk] I understand. [cross-talk] --

Donna Sullivan: -- management.

Kavita Chawla: Now, thank you for taking that feedback. Go ahead, Peter.

Peter Barkett: I was just going to say, Zoey, I think kind of what you are getting at on the one end of the extreme would be essentially an attestation to the criteria versus

providing a bunch of clinical information and then having somebody review it. And with the other health plan I sit in these kinds of committees for --we have looked at that, and it's really difficult to do an attestation because people are so busy that they end up kind of skimming through it or not reading it too closely and just sign their name or click a [cross-talk] --

Zoe Taylor: [Cross-talk] Yeah, I know. [cross-talk] --

Peter Barkett: [Cross-talk] check a box. [Cross-talk] --

Zoe Taylor: -- I agree with that. [Cross-talk] Yeah. I'm thinking attestation makes sense. I just think like, a clue that is like, if you clicked No here, like, stop. This isn't going to get approved, which a lot of the, like, HCA imaging ones have that kind of thing on them, and it's --

Peter Barkett: Having the link to the policy is nice. But we've actually built that into the EMR for the other health plan that I work at, and nobody clicks on it. I mean, like, very few people actually look at the criteria. It's like, I agree, it's really nice to have, and I think we should do it. It's just, it doesn't get as much traffic as you would like.

Kavita Chawla: Kavita here. I think it gives the provider at minimum some sense of autonomy that, okay, I have control over this information whether I choose to access it or not before filling out the form. But okay, great points. Other comments? It's a great discussion. I feel like I am having Deja vu about this policy number thing, though. I feel like we had this discussion like couple years ago, as well, that the policy number would be included at the top of the form for reference. So I am glad. I am glad that we are discussing this. And if not, then we can move forward to the motion for this policy.

Marissa Tabile: Okay, this is Marissa. The motion should be here. Hopefully, you can see it.

Kavita Chawla: Yeah. Yes, we see it.

Marissa Tabile: Okay.

Kavita Chawla: Yeah, so whenever the Board is ready, yeah.

Peter Barkett: Hi. This is Peter Barkett. I can make the motion. I move that the Apple Health Medicaid Program implements the clinical criteria listed on policy 62.38.00.AA-1 as recommended.

Kevin Flynn: This is Kevin Flynn. [Cross-talk] --

Laura Beste: [Cross-talk] This is Laura Beste. I second the motion.

Kavita Chawla: All in favor [cross-talk] --

Laura Beste: Flynn got it.

Kevin Flynn: Hi.

Kavita Chawla: Any opposed? And the motion passes. All right. Moving on. And I think we are going over to Ryan for the Antihemophilic Agent.

Marissa Tabile: This is Marissa. Sorry. Hold on one second. I am just going to save all of our wonderful work, so I don't lose any of it. We have been getting updates to our windows, and I just want to make sure that nothing freaks out on me, and I don't lose any of this, even though this meeting is transcribed. Okay. So let me enter that. Okay. And Ryan, I will get your policy up in just a minute. Let me close some of these windows. And there is this one. Okay. Ryan, your policy should be displaying. If it's not, let me know. But you should be good to go.

Ryan Taketomo: All right. Hi, this is Ryan Taketomo. Yes. Thanks, Marissa. So I will be going over the Hemgenix clinical policy. A little background before we get started. Congenital Factor IX deficiency, also known as hemophilia B as an X-linked disorder that predominantly impacts males and manifests as leading from impaired hemostasis and bleeding-related complications. Hemophilia B is categorized by the disease severity, which is determined by the amount of clotting factor in the blood. Severe disease is defined as Factor IX levels less than 1 IU/dL or less than 1% of normal. Moderate disease is defined by Factor IX level of 1 to 5 IU/dL or 1% to 5% of normal, and mild disease is 5 to 40 IU/dL or 5% to 40% of normal. The current standard of care for hemophilia B is to replace the deficient coagulation factor either through episodic or on-demand treatment given at the time of bleeding or through continuous prophylaxis to prevent bleeding. People who are on a prophylactic regimen may still require on-demand therapy with Factor

replacement. And so moving on to Hemgenix. Hemgenix is a gene therapy for hemophilia B, which aims to kind of eliminate the need for Factor IX replacement. Hemgenix is given as a single-dose by IV infusion that delivers and adeno-associated virus 5 vector containing a copy of the gene that encodes for Factor IX. The short-term results are promising and demonstrate a reduction in factor IX replacement or the durability of the response to this gene therapy has not been established and patients may need to Factor IX treatment again. The long-term extension trials for this therapy are still ongoing. And so that covers kind of the background, and we can move on to the criteria for this. So etrenacogene, dezaparvovec, Hemgenix may be approved when all of the following criteria are met: Criteria 1: patient is 18 years of age or older, and Criteria 2: it is prescribed by or in consultation with a hematologist or specialist in hemophilia, and Criteria 3: the patient has not received a prior gene therapy that is in reference to another gene therapy for hemophilia B, and Criteria 4: there is a diagnosis of moderately severe or severe congenital Factor IX deficiency defined by Factor IX less than 2 IU/dL or less than or equal to 2% of normal as confirmed by blood coagulation testing, and Criteria 5: is either a contraindication, intolerance, or history of failure to continuous routine Factor IX prophylaxis with greater than 150 prior exposure days to Factor IX therapy. Failure to continuous routine vaccination prophylaxis is defined as one of the following: a.) current or historical life-threatening hemorrhage, or b.) history of repeated serious spontaneous bleeding episodes, and Criteria 6: is documentation that the patient is negative for Factor IX inhibitor titers, and Criteria 7: the patient has a baseline anti -- adeno-associated virus 5 antibody titer of less than 1 to 678 measured by Elisa. And Factor IX prophylaxis therapy will be discontinued upon achieving Factor IX levels of at least 5% following treatment, and Criteria 9: documentation is submitted that includes the client's weight and then liver function tests within the past few months. And then once all the criteria are met, this will be authorized for 12 months for one dose. For the reauthorization, this is a single-dose therapy, so there will be no preauthorization for this treatment. And then [indistinct] covers the clinical criteria before this kind of dosing limits, and then the background so they can move to the form that has -- yeah, the forms. This helps facilitate the prior authorization process. And that kind of covers it, so I will give the Committee a few minutes to look over the form, and then I will open up for questions and discussion. Thank you.

Nonye Connor: We do have a stakeholder for this topic.

Kavita Chawla: Yes. So I see Jonathan Abdul-Haqq. Are you online?

Nonye Connor: Yeah. [Cross-talk] Jonathan is.

Kavita Chawla: [Cross-talk] I'm sorry.

Jonathan Abdul-Haqq: [Cross-talk] Can you hear me?

Marissa Tabile: I am just going to pull up the questions and then the timer. Just give me one minute.

Kavita Chawla: Thank you. And I believe we do have a completed COI for Jonathan. So I think if we can have -- once we have the timer on the screen, Jonathan will have you get started.

Jonathan Abdul-Haqq: All right.

Marissa Tabile: [Cross-talk] It should be ready to go.

Kavita Chawla: [Cross-talk] All right. [Cross-talk]

Jonathan Abdul-Haqq: Okay. Good afternoon. My name is Jonathan Abdul-Haqq. I represent CSL Behring in Medical Affairs. I am not a provider or a patient, and then my only conflict of interest is as a CSL Behring employee. So I very much appreciate the opportunity to provide a few comments on the proposed Hemgenix policy. I just wanted to before I get into those, I have two comments. But I just wanted to point out, we do have a three-year data readout from our pivotal trial, which is called HOPE-B, and that did show very good durability in terms of Factor levels approaching the lower limit of normal, 38.6 was the mean factor activity at three years, so we do have good durability data from our pivotal trial out to three years. But my first comment on the proposed policy relates to the criteria requiring a factor night activity level of less than or equal to 2%. So this requirement was part of the inclusion criteria for our Phase III trial, which, again, was called HOPE-B, and the purpose of this requirement in that trial was to facilitate pharmacokinetic analyses that were conducted as part of that study. A Factor IX activity level of less than or equal to 2% was not intended to define any real-world population that could benefit from Hemgenix, and so including this requirement and coverage policies could potentially limit access for patients living with bleeding phenotypes that the FDA has deemed appropriate for this treatment. It is

important to note that our FDA-approved label or FDA-approved Indication does not require any specific endogenous Factor IX activity level but rather focuses on adults with hemophilia B, who currently use Factor IX prophylaxis therapy or have current or historical life-threatening hemorrhage or have repeated serious spontaneous bleeding episodes. My second comment relates to the proposed criteria requiring an AAV5 neutralizing antibody titer of less than or equal to 678. The presence of neutralizing antibodies to AAV5 was not exclusion criteria in our Phase III trial, and patients with pre-existing neutralizing antibodies were allowed to participate in the trial. Our FDA-approved label does not require testing for AAV5 neutralizing antibodies, and there is also no FDA-approved companion diagnostic for such antibody testing. In addition, there is currently no guidance on an appropriate exclusionary neutralizing antibody titer threshold at this time. Providers are encouraged to test patients for AAV5 neutralizing antibodies and use their clinical judgment and interpreting results according to currently available data. The Athen Gene Therapy Registry will be conducting -- collecting data for additional understanding in this area. So those are the comments I had to share on this policy. Thank you very much for the opportunity to speak, and I would be happy to take any questions you may have.

Kavita Chawla: Thank you for your comments, Jonathan. Do we have any other stakeholders? And any questions from the Board for Jonathan? Okay. So with that we can go back to looking at the policy and the form. So I guess as I was hearing you talk about the policy Ryan, I was wondering, like, that list of tests that need to be done for the patient to get this treatment. Is that -- are those criteria included in the FDA approval? Because I just think about, like, the cost of the testing and the accessibility of these very specific tests, depending on where the patient is.

Ryan Taketomo: Hi, this is Ryan Taketomo. And yes. I am assuming you are referring to Criteria 6 and 7, is that correct?

Kavita Chawla: Um, yes, 6, 7, yeah. I think those are the main ones.

Ryan Taketomo: Yep. And this is Ryan Taketomo again. So Criteria 6 is in the FDA label [cross-talk] that they are required to have a negative Factor IX inhibitor titer. Otherwise, it is recommended not to administer Hemgenix. With Criteria 7 with the baseline anti adeno-associated virus anybody titer, it is important to note that that was like a companion diagnostic that was not validated, and do that kind of -- what that lab the purpose was to show that if -- whether or not

a patient has some exposure to, like, wild type virus and that they might develop some resistance if they were to receive a [indistinct], that might make the therapy less effective and potentially impact the safety. In the study, there was one participant who had a really high titer, and the Hemgenix was not effective. It's important to know that Hemgenix is a multimillion dollar therapy, so we want to make sure that when we are giving it, we are trying to maximize the benefit of this therapy and to make sure you know, it's not -- we are not putting those millions of dollars to waste. There is guidance from The World Hemophilia Foundation that recommends that they still get this assay completed and to help use it as a guidance for whether or not they want -- they make into prescribing this therapy. And then I think in the HOPE-B trial it was up to 18 months, I think, at that specific level. There was no there was no correlation with the antibody to Factor IX activity at 18 months after treatment. So that was kind of a low where it might not have an effect. But again, this assay is not validated. There really is no companion diagnostic available yet, but this is all we have. Hopefully, that answered your question. Let me know if there is any follow up.

Kavita Chawla: That does, yeah. Thank you, Ryan. Yeah, a great point about how expensive this is, so we should remove any risk of serious effects or any risk of resistance. I just hope that this is an accessible test, which I imagine if we are getting to a point where the hematologist is prescribing this, they should have access to it. Other comments from the Board? I see Jon's hand up. Hey, Jon.

Jon MacKay: Hi, there. Um, this is Jon MacKay. So this is probably for Donna or Ryan. I don't know if it's under the purview of this Committee, but I'm just wondering, is this going to be a carve-out medication? If so, have there been -- can you discuss, is this going to be possibility for an outcome space reimbursement kind of given the excessive cost of the medication and the possibility of treatment failures kind of like one and done?

Donna Sullivan: Uh, [cross-talk] this is Donna. [Cross-talk] It is a carve out from the managed care plan, so it will be covered through the fee-for-service program. As far as value-based, outcomes-based agreements, I believe CMMI is creating a cell and gene therapy model around this particular gene therapies for -- is this for sickle cell? No. This is for hemophilia. So no, I am mixing up my [laugh] [indistinct]. So it is a carve-out. It's covered under fee-for-service. The outcomes-based contracting sounds really great on the front

side. They are very difficult to administer, depending on trying to negotiate the actual outcomes, exclusion/inclusion criteria with manufacturers. So I am not sure if we are going to be entering into an agreement at this point in time, but we continue to look at it when -- as resources -- are available.

Kavita Chawla: Peter, go ahead. Oh, Peter, I think you are still muted.

Peter Barkett: There we go. Hopefully, you can hear me now.

Kavita Chawla: Yes.

Peter Barkett: I just want to make sure I understand the point from the industry representative about the Factor IX levels. It sounded like they were saying that was an inclusion criterion in the Phase II studies but not the Phase III studies, and I just wanted to make sure I am understanding that correctly. Or was that also a requirement for the -- an inclusion requirement for the Phase III studies?

Jonathan Abdul-Haqq: Can you hear me?

Kavita Chawla: Yes, we can.

Jonathan Abdul-Haqq: It was an inclusion requirement for our Phase III study, but it was an inclusion requirement tied to specific pharmacokinetic tests. So including it in coverage criteria doesn't -- would not be clinically appropriate because the FDA doesn't require any particular endogenous factor activity for in our Indication. And as your colleague pointed out, 2% doesn't define any clinical phenotype or medical necessity at all. It was in there to facilitate specific pharmacokinetic analyses, so it's not appropriate to define medical necessity in a coverage policy. And if I could just say one more clarification. The AAV5 neutralizing antibodies, that whole requirement. So that is not in our label at all. So the FDA does not require any testing period, and the test is offered by us free of charge to clinicians that want to use it in the shared decision-making process. It's the test that was used in HOPE-B, it's going to be updated, so 678 won't even be a valid titer anymore. And requiring the test is what The World Hemophilia Federation suggests, but a specific cut off. There is no clinical rationale for a threshold. That is why we offer it to be used in shared decision-making, and clinicians can decide. Because we had one patient -- all the patients that -- of the 54 patients in our trial 21 had neutralizing antibodies, 33 did not. All patients, regardless, there wasn't a

correlation between Factor IX production and having antibodies or not. So that is one point. The other point is, all of the patients that had neutralizing antibodies were 678 or below, except for one gentleman who was very high in excess of 3000, who never produced his own Factor IX, but there are no data points between 678 and 3000. So there is no threshold that anyone's recommending to determine appropriateness and, again, the FDA doesn't even require testing at all. And the World Hemophilia Federation suggests doing the test, but there is no threshold that can responsibly be applied. And again, 678 won't even be a valid number given that this test is going to be updated by CSL.

Kavita Chawla: Thank you for your comments, Jonathan. All right. So I think with those with those comments with that context, how would the Committee like to address the language in this section, if at all?

Peter Barkett: Hi, this is Peter. This is a very expensive medication, and we are kind of in uncharted territory, and as we -- over time, we'll get more experienced with the medication and possibly having a chance to address this again, but I am comfortable with the way that the language is written. Our industry representative said it's basically not appropriate to determine medical necessity beyond compendia use the FDA-approved Indication, and that is just not the way that the industry works with these very expensive medications. That is absolutely appropriate to determine some higher thresholds than simply an FDA approved Indication. That is the whole point of these policies, and I think the policy has been crafted well, and it's thoughtful, and maybe we will revise it in the future, but I think for now this looks pretty good.

Kavita Chawla: Thank you, Peter.

Christy Weiland: This is Christy Weiland. Peter, I appreciate that comment. I feel like how it is written currently seems to mirror the inclusion criteria of the patient population that has been studied from what I can understand, so I agree with you.

Kavita Chawla: I think most of us are in consensus. Any opposing viewpoints or feel like any of this language needs to be modified? I'm looking at your faces, too. I am seeing head shaking. Okay. All right. So with that, let's look at the form again and then move on to the motion. Thank you so much, Marissa. Okay. So this

looks pretty much -- yeah, it mirrors the policy well. Comments on this from the Board? And if not, then we can move on to the motion.

Kevin Flynn: This is Kevin Flynn, and I move that the Apple Health Medicaid Program implements the clinical criteria listed on policy 85.10,25.AA-1 as recommended.

Peter Barkett: This is Peter Barkett. I will second the motion.

Kavita Chawla: All in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstained? And the motion carries. All right. Thank you, Board. Great discussion. And I think that takes us back to you, Marissa, for the Immunomodulators.

Marissa Tabile: This is Marissa. Yes. Let me go ahead and just -- we didn't have any comments on the Hemgenix, but I am just making sure I save everything.

Kavita Chawla: Thank you.

Marissa Tabile: And then I will go ahead and get to the thalidomide. Okay. Okay. So this is Marissa again, and I will be going through the Immune Modulators: Thalidomide Analogs clinical policy. So just to give you a very high-level overview, these particular drugs can really treat a plethora of different -- they have a plethora of different Indications, so I am not going to get very Indication specific. I will just really get into disease and kind of drug information on it. So as a high-level overview, these immunomodulatory drugs are indicated for several different oncology and non-oncology Indications. So lenalidomide is commonly used in the first-line setting, while pomalidomide is indicated in the relapse refractory setting. Thalidomide has generally fallen out of favor given newer second-generation immunomodulatory agents. When used for the treatment of MM, thalidomide analogs are part of the standard three-drug backbone based on the superiority over two drug regimens. The place in therapy for four-drug regimens is still evolving and should be limited to clinical trials. The thalidomide is considered a first-line therapy for MDS but is generally used in the relapse refractory setting for other Indications such as follicular lymphoma, marginal zone lymphoma, and mantle cell lymphoma, so different

types of oncology and non-oncology Indications. So this is a little bit of a long policy, so just bear with me. As far as the clinical criteria, the language at the top of the policy is pretty much the same as the other two policies that you have seen. But just to mention, again, this policy really encompasses the three products that you will see here, so brand names are Revlimid, Pomalyst, and Thalomid. Getting into Indication specifics, so this is where I said "hold on" because there is quite a bit. The first one is erythema nodosum leprosum (ENL). For two, the patient has a diagnosis of ENL, and the medication will be used for the acute treatment of cutaneous manifestations of moderate-to-severe ENL. And if moderate-to-severe neuritis is present, the medication will be used in combination with corticosteroids unless that is not contra-, -- unless it's not tolerated or it's contraindicated, or the medication will be used as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence. And these are really just based off of the label [laugh], so that is really where some of these criteria came from. If the patient meets all of the criteria, we will authorize it for 6 months. And then for the reauthorization criteria, I will say it's pretty standard across the Board for all of these Indications. It's pretty blanket statement type of reauthorization criteria. So we would just be looking for a documentation of response to treatment defined by improvement or stable stabilization of disease or symptoms, so very broad language for that. And for the reauthorization, if they meet that and if we see that they are having clinical improvement or no progression, then we will reauthorization it for another 6 months. So it's a little bit different as far as the yearly approvals that you will see at least in like the other policies that we presented today. Well, except for Hemgenix that was not reauthorization. But typically, we tend to go with either 12 months or 6 months. Special occasions, sometimes we'll do less than that, but because there is just frequent monitoring that we want to make sure it gets done, that is why we did the 6 months for these. So getting into the next Indication, Follicular Lymphoma (FL). It applies to the drug lenalidomide or Revlimid. For this, it's kind of the same criteria for that, it's just prescribed same specialists that we would be looking for, so oncologists or hematologists. We would want them to have the diagnosis of follicular lymphoma. And then for 3, this is really mirroring the labeling. And then also some of -- we did take into account some of the NCCN Guidelines that are written, so that is why you will see for 3 it's either 3 or 4, but for 3, it would be if used as first-line treatment, lenalidomide will be used in combination with another medication. So you would probably see rituximab or obinutuzumab -- hopefully, I pronounced that correctly -- or the patient was previously treated with at least one prior

regimen for follicular lymphoma. So examples of those kind of treatment cycles that we would be looking for, and these are really pulled from NCCN and, like Imogen. Same reauthorization is 6 months. Same reauthorization criteria as above and the same reauthorization duration. For the next Indication, it is Kaposi sarcoma, it applies to pomalidomide. For this one, the specialists are a little bit different. It looks like there are oncologists, dermatologists, or infectious disease specialists that we will be looking for. We would want, of course, the diagnosis of Kaposi sarcoma. For this one, the patient has progressed on at least one prior systemic treatment, so that would be liposomal doxorubicin or paclitaxel unless it's contraindicated, and if the patient is HIV positive, the patient remains on an antiretroviral therapy. For this one, same reauthorization, same reauthorization criteria, and same reauthorization duration of 6 months. And then, of course, the disease stability or no progression. For this one, it is mantle cell lymphoma, for lenalidomide. This one has pretty simple criteria. Oncologists and hematologists prescribe it or in consultation, diagnosis of mantle cell lymphoma. And lenalidomide will be used in combination with rituximab. Same reauthorization duration and then reauthorization criteria. The next Indication is marginal zone lymphoma for lenalidomide. For this one, same specialists as the criteria above, the diagnosis of marginal cell lymphoma. For this one, we did also take into account NCCN guidelines as well, so that is why you will see the or here for this. This is pulled from the label, so it's used as first-line treatment. Lenalidomide will be used in combination with another medication, so rituximab or obinutuzumab, or they have been previously treated with at least one prior regimen for marginal cell lymphoma, and these are the examples of the treatments that we will be looking for. Same duration of 6 months, same reauthorization criteria and reauthorization duration. Next is multiple myeloma. This applies to all three of those drugs. And just to note, we do have all of these products preferred with PA on our Apple Health Preferred Drug List, so in order for a patient to get these medications, they would just need to meet these criteria for this. And regardless of what drug they are requesting, as long as they meet them, they could possibly get approved for it. So for this same specialist, oncologist, or hematologist, diagnosis of multiple myeloma. For lenalidomide, specifically, or Revlimid, we would be looking for that the medication will be used with dexamethasone as part of a doublet or triplet regimen, or if it's used as a maintenance therapy, the medication may be used as monotherapy. For pomalidomide, we would be looking for the patient has received at least two prior treatments for multiple myeloma, including one with lenalidomide and a proteasome inhibitor, and the patient has demonstrated disease

progression on/or within 60 days of completion of the last therapy, and c.) the medication will be used with dexamethasone as part of a doublet or triplet regimen. Or for thalidomide, this one the medication will be used with dexamethasone or prednisone. Same duration of 6 months, same reauthorization, and same reauthorization duration. For myelodysplastic syndrome -- that is for lenalidomide -- same specialist, diagnosis of myelodysplastic syndrome. 3.) the patient has lower risk disease, so IPSS Low or Intermediate-1. These are the different risks that we would be looking for. And four, the patient has transfusion-dependent anemia defined as two or more units of red blood cells in the previous 8 weeks, and we would be looking for MDS, so myelodysplastic syndrome, with a Del(5q) abnormality, or if the patient has MDS without the Del(5q) abnormality, we would be looking for these particular lab values. So serum erythropoietin levels are less than 500, and they had a history of an inadequate response to erythropoiesis stimulating agents with or without granulocyte colony stimulating factor, or if they have serum erythropoietin levels greater than 500, we will also be looking for a history of failure, contraindication, or intolerance to immunosuppressive therapies; so anti-thymocyte globulin with or without cyclosporine A, or demethylating agents, azacitidine or decitabine, or a verified SF3B1 mutation. That was mouthful. Same duration of initial approval duration of 6 months, same reauthorization criteria and duration that we would be looking for 6 months. And then for this one it is POEMS syndrome, for lenalidomide. This one, same specialists, oncologist or hematologist, diagnosis of POEMS syndrome. 3.), the patient has disseminated disease, -- so we will be looking for more than three bone lesions, and the patient is not a candidate for radiation-only therapy, and 4.) the provider attest that the patient is not a candidate for hematopoietic cell transplant. And 5, the medication will be used in combination with dexamethasone. So same 6 months, disease improvement, or no progression, and then same reauthorization of 6 months. These are the dosage and quantity limits. It is pretty extensive. Well, I guess it looks a little long, but these are all the Indications. And then the background. And then looking at the form -- let me pull that up here. Where is it? Sorry, it's not -- there we go. Okay. This is the form that goes with this policy. And I will go ahead -- let me just see. Okay. I will try to do it slowly, but I will go ahead and stop for any questions as I slowly scroll through the form for you all.

Kavita Chawla: Thank you, Marissa. While Marissa does that, any questions from the Board for Marissa?

Jon MacKay: Marissa, this is Jon MacKay. I'm just wondering if there are any non-oncological Indications that we might have to call, like a pregnancy contraindication or anything like that?

Marissa Tabile: This is Marissa. Sorry. [cross-talk] So you are asking to include that in [cross-talk] --

Jon MacKay: [Cross-talk] Just from the safety profile for pregnancy? Is there any place in there with that, where that would be warranted in terms of monitoring or a contraindication for, like, the non-oncological Indications? Or are they all for cancer?

Marissa Tabile: Um, it looks like for the most part -- and I apologize, I did not draw up this policy -- but for the most part, I believe most of these are the cancer Indications. The ones that they are not the cancer Indications, I can take a look at that and see if we want to consider adding that to the policy for those non-cancer Indications, I think, is what you were asking. Right?

Jon MacKay: Mm-hmm.

Marissa Tabile: Okay. I just want to make sure I understood. I could take that back and see if we want to consider adding that to the criteria.

Kevin Flynn: The one [cross-talk] that this has a pretty strict REMS regardless of the Indication, so you don't really need -- I don't think you need to put that in the policy. There is a lot of paperwork the provider has to do in order to -- like you literally have to write the prescription every month and, like, check the type of birth control the patient's on, so I don't think we need to be that redundant.

Jon MacKay: Okay. There is a strict REMS for it?

Kevin Flynn: Yeah, for all of these were.

Jon MacKay: Okay.

Kevin Flynn: I mean, thalidomide is like the classic drug that we remember from all the birth defects that I am sure you are referring to.

Kavita Chawla: I think Laura had her hand up for a second. Okay.

Laura Beste: I had the same comment.

Kavita Chawla: Okay. Other questions or comments? And then if there are any stakeholders. There are none listed.

Nonye Connor: Um, looking at the list, I don't see anyone's hands raised. No.

Kavita Chawla: Thank you, Nonye. Kavita here. I guess my question is a basic one. The reason for authorizing for 6 months at a time is because that is the usual length of treatment, or the risks -- or the adverse effect risks go too high after that? Usually the authorization is for a year at a time.

Marissa Tabile: Yeah. This is Marissa. So we just made it 6 months just because of the continuous monitoring that we would want to be looking for these drugs, so that is why it's a little shorter than what you typically see in most policies where it would be a year, so that is why it's a little bit shortened. We would just want to make sure that that monitoring is being done, and then on our end where we are looking for those monitoring parameters. So that is why. I am not sure if the treatment duration -- I apologize -- if those are 6 months or not, but it's really just from like a safety and monitoring perspective.

Kavita Chawla: All right. Other questions or comments? And if not, then we can move to the motion.

Michael Corsilles: This is Michael Corsilles. I would like to make a motion. I move that the Apple Health Medicaid program implements the clinical criteria listed on policy 20-1 has recommended.

Christy Weiland: This is Christy Weiland. I second.

Kavita Chawla: All in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstained? Okay, and the motion carries. Thank you, Board. And I know that with that we would move on to Anticonvulsants, but I also realize that our lunch started a little earlier. Is the Board okay continuing? I see. Okay, good. I see nodding, so all right. Umang.

Umang Patel: All righty. Can you hear me?

Kavita Chawla: Yes, we can.

Umang Patel: Okay. So I think my video stopped, so I don't know if you can see me, but --

Kavita Chawla: Yeah, we can see you.

Umang Patel: You can't? Okay.

Kavita Chawla: Yeah.

Umang Patel: Okay. Well, that's okay. [Cross-talk] --

Marissa Tabile: [Cross-talk] This is Marissa. Sorry, Umang. [cross-talk] --

Umang Patel: [Cross-talk] Marissa is going to show [cross-talk] --

Marissa Tabile: I'm going to go ahead and pull your slides up.

Umang Patel: That's okay.

Marissa Tabile: Just give me one second.

Umang Patel: Yeah, [cross-talk] no worries. [cross-talk] --

Marissa Tabile: [Cross-talk] A lot of documents to sift through today.

Kavita Chawla: You are doing an amazing job, Marissa. Thank you.

Marissa Tabile: Thank you. Let me pull everything up here. We'll get at your slides. Okay. I'm almost there. I just got to get the motion slide pulled up, and then we should be good to go so then have everything at once. Okay. All righty. Let me share this. All right. All right, Umang, I think you should be good to go.

Umang Patel: Okay. All righty. Um, perfect. Well, I will be reviewing the next few topics here. Just a quick reminder to some of the Committee members, some that are new or some who may have forgotten, what I will do is when we review significant clinical updates within the last 12 months or so. I will provide some background, some guideline updates, if they are relevant, within the

last few years, and then we'll go right into the significant clinical updates. So the first one being Anticonvulsants. So if we could just go to -- perfect -- and again, just a reminder for some of the Committee members, if you see on the title page of each subclass, we have what the class is in our Magellan prime system, which is anticonvulsants, and then we also have the Apple Health PDL and how it is listed in the PDL. So anticonvulsants are broken down by a mechanism of action which includes Ampa Glutamate Receptor Antagonists, Benzodiazepine Rescue Agents, Miscellaneous, Neuroactive Steroid- GABA Modulators, and Succinimides. So moving onward, a little bit of background here. So epilepsy is one of the most common disorders of the central nervous system. It is defined when a person has two or more seizures. It affects about 2.2 million Americans with 150,000 new cases diagnosed each year. The risk is estimated to be 1% from birth to age 20 years and 3% at age 75. Isolated seizures may also occur during a febrile illness after head trauma or as a result of withdrawal from alcohol or sedative hypnotics. A seizure is traceable to unstable cell membrane or cluster of cells, and excessive excitability spreads either locally which is defined as a partial seizure or more widely, which is a generalized seizure. Partial seizures began in one hemisphere of the brain and unless they become secondary generalized, they can cause alterations in motor functioning, sensory symptoms, or automatisms. In terms of if there is no loss of consciousness, they are called simple partial. If there is loss or impairment of consciousness, they are called complex partial, and about 70% of patients with epilepsy can be maintained on one drug. Noncompliance and evolving refractory epilepsy are common reasons for treatment failure, and if control is not achieved with one drug, alternative medication should be attempted before others are added to current therapy. On the next slide here, we will give a little bit of a guideline update. So in 2022, the International League Against Epilepsy developed classifications for epilepsy syndrome. An epilepsy syndrome is defined as a characteristic cluster of clinical and EEG features often supported by specific ideological features such as structural, genetic, metabolic, immune, or an infectious. Through a series of publications, the ILAE provides definitions and classifications of syndromes according to categories divided by age of onset. They commonly have age-dependent presentations, features, and specific comorbidities. Diagnostic criteria include age of onset, neurological exam, genetic studies, and, of course, illness. The classification of epilepsy syndromes in neonates and infants focuses on the clinical and laboratory features of epilepsy syndromes with onset from birth to two years of age and includes two major groups of syndromes, self-limited epilepsy syndrome and developmental and epileptic encephalopathies. Generally, children with

epilepsy developing very early in life, experience significant cognitive and behavioral comorbidity, and have a higher rate of drug resistance. And the classification of syndromes with an onset between ages two and 12 years are categorized broadly as self-limited focal epilepsies, generalized epilepsy syndrome, and developmental and/or epileptic encephalopathies. Childhood syndromes may evolve from syndromes of infancy or may present with severe acute encephalopathy following prior to normal development. Idiopathic generalized epilepsy syndromes and syndromes that occur with a variable age of onset either in childhood or beyond the age of 18 are further described and categorized by the ILAE. On the next slide, again, as you can imagine, there -- anticonvulsants can have a lot of subsections, so I will do my best here to give you a breakdown. First, we have Lennox-Gastaut syndrome. It is one of the most severe forms of childhood epilepsy and is one of the hardest forms to treat, characterized by mental retardation and multiple seizure types. Patients have seizures daily, sometimes experiencing several seizures within a day, and patients may also experience drop attacks, which is defined as a loss of muscle control, causing the patient to fall abruptly to the floor. Next, we have infantile spasm primarily consists of sudden bending forward of the body and stiffening of the arms and legs. West syndrome is characterized by infantile spasms, developmental regression, and a specific pattern on the EEG testing called hypsarrhythmia, so it's chaotic brainwaves. The onset is usually in the first year of life, typically between four and eight months, and usually stops by age five but may be replaced by other seizure types. Then we have Dravet syndrome, a rare catastrophic form of epilepsy that presents in the first year of life and is characterized by frequent prolonged seizures. Patients may experience multiple seizure types during their lifetime. Infants with Dravet syndrome often experienced multiple comorbidities over their lifetime related to the persistent seizure activity, including behavioral and developmental delay. Dravet syndrome is also associated with a 15% to 20% mortality due to sudden unexpected death in epilepsy. The goals of treating epilepsy are to reduce the frequency of seizure occurrence along with providing the best possible quality of life for the patient. Treatment will depend on the type of seizure. Many different classes of drugs are available to treat the different forms of seizures. and some patients will require more than one drug to control said seizures. Let's see, on the next slide here. Okay, we'll go into drug-specific updates. So first new generics. In March of last year, the FDA approved topiramate, the first generic to the 200 mg ER oral capsule of Supernus Trokendi XR from Zydus. Then we have methsuximide. In May of last June, the FDA approved the first generic for the 300 mg oral capsule of Parke Davis Celontin from Novitium.

We did have a manufacturer communication April of last year, for Fintepla. The DEA published a final ruling declaring the removal of fenfluramine and associated salts, isomers, and salt of isomers from the schedules of the Controlled Substance Act, effective December 23, 2022. Fenfluramine was previously a Schedule IV controlled substance since 1973, and UCB Pharma filed with the FDA for a labeling supplement to remove the schedule for designation from the label. And then a new dosing for Vimpat. May of last year, the package insert updated to include loading dose and/or higher initial dose during week 1 as an alternative option for initiation of lacosamide in patients 1 month or greater to less than 17 years of age, with partial onset seizure for monotherapy or adjunctive. Treatment and for patients four years of age or older to less than 17 years of age with primary generalized tonic clonic seizures for adjunctive treatment. This new dosing can be applied for all Formulations of the drug and can be utilized when reaching the maintenance dosage in a shorter timeframe is indicated. Labeling includes a table with the recommended loading doses according to patient age and weight. We will go on to the next slide here. All righty. So next we have Motpoly XR. May of last year, FDA approved a new Formulation for the treatment of partial onset seizures in adults and pediatric patients weighing 50 kg or more. So, there are some Warnings here: Fetal Toxicity, so use during pregnancy can cause cleft lip and/or palate and being small for gestational age, suicidal behavior and ideations, and cardiac rhythm and conduction abnormalities. In terms of Dosing, it is stratified by age and weight for adults defined as 17 years of age and older. Initial dose for monotherapy is 200 mg daily. Initial dose for adjunctive therapy is 100 mg daily. And the maximum dose for mono- or adjunctive therapy is 400 mg daily. And for pediatric patients weighing at least 50 kg, the initial dose is 100 mg daily. As you can imagine, the Availability are extended-release capsules in 100 mg, 150 mg, and 200 mg dosage forms. All righty. And I am going to pause right there for the Committee. Any questions?

Kavita Chawla: Thank you, Umang. And the Board, any questions for Umang? And if there are any stakeholders.

Nonye Connor: It looks like we have one hand raised.

Kavita Chawla: Okay. Wait. Call on it, Nonye, I don't see it.

Nonye Connor: Okay. The first one we have is Regina Amin, and I am so sorry if I am pronouncing your name incorrectly. Regina, you can unmute now.

Regina Amin: Can you hear me now?

Nonye Connor: Yes.

Kavita Chawla: Yes, we can.

Regina Amin: Thank you. Yes, I did not fill out the form, so I am not a provider for Washington. I am not a patient. I don't have any conflicts besides where I work for UCB Pharma. I wanted to present the Nayzilam, so that is what I am going to do right now. Good afternoon. My name is Regina Amin. I am the Medical Outcome Liaison for UCB. I am here today to discuss seizure clusters, specifically the unmet need, treatment need, and socioeconomic burden and UCBs product, Nayzilam, wins request for his placement on the Preferred Drug List. Seizure clusters are a seizure emergency which is defined as having two or more seizures in 24 hours, no different from a patient's typical seizure pattern. Seizure clusters are serious medical events that need to be stopped promptly to avoid potential serious consequences, such as increased rates of status, hospitalization, and greater use of emergency services. [indistinct] prospective in the State of Washington, you can anticipate roughly about 74,000 patients with epilepsy of which 11,000 experience seizure clusters. Seizure -- Nayzilam is the first FDA-approved nasal Formulation for acute treatment of seizure clusters in the outpatient setting in patients 12 years and older. It is the only midazolam-based option approved for the treatment of seizure clusters. Nayzilam is a benzodiazepine indicated for the acute treatment of intermittent stereotypic episodes of seizure activity or seizure clusters in patients 12 years and older. It has a T-max of 17 minutes followed by single-dose and a half life of two to 6 hours. Nayzilam demonstrated efficacy in stopping seizure cluster in a Phase III double-blind and placebo-controlled study of 292 patients in which significantly more patients received a single-dose of Nayzilam experienced treatment success versus placebo, 53.7 Nayzilam arm versus 34.3 in the placebo arm, and 81% of Nayzilam-treated patients, seizure terminated within 10 minutes, and 50% of patient had no risk of recurrence within 10 minutes to 6 hours. Additionally, more patients have a no problem of a seizure recurrence for 24 hours after Nayzilam treatment. After treatment, return to baseline function was assessed by the caregiver, and the medium you are trying to full baseline functionality after treatment with Nayzilam was 190 minutes. Like all benzodiazepines, Nayzilam does have a Box Warning for risk of concomitant use of opiates, risks of abuse, misuse,

addiction, independence, and withdrawal. Please refer to the PI for our full Box Warning. And has otherwise other important information. The most common adverse reaction are somnolence, headache, nasal discomfort, throat irritation, and rhinorrhea. Nayzilam is supplied in a single-dose strength in a box containing two 5 mg nasal spray units and does not require weight-based dosing. While the majority of Nayzilam patients in the clinical trails did not have a recurrent second dose. You can administer a second dose as early as 10 minutes after the first. Thank you for your time today, and please consider putting Nayzilam as a preferred status and for Washington Medicaid patients. Thank you.

Kavita Chawla: Thank you, Regina. Any questions from the Board for Regina? Great. And any other stakeholders, Nonye?

Amanda Rendell: Hello? Can you hear me?

Kavita Chawla: Okay. Hi, Amanda.

Amanda Rendell: Hi. How are you?

Kavita Chawla: Well, go ahead. And so if you can answer those questions, then we'll start your timer.

Amanda Rendell: Yep. My name is Amanda Rendell. I am an employee of Neurelis, and I am not a patient, I'm not a provider, and I don't have any other conflict of interest to report besides being an employee of Neurelis.

Kavita Chawla: Great. Thank you. Go ahead.

Amanda Rendell: So we request that Valtoco remained in a preferred position without restrictions. With that, we would like to use this time to review a few key highlights on Valtoco. Valtoco is an intranasal diazepam spray for emergency rescue treatment of seizure clusters and is the first and only intranasal rescue treatment for adults and children down to the age of six. Neurelis is currently conducting a clinical trial on patients two to five where we are investigating in the Safety and Pharmacokinetics of Valtoco for label expansion to include these younger two to five year old children. Valtoco was designated clinically superior to Diastat, the diazepam rectal gel by true effect FDA. Valtoco is the only intranasal rescue medication that allows for customized dose based on age and weight, with 5 mg, 10 mg, 15 mg, and 20

mg doses available. An optimal dose may be administered to pediatric and adult patients alike. Each box contains two doses of Valtoco. If a second dose is needed, it may be administered at least 4 hours after the initial dose. Our PK studies demonstrated consistent and reliable dosing with 97% absolute bioavailability of diazepam relative to IV. And PK parameters that were two to four-fold less variable when compared to Diastat. When treating seizure clusters with rescue medication, the primary goals are to stop the initial seizure and prevent reoccurrence of seizure activity over time. Valtoco has a half life of 49.2 hours, which would allow coverage within the expected 24-hour timeframe of a seizure cluster. In an exploratory analysis from a long-term safety study, patients with epilepsy and their care partners reported rapid Valtoco administration and seizure cessation. With a median time to administration of two minutes and a median time to seizure cessation of four minutes. A separate exploratory analysis demonstrated that almost 4000 seizure cluster events treated with Valtoco, and 87% of events were treated with a single-dose over a 24-hour period. Valtoco has a Boxed Warning as do all benzodiazepines, regarding concomitant use with opioids, abuse, misuse, and addiction, and dependence and withdrawal reactions. The most common local AEs were nasal discomfort, dysphasia, epistaxis, and in a long-term safety study the rate of somnolence was 1.8%. For additional prescribed and important safety information, please refer to the Full Prescribing Information for Valtoco. I would like to thank you for your time and ask that you please continue to allow patients to have unrestricted access to Valtoco. And I am happy to take any questions you may have.

Kavita Chawla: Thank you, Amanda. Any question from the Board for Amanda? Okay. And any other stakeholders, Nonye?

Nonye Connor: No, I don't see any other stakeholders. I realized earlier that I was talking while muted, but [laughter] --

Kavita Chawla: And Marissa. [Cross-talk] Oh, okay. Thank you. Marissa, I know you were starting to show us the list on the Apple PDL.

Marissa Tabile: This is Marissa. Yep. So I will go ahead and go through the PDL for you all. So I'm just going to go class by class for all the Anticonvulsants. So the first one is the Ampa Glutamate Receptor Antagonists. The only product in that class right now is Fycompa, and we have that preferred with the tablets and the suspension. For the Benzodiazepine Rescue Agents, our preferred products in this class are the Diastat, so those are the diazepam rectal gels, various

midazolam. I believe these are injections for IV. And then we do have Valtoco preferred, which is a diazepam nasal spray. For the Anticonvulsants : Miscellaneous, the preferred products in this class we have Briviact, which is brivaracetam. That looks like that is an IV. We have carbamazepine, which is different Formulations, chewables, suspension tablets, ER capsules, ER tablets, everything. We have Epitol, gabapentin capsules, solutions. Those are preferred. Generic lacosamide solutions and tablets. I apologize for the scrolling. Lamotrigine tablets and various levetiracetams. So we have some injection IV solutions, oral solutions, tablets, ER tablets. And oxcarbazepine suspensions and tablets. Pregabalin capsules, solutions. Primidone tablets. This looks like it is a brand name. This is Roweepra. It looks like that is a levetiracetam 500 mg. We have the preferred. We have Subvenite, which is lamotrigine. Different carbamazepines, Topiramate different Formulations, sprinkle, capsules, and tablets. And I think I mentioned everything. Oh, and some zonisamide capsules and oral suspensions. And the Neuroactive Steroid - GABA Modulator, it is Ztalmy. We do have that non-preferred. And then for the succinimides, our preferred product in that class is the ethosuximide products. It looks like it's the capsules and solutions. And I will go ahead and pause there for any questions about the PDL.

Kavita Chawla: Questions from the Board?

Zoe Taylor: So you mentioned that the diazepam for the rescue, there is rectal and inhaled -- or intranasal preferred. But for midazolam, there is just injectable preferred? I think. Not the nasal [cross-talk] to choose [cross-talk] --

Marissa Tabile: [Cross-talk] That's correct. We don't have the nasal preferred.

Zoe Taylor: Okay.

Marissa Tabile: Yep.

Zoe Taylor: Are there, like, compelling reasons for that? Is it really new? Is it really expensive? Or do you know?

Marissa Tabile: This is Marissa. Yeah, when we did take a look at it, there were some cost considerations that we took into account. So that is part of the reason why.

Zoe Taylor: Do you know if there is anything, like, about if somebody fails the diazepam then they can get that still, or what the details of that are at all?

Marissa Tabile: Yeah. So that would be the expectation. This is Marissa. Sorry. That would be the expectation for someone if they wanted to get midazolam nasal spray is that they would have stepped through either the diazepam rectal, and it didn't work out, or the nasal spray didn't work out. That would be the expectation, and then they would be eligible for the nasal.

Zoe Taylor: Okay, sounds good.

Marissa Tabile: Yeah.

Zoe Taylor: Thank you.

Marissa Tabile: Mm-hmm.

Kevin Flynn: And the IV is covered. Right? So, like, if you just had an atomizer, it's probably what I guess you were thinking of and confused that.

Marissa Tabile: This is Marissa. I'm sorry, Kevin. Can you repeat that question one more time?

Kevin Flynn: Because if you have an atomizer you [cross-talk] nasally, so like I'm guessing that's what you were thinking [cross-talk] --

Multiple Speakers: [Cross-talk] [indistinct].

Donna Sullivan: [Cross-talk] Kevin, this is Donna. Yes, that was originally before Nayzilam came to market. That was the intention of having the injectables preferred.

Kevin Flynn: Got it. All right.

Zoe Taylor: Okay, thanks.

Laura Beste: This is Laura Beste. I don't think that the Nayzilam product is indicated for children under age 12, and the diazepam it is for like ages five and [audio cuts out], so you got better coverage age wise for the diazepam nasal versus midazolam.

Donna Sullivan: This is Donna. Yep, I agree.

Kavita Chawla: All right. Other questions for Marissa? Okay. And [Cross-talk] --

Zoe Taylor: [Cross-talk] Kavita, sorry. Does the HCA ever have or bring, like, data on I guess maybe you already use the to decide what you want to propose to us but, like, data on which if there are any things that are like frequently requested that are not preferred or -- because we like we hear from the stakeholders from the pharmaceutical companies, but we don't always have doctors on our Committee who have personal experience with all of these things, and so I just feel like the best data would be like what are people requesting out in the real world? Do you already take that into account before this? Or do you ever have that to [cross-talk] yeah --

Donna Sullivan: [Cross-talk] So this is Donna. That's a tricky question to answer, Zoey. Sometimes what is being most requested as a result of a very good marketing campaign of the manufacturers rather than what is the more effective or cost effective treatment, I don't -- I haven't seen any -- I won't say I haven't seen any requests for Nayzilam. I haven't seen any provider complaints get escalated up to our attention about the diazepam nasal spray being preferred over the [cross-talk] --

Zoe Taylor: Yeah, no. No worries.

Donna Sullivan: [Cross-talk] Yeah. So [cross-talk] --

Zoe Taylor: [Cross-talk] I was just wondering [cross-talk] if there was, like how that gets brought into account.

Donna Sullivan: We would probably look at how often we are prefer -- approving it and then at what point in time. If there is a rebate on it, are we leaving money on the table? And at what time does it make sense for us to -- based on utilization, volume, we would adjust and maybe make it preferred because there would be additional savings. But we monitor that pretty much on a quarter-to-quarter basis.

Zoe Taylor: Okay. Cool. Thank you.

Kavita Chawla: Go ahead, Peter.

Peter Barkett: Hi, Donna. This is just a follow up to Zoey's question. Maybe one other way of getting at I think what she was driving at is -- do you have a process for

tracking outcomes of appeals, overturn rates, and then reviewing that data and triggering something to come to P&T?

Donna Sullivan: We track our prior authorizations and what is approved and denied. Unlike a commercial health plan, we don't have what we call appeals. We might get a request for reconsideration, which I believe gets counted as just another Request for Authorization in our data, so we don't track it from the client. We got a request for client A. It was denied. Provider requested a second -- a reconsideration or what in commercial world would be an appeal, and then it got approved. We don't track it linearly like that, so I can't really answer your question there.

Peter Barkett: Okay. No. And I guess I didn't realize that you don't follow the same appeal process. What about -- and you do follow like peer-to-peer, right? Like [cross-talk] --

Donna Sullivan: [Cross-talk] There is a period -- I mean, there is a request for reconsideration. You can request a peer-to-peer. You can go straight to an administrative hearing, also. But again, they are all -- they are not tracked. The hearings are tracked completely separately because that is a daily administrative function, but we don't -- if you had a peer-to-peer, and the decision was to reverse the original denial, it doesn't -- like, again, I don't track -- it will get put in as a new authorization. It doesn't get tracked back to that original denial to have that -- here is the full story for this person's request for this drug.

Kavita Chawla: Did that answer your question, Peter?

Peter Barkett: Yeah, that is helpful. I wasn't aware of like some of the differences. That is helpful. Thank you.

Kavita Chawla: Any other questions for Marissa or the HCA team? And Marissa, if you can get the motion on the screen in the meantime. Okay. And whenever the Board is ready.

Greg Hudson: This is Greg Hudson. I can read the motion. 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 the HCA. Products in these classes 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.

Peter Barkett: This is Peter Barkett. I will second the motion.

Kavita Chawla: All those in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstained? Okay, with that the motion carries. And back to you, Umang, for Antidementia Agents.

Umang Patel: All righty. So the next subcategory we have are Alzheimer's agents, which are Antidementia agents overall and Anti-Myeloid antibodies. So a little bit of background here on the next slide. Dementia is characterized by irreversible loss or decline in memory and other cognitive abilities. Approximately six and a half million Americans aged 65 and older suffer from Alzheimer's. It is the most common type of dementia, accounting for 60% to 80% of dementia disorders in the elderly and is the fifth leading cause of death in the United States. Other types of dementia include vascular dementia, dementia with Lewy bodies, mixed dementia, and frontotemporal dementia. It may be associated with HIV, normal pressure hydrocephalus, Huntington's disease, Korsakoff's syndrome, MS, Parkinson's, and Creutzfeldt-Jakob disease. Many other conditions can cause delirium symptoms, such as thyroid disorder, vitamin deficiencies, but are reversible once the underlying condition is addressed. In terms of Alzheimer's, it is characterized by progressive cognitive decline associated with impairment of activities of daily living and behavioral disturbances. Patients with Alzheimer's eventually lose all cognitive, analytical, and physical functioning. Ten Warning signs of Alzheimer's include memory loss that disrupts daily life, challenges in planning or solving problems, difficulty completing familiar tasks, confusion with time or place, trouble understanding visual images and spatial relationships, new difficulties with speaking or writing, misplacements of items or losing the ability to retrace steps, decreased or poor judgment, withdrawal from work or social activities, and mood or personality changes. In addition, there are three stages of Alzheimer's over the course of the disease characterized by symptoms severity, rate of disease progression, and level of necessary supportive care for activities of daily living. On the next slide here, in January of last year, we have Leqembi. FDA granted an

accelerated approval for Leqembi, which is an amyloid beta-directed antibody indicator for the treatment of Alzheimer's. Labeling states treatment should be started in patients with mild cognitive impairment or mild dementia stage of disease in the population in which the treatment was initiated and clinical trials as there is not Safety and Efficacy data on starting treatment in earlier ages or later stages of the disease than were studied. In terms of Limitations, pregnancy is one of them. Based on animal data, it may cause fetal harm, and there is a Blackbox Warning for monoclonal antibodies directed against aggregated forms of beta amyloid, including Leqembi can cause amyloid-related imaging abnormalities (ARIA). characterized as ARIA with edema and ARIA with hemosiderin deposition. ARIA is usually asymptomatic, although rarely serious and life-threatening events can occur. Serious intracerebral hemorrhage greater than 1 cm has occurred in patients treated with this class of medications. The Dosage is 10 mg/kg that must be diluted then administered as an IV infusion over approximately 1 hour every 2 weeks. And the Availability is an injection form a single-dose vial in 500 mg/5 mL and 200 mg/2 mL solutions. Moving onward, CMS Communication, in June of last year announced that Medicare Part B will cover drugs that slow the progression of Alzheimer's disease if: 1.) the drug is granted traditional FDA approval rather than the accelerated, 2.) patient is diagnosed with mild cognitive impairment or early dementia due to Alzheimer's, and 3.) the patient is followed by a qualified physician participating in a registry that has appropriate follow-up care. And lastly, there was a drug discontinuation earlier this year, Aduhelm, in February. Biogen announced a realignment of resources in their Alzheimer's disease portfolio resulting in the discontinuation of the development and commercialization of Aduhelm. They stated that the decision to withdraw resources was not the result of any Safety or Efficacy concerns but allows for reprioritization to focus on Leqembi as well as potential pipeline products. The rights to this will revert to Neurimmune, and the Phase IV post-marketing confirmatory envision study will be terminated. And just an FYI, this did receive accelerated approval back in 2021. So I will pause there for the Committee.

Kavita Chawla: Thank you, Umang. Questions from the Committee for the Board? [laugh] -- for Umang, I mean. Peter, go ahead.

Peter Barkett: Thanks, Umang. Yeah, I was curious, first, about the Aduhelm. And it sounds like -- well, you answered it. They just want to double down on what can be. But the other thing I was curious about was donanemab, so I know it's not FDA approved yet. I was kind of waiting for the word on that -- anytime now.

I am curious, if you have seen any of that data, if we are going to bring this class back when there is a verdict on donanemab, particularly if it gets FDA approval? Or how are you thinking about that agent?

Umang Patel: Yeah, Dr. Barkett. So this is Umang. So I haven't seen the data yet. We usually focus on -- we kind of dive more into the data once it is officially approved. Once it is approved, we do take a look at it. We do update these clinical review documents that we provide the Committee. I may defer the second part of your question to Marissa or at least have her verify what I am saying is honest. But I believe, based on the scheduling of these disease states, this would be revisited again next year in 2025. And that is when if it is approved between now and then then it would fall into that review cycle.

Marissa Tabile: This is Marissa. Yeah. So just to verify we typically want to review classes annually, especially the same types of classes. But of course we could, possibly, depending on kind of where it lands in our PDL if it has to be like a one off class, we could certainly bring it -- not to an April meeting, but maybe to another one. So we do try to keep as closely to that annual schedule as we can. But if we do have to do a one off, we certainly can for sure.

Peter Barkett: Yeah. I was anticipating the differential interval dosing. But I believe Leqembi is also trying to come up with a one-month interval dose, too, so that might be a moot point. But we are kind of -- I was anticipating there might be a lot of interest in donanemab other than Leqembi based on the difference in interval.

Kavita Chawla: I guess I have a question, probably more for like Marissa and Donna. For something like this where there is a relatively newer medication, and we know it's very expensive, remind me again when we would look at the policy for that versus just approving it to be included in the PDL.

Marissa Tabile: This is Marissa. So policy-wise, it probably, to be quite honest with you, as soon as -- if a drug were to come out tomorrow, for example, like an FDA approval, you probably wouldn't see a policy for that probably until a couple months later, depending on the need, or even the next year just because we do try to schedule our policies at least for the whole year and try to keep to that schedule. But depending on kind of the urgency that policies need to be created, we do tend to prioritize those, especially those that might have higher utilization than others. So especially for some of the more rare diseases, they typically tend to get kind of prioritized a little lower, just

because one, they are a little rare, so the patient population for them is a little bit smaller, but you wouldn't see very many requests for that one, and also the urgency of them may not be necessarily needed because they are very rare orphan diseases that we typically probably wouldn't see. So [cross-talk]

Kavita Chawla: [Cross-talk] for this?

Marissa Tabile: It may take like a year for a policy for these products to come out from inception to really getting implemented.

Kavita Chawla: Okay, so for Leqembi, specifically, the policy is not out yet. Is that --

Marissa Tabile: This is Marissa. That's correct. Yeah. We don't have a policy for it, and we don't have a policy that we are working on right now for that one yet.

Kavita Chawla: Got it. Thank you. Go ahead, Kevin.

Kevin Flynn: I just -- and Donna and Marissa, clarify if I am wrong just for everyone's knowledge. All right? Because most of these patients are going to have Medicare, right? So you don't -- if Medicare approves it, you don't -- like as their secondary -- you don't deny it or put any additional requirements on top of it, so there is really not a need for a policy for the vast majority of patients.

Marissa Tabile: This is Marissa. That is a good question. Donna, I am not exactly sure how to answer that to be quite honest with you. I think we can still apply criteria to them if we need.

Kavita Chawla: Okay, yeah. Kavita here. I suppose, like, because we are reviewing the agents here, and the motion we are about to vote on says that we are approving their inclusion on the PDL, I assume that all of those medications that are on the PDL would require some kind of policy.

Kevin Flynn: I just mean practically in terms of, like, approval. Like, almost -- not all, but a vast majority of patients are going to be of Medicare age. So in terms of, like, waiting for approval for any new agents that come out, a lot of them are going to, if Medicare agrees to cover them, by default, Medicaid would just cover the remainder, like, their 20% copay, what's left for Part B, right?

Marissa Tabile: This is Marissa. I do believe there is that coordination that you are speaking of. But as far as putting prior authorization on some of them, I do believe we still have the ability to do that, so they can still go through, at least for Medicaid, a clinical review for appropriateness for those. The coordination of as far as Medicare and Medicaid, that is like a whole -- I apologize, I am not privy to kind of how that works, but I do know that we can create policies for those products.

Kavita Chawla: Go ahead.

Peter Barkett: [Cross-talk] I think on the coordination of benefits, unless Medicaid operates under a different set of rules than commercially, you are not allowed to apply any prior auth as a secondary insurance, so you just have -- you get stuck with the bill. And as far as the kind of Medicare versus non-Medicare insurances covering it, you are probably right. Most -- well, maybe not most, but a disproportionate number of the patients that would get this medication would likely be of Medicare age, at least, but not everybody qualifies for Medicare. And also because the medications are indicated for the very early stages of Alzheimer's dementia, you are going to pick up some patients in their 50s and early 60s before they become of Medicare age, so it's not exclusively Medicare. But, overall, my understanding of utilization of this agent is very, very low so far.

Kavita Chawla: And these would be the dual-eligible patients, right? Because we are talking about Medicaid, so. Okay, any other questions before we look at that motion? Okay, Marissa, if we can pull up our motion. And I did see that we did have some written stakeholder testimony that was submitted to us ahead of the meeting, which I am sure we all had a chance to review. Okay. So here is our motion, whenever the Board is ready.

Zoe Taylor: So I am confused about, like, do we also look at an Excel of these ones? Or no, just because there are so few? And is this the same process that we just did with the [cross-talk] --

Marissa Tabile: Oh. This is Marissa. Actually, yeah. Thank you for pointing that out. Let me -- I did not show you all the PDL. Let me show you [cross-talk] --

Zoe Taylor: [Cross-talk] All right, great. Thank you.

Marissa Tabile: -- what that is looking like. Okay.

Zoe Taylor: Perfect.

Marissa Tabile: Thank you. I forgot myself. Okay. So we will go through the Antidementia agents. So there is, like, this class and then a subclass, which I will show below. So for this particular drug class, this has really the traditional antidementia products that you would think of, so then the non-Aduhelms if you will. So the preferred products that we have in this class are Donepezil with various types of Formulations available. We have tablets, ODTs. We also have rivastigmine, so the patches. Memantine tablets and [audio cuts out] capsules, those are preferred. And then it looks like the preferred products are the rivastigmine patches, the memantine capsules, and then Donepezil tablets and ODTs. And then for the Anti-Amyloid Antibodies, which is where Aduhelm and Leqembi live. That is where that houses those two products. Aduhelm is still included on our PDL right now, even though I know Umang did mention that it got withdrawn, just on our drug file of where we get our source of truth for drugs, it hasn't been officially pulled from that database, so that is why it shows up on our PDL. But for those two products, we do have them nonpreferred on our PDL and, of course, there is PA on them. I don't believe -- I haven't heard of us getting, to be quite honest with you, any requests for those two products yet, so I am just throwing that out there as like an FYI. And I can answer any questions you might have about the PDL.

Zoe Taylor: So by approving that motion, are we saying that all of the drugs on this list are safe and efficacious? Even the ones that are not preferred?

Marissa Tabile: This is Marissa. Yep, that is correct.

Zoe Taylor: Okay.

Marissa Tabile: Yep.

Peter Barkett: So it looks like Leqembi is non-preferred, right? And there is a prior auth criteria. But if we approve the motion, Leqembi could be listed as a preferred agent.

Zoe Taylor: Yeah, that's the problem.

Peter Barkett: Yeah. Right. And I think there were, like, [cross-talk] one or two deaths in the study [cross-talk] --

Zoe Taylor: [Cross-talk] So it's not true.

Peter Barkett: Yeah. Like, it is just not terribly efficacious, and there [cross-talk] is still some lingering Safety concerns.

Marissa Tabile: This is Marissa. And to speak to that, Peter, that is really why we made it nonpreferred. I mean, even though there are two products in the class, it's just because the evidence that has been submitted for these drugs is not very strong for them. We didn't feel very strongly about making them preferred, so that is why you will see that nonpreferred positioning on our PDL.

Zoe Taylor: Yeah. I just think it should be part of the motion. Like this is kind of the whole point of this Committee is, like, when there is a drug like this, that is, like, super expensive, has a ton of marketing behind it, but it doesn't do anything, we are like the ones who say, no. Right? And so I think, even though right now it is nonpreferred, which is great, like, our motion is still saying, like, we think this drug is safe and efficacious. So I think can we change that? Like --

Kavita Chawla: What does the Committee think about that, about maybe just having a sentence in there about the Anti-Amyloid Antibody agents that currently exist are not considered efficacious enough to be included in the PDL? And I think Donna and Marissa, I will have you weigh in on that as well because I don't think we have specifically excluded medications like that. Go ahead, Laura.

Laura Beste: So my question would be, what about making it into its own class? I know sometimes even though it is for antidementia, it could be its own class, so then it wouldn't be part of the standard of care classes.

Donna Sullivan: This is Donna. Which drug are we talk -- are we talking about Aduhelm?

Kavita Chawla: Leqembi as well.

Donna Sullivan: Leqembi as well. Um, I think they are in their own classes. Marissa, are they both being pulled from the market at this point in time?

Marissa Tabile: This is Marissa. So as far as I know it is just the Aduhelm. They are housed in their own Anti-Amyloid Antibody subclass, but I think what Laura was alluding to was instead of you know how for the motion we list all the drug

classes and say all of these classes on Slide 4 are safe and efficacious [cross-talk] what I'm hearing it sounds like Laura was suggesting splitting it out, so having two different motions for them. And then, I don't know, wordsmithing for the anti-amyloid antibodies for that. I think the same kind of [cross-talk] --

Donna Sullivan: [Cross-talk] I think you could just leave -- you could, um, [cross-talk]. If I have got Aduhelm as off the market, just because it is listed here doesn't mean that it is on the PDL. I mean we can officially make it not covered on the posted PDL, but you could put all available drugs listed on slide XYZ because that would [cross-talk] --

Kavita Chawla: [Cross-talk] I think, Donna, Kavita here. I think the concern is also what Leqembi that the evidence is not compelling to even include in on the PDL.

Donna Sullivan: Well, we have to cover it. This is Donna. So we have to cover it. So we can either -- you know, it is on prior authorization, and so we have listed it as a covered drug. It can be non-preferred rather than preferred. It makes no difference, really, in how it's treated, but we do have to cover it, so that is why we list it on the PDL.

Peter Barkett: Yeah. So my understanding is that the PDL is really about, essentially step therapy, right? And regardless of whether Leqembi gets listed as a preferred drug, it's still going to have prior authorization criteria for medical necessity review.

Donna Sullivan: Right.

Peter Barkett: So until we have, like, more than two agents in this class, which we may eventually have, the PDL is kind of a moot point. But I agree it feels uncomfortable saying that it's safe and efficacious. [Cross-talk]--

Zoe Taylor: Can we say, like, the jury is still out on that class, in general, like, instead of putting it in the safe and efficacious bucket. Can we say, like, the Committee has decided that there, like, isn't sufficient evidence to, like, make a decision about [cross-talk] to the --

Donna Sullivan Typically, [cross-talk] if you are going to say anything, I would say nothing about them rather than say that they are unsafe or an efficacious when they are an FDA-approved drug, Because then you are going against what the FDA

has said, and we generally recommend that you don't make those types of statements.

Peter Barkett: Yeah. I can get -- well, yeah. And the Advisory Committee, when it came to Aduhelm, like, almost unanimously said, "No, they are not safe and efficacious." And then they are FDA-approved anyway. But Aduhelm is gone now. So, Donna, I am comfortable doing kind of what you recommend and making a motion on everything other than the anti-amyloid antibodies, and just [cross-talk] be quiet on the anti-amyloid antibodies, and they will continue to get treated the way they are now not being on the PDL and having medical necessity review.

Peter Barkett: Right. Can I just give everyone food for thought? I know all the concerns I think are very valid about the Efficacy and the Safety with the deaths, but, I mean, consider the disease state, and you know we don't make those kind of statements for, like, oncology agents, right? Some of them have very poor data -- uh, are, like, incomplete data on their Efficacy and, like, high risks with side effects [cross-talk] as acutely for this drug but, you know, definitely, obviously, dementia is clear -- we all clearly know the outcomes there, so I'm just thinking we should [cross-talk] kind of get to that too.

Zoe Taylor: Yeah, that's fair.

Kavita Chawla: Marissa, can you get the motion up again? I think that will also help us think about the wording there and see if Slide 4? And so, basically, I think the point was from Slide 4, do we just remove anti-amyloid antibodies as a drug class? And then we are not commenting on it. Does the Committee agree with that on Slide 4, removing the anti-amyloid drugs? Yes? No? Maybe? I see one head nodding.

Peter Barkett: Yeah. Yeah, I would pull the entire amyloid antibodies and just put in all the others.

Laura Beste: I agree.

Kavita Chawla: Okay. Okay. Any opposed to that? Any want to leave it on? Okay. So then let's go to the motion.

Peter Barkett: This is Peter Barkett. I can make the motion. I move that all products in the drug class listed on Slide 4 are considered safe and efficacious for their

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

Jon MacKay: This is Jon MacKay. I second.

Kavita Chawla: All right. All in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstained? Okay. And with that the motion carries. So I think we are on schedule, and this is very well earned at this point. A break would be tidy for 10 minutes [cross-talk], and then we'll see maybe Marissa and team, you can look at the rest of the agenda and see what all we can get through by 4:00.

Marissa Tabile: This is Marissa. Yeah, that sounds good.

Nonye Connor: [Cross-talk] You guys want to be -- sorry, go ahead. Go ahead.

Kavita Chawla: Yeah, that is what I was going to say. We'll see you back at 3:12.

Nonye Connor: Okay.

Kavita Chawla: Thank you.

Nonye Connor: Thank you.

[break]

Kavita Chawla: All right. Let's have our Board members come back on camera, please. Wonderful. All right, we have quorum. Next, is the -- oh, Marissa, any updates on the topics, or shall we just move forward with the Atopic Dermatitis Agents?

Marissa Tabile: This is Marissa. Yeah. So, Kavita, I think we'll just move forward and see how far we get. We may just only be able to [audio cuts out] --

Kavita Chawla: Oh, you cut out for me, but okay. What I heard was we move forward. So go ahead, Umang. We'll get started with the Atopic Agents.

Umang Patel: Perfect, no problem. I did want to clarify Dr. Chawla, on the slides I have Cytokine and CAM Antagonists, and that will encapsulate both Cytokine and CAM Antagonists and Atopic Dermatitis : JAK Inhibitors. So this will be an overarch of all Cytokine and CAM Antagonists, so [cross-talk] we'll be --

Kavita Chawla: [Cross-talk] Sounds perfect.

Umang Patel: It will be a bit so, everyone, I hope you have some coffee. Okay. As you can imagine, everyone on the Committee, this has a lot of disease states within it because these are disease-modifying agents in here. I did my best to kind of give us backgrounds for the relevant disease states that hit the drug updates in this class. So moving right along, a very, very overview here. Cytokine and cell adhesion molecules (CAMs) are chemical mediators involved in the inflammatory process throughout the body. Cytokines are small proteins secreted in response to an immune stimulus for the purpose of mediating and regulating immunity, inflammation, and hematopoiesis. The actions of the individual cytokines are widely varied, and they contribute to fibrosis, tissue degeneration associated with chronic inflammation, primarily by inducing the proliferation of fibroblasts and collagenase. The pro-inflammatory cytokines, TNFs, IL-1s are involved in tissue destruction in many chronic inflammatory diseases affecting various organs. So cell adhesion molecules are CAMs. They are cell surface proteins involved in the binding of cells, usually leukocytes to each other, endothelial cells, or the extracellular matrix. Specific signals produced in response to wounds and infection control the expression and activation of these molecules. Most of the CAMs categorized fall into the three general families of proteins. We have the immunoglobulin, the integrin family, and the selectin family. And the different CAMs here have been implicated in the inflammatory, fibrotic, and autoimmune diseases. For the Committee, I know on some of these backgrounds there is a lot of information. I have tried to just kind of highlight the key points here. Moving right along to disease background. First, we have hidradenitis suppurativa. It is a chronic condition that affects the terminal follicular epithelium in the apocrine gland-bearing skin, such as the armpits and the perianal area. It typically occurs in adolescents, generally after puberty, and adults. It is generally diagnosed clinically and affects approximately 1% to 2% of the population in the US. Select signs and

symptoms include erythema, raised bumps and lesions, painful lesions, and local arthritis and arthralgia. In addition to non-pharmacological treatments, pharmacological treatments include anti-inflammatories, antibiotics, anti-androgens, and biologics such as infliximab. Surgery may also be considered in some patients. Again, the guideline for this is very old. It's almost a decade old, so it's here for your referral. But the European dermatology forum does have a recommendation that is about nine years old now here. Next, we have uveitis. So this is a noninfectious, intermediate and posterior uveitis is the inflammation of the intermediate and posterior uvea, while panuveitis is the inflammation of the anterior chamber, vitreous humor, and the choroid or retina simultaneously. Together, these represent the most severe and highly recurrent form of uveitis. The incidence of all cases is approximately 25 to 52 cases per 100,000 patients per year, and anterior uveitis is the most common form. Initial treatment is typically topical corticosteroids. Adalimumab is generally reserved for patients with disease nonresponsive to initial treatment, and other treatments include systemic glucocorticoids, immunosuppressives, and intraocular implants. In terms of treatment, on the next page, we have guidelines from the ACR and Arthritis Foundation. It's about five years old now from 2019. Again, just a quick overview, they recommend select topical glucocorticoids in patients with GIA and active chronic anterior uveitis for short-term control. But for those who are unable to control symptoms with short-term therapy, they recommend systemic therapy in order to taper topical glucocorticoids. Regarding specific agents, they recommend sub-q methotrexate conditionally over oral methotrexate. However, use of a TNF antagonist with methotrexate in severe active disease and site threatening complications is conditionally recommended. Abaticept or tocilizumab as biologics and mycophenolate, leflunomide, or cyclosporin as non-biologic options are conditionally recommended in patients who have failed methotrexate and two monoclonal TNF antagonists. And for pediatric patients with spondyloarthritis, they do recommend topical glucocorticoids prior to a change in systemic therapy. And notably, the only agent approved for uveitis in this class back when these guidelines were written was adalimumab. On the next slide here we have Ankylosing Spondylitis. So axial spondyloarthritis is an inflammatory condition generally affecting the spine and can be further subdivided into ankylosing spondylitis and non-radiographic ankylosing spondylitis. The American College of Rheumatology, The Spondylitis Association of America, and The Spondyloarthritis Research and Treatment Network published a collaborative 2019 update on the treatment guidelines for ankylosing spondylitis and non-radiographic axial spondyloarthritis. In general, recommendations for both ankylosing and non-

radiographic axial are similar. TNF antagonists -- not a specific one was listed -- are recommended as first biologics over Cosentyx and Tremfya, which are then recommended over a second TNF antagonists of the first does not produce a response. All the prior mentioned agents are recommended over Xeljanz. Concurrent low-dose methotrexate with TNF antagonist is not recommended. They recommend against a strict treat the target strategy. If a patient's disease is stable, guidelines recommend against discontinuing or tapering of biologics, and sulfasalazine provides a viable option for select patients who cannot take a TNF antagonist. Next slide here, we have Recurrent Pericarditis. So acute pericarditis is the inflammation of the pericardium, and symptoms include chest pain, ECG changes, pericardial effusion, and pericardial friction rub. Typically lasts up to 6 weeks, although symptoms may recur, and recurrence may be as high as 15% to 30% in select patients with idiopathic pericarditis. In recurrent pericarditis, the symptoms returned after a symptom-free period of at least four to 6 weeks. Symptoms of recurrent pericarditis include pleuritic chest pain with fever, pericardial rub, ECG changes, new or worsening pericardial effusion, and/or elevation of markers of inflammation. Patients may feel well in between attacks, and others may have a more persistent disease course. Studies have suggested that many cases of recurrent pericarditis are caused by an autoimmune disorder, although other causes are possible, such as infection, and there are no well-established predictors of recurrence. In terms of treatment, the pharmacologic treatment of recurrent pericarditis is similar to the treatment of acute pericarditis and includes NSAIDs or aspirin plus colchicine as typical first-line agents. Steroids or combination therapy may also be considered, and other agents that may be used for treatment and late-lying therapy include rilonacept and the off-label use of anakinra, azathioprine, or immunoglobulins. And pericardiectomy may also be considered in select patients. Right. Next, we have Polymyalgia Rheumatica. So this is an inflammatory disorder characterized by pain and stiffness in the shoulders, upper arms, hips, and neck, and is worse upon waking or after rest. Flu-like symptoms, fatigue, and weight loss may also be present. Onset is typically seen after 50 years of age, and most often occurs in Caucasian and in women. The condition is associated with development of GCA in approximately 10% to 15% of patients, and treatment guidelines are lacking. The 2015 collaborative initiative strongly recommends treatment with glucocorticoids to treat PMR episodes. The addition of methotrexate may be considered, particularly in patients at high risk for relapse and/or prolonged therapy, or with comorbidities-prone, steroid-related adverse events. The panel also strongly recommends against the use of TNF-alpha inhibitors for PMR. It is

estimated that up to 29% to 45% of patients do not adequately respond to glucocorticoid therapy within three to 4 weeks, and relapses and long-term glucocorticoid dependency are common. In 2023, the FDA approved Kevzara as the first biologic treatment for treatment of adults with PMR who have an inadequate response to corticosteroids or who cannot tolerate corticosteroid taper. Next, we have Atopic Dermatitis, which is a chronic pruritic inflammatory disease of the skin resulting in combination of genetic and environmental factors, often referred to as eczema. It can affect up to 15% of children and a little over 7% of adults in the US, commonly occurs in patients affected by asthma and other allergic conditions and is associated with elevated serum Immunoglobulin E levels. It is characterized by extremely dry itchy skin on the insides of the elbow, behind the knees, and on the face, hands and feet. The American Academy of Dermatology last year had guidelines which only address topical therapies for the management of atopic dermatitis. But they state that moisturizers, topical corticosteroids, topical calcineurin inhibitors, topical PDE4 inhibitors and topical JAK inhibitors are options with strong evidence for treatment of atopic dermatitis. Systemic immunomodulating agents are indicated for patients whose atopic dermatitis is not adequately controlled by topical regimens and/or phototherapy. Like the guidelines, the American Academy of Allergy Asthma and Immunology 2012 Guidelines state first-line options include hydration, such as emollients, moisturizers, and topical corticosteroids, and they also recommend careful consideration of risks and benefits of systemic agents in patients who not respond to topical agents or phototherapy. Abrocitinib and upadacitinib were also not addressed in those guidelines. Next, we also have Ulcerative Colitis, which is a chronic inflammatory disease primarily affecting the colon and rectum. It affects approximately a million people in the US, and the incidence continues to increase worldwide. The CDC estimates the current prevalence is 249 per 100,000 adults. It may present at any age, and onset typically peaks between 15 and 30 years of age. The disease is characterized by superficial infiltration of the bowel wall by inflammatory white cells, resulting in multiple mucosal ulcerations and crypt abscesses. The predominant symptom is diarrhea, which is usually associated with blood in the stool. Additional symptoms may include pain in the lower quadrant or rectum along with systemic features including fever, malaise, and weight loss. The initial attack may be fulminant with bloody diarrhea, but the disease more commonly begins indolently with non-bloody diarrhea progressing to bloody diarrhea. It can present initially with any extent of the anatomic involvement ranging from disease confinement to the rectum to the entire large intestine defined as pan colitis. And most

commonly, ulcerative colitis follows a chronic intermittent course with long periods of quiescence interspersed with acute attacks lasting weeks to months, and a significant percentage of patients suffer a chronic continuous course. Next, we have Crohn's disease. In 2021, the American Gastroenterological Association issued a guideline on the medical management of moderate-to-severe luminal and perianal fistulizing Crohn's disease, and notable recommendations regarding agents within the class are described below. In adult outpatients with moderate-to-severe, they recommend the use of a TNF antagonist or ustekinumab over no treatment for induction and maintenance of remission, and the AGA suggests the use of the vedolizumab over no treatment for induction and maintenance of remission. In biologic treatment naive adult outpatients with moderate-to-severe, the guidelines recommend the use of infliximab, adalimumab, or ustekinumab over certolizumab and suggest the use of vedolizumab over certolizumab for the induction of remission. In adult outpatients with moderate-to-severe Crohn's, who never respond to TNF antagonists, the guidelines recommend ustekinumab and suggest vedolizumab over no treatment of the induction of remission. And if patients had previously responded to infliximab, they recommend adalimumab or ustekinumab over no treatment -- excuse me -- and suggest vedolizumab over no treatment for induction of remission. And the group also recommends the use of biologic drug monotherapy over thiopurine monotherapy for the induction of remission. In adult outpatients with moderate-to-severe Crohn's, who were treatment naive to biologics and immunomodulators, they recommended infliximab plus thiopurines over infliximab monotherapy, and adalimumab plus thiopurines over adalimumab monotherapy for induction and maintenance of remission. They do not make recommendations regarding the use of ustekinumab or vedolizumab. The AGA does suggest the early introduction of a biologic over waiting until failure of five ASA and/or corticosteroids. For those with active perianal fistula, the guidelines recommend infliximab over no treatment for the induction and maintenance of fistula remission and suggests adalimumab, ustekinumab, and vedolizumab over no treatment for the induction or maintenance of fistula remission. And risankizumab and upadacitinib were not approved for Crohn's at the time these guidelines were developed. And the role of Tysabri and other agents not in the therapeutic class are also addressed in the guidance. Now moving right along to drug-specific updates. First, we have Kevzara. Now, up until my presentation today we have pretty much had new drugs. Just to remind the Committee when there are significant clinical updates but not a new drug, I try to bold the relevant portions. So here, as

you can see Kevzara, the FDA approved for the treatment of adults with polymyalgia rheumatica, who have had an inadequate response to corticosteroids, who cannot tolerate a steroid taper, previously approved for the treatment of rheumatoid arthritis. So as you can see, it does already contain an additional Indication. No changes to Precautions or Formulations. And with this new Indication comes, of course, a new Dosing. So the recommended Dosage is 200 mg subcutaneously every 2 weeks in combination with the tapering course for the corticosteroids. And for this Indication, it can be used as monotherapy following discontinuation of the corticosteroid. Next, Cyltezo had a busy year last year. In March of last year, the FDA approved Cyltezo, which was an interchangeable Humira biosimilar for the treatment of moderate-to-severe hidradenitis suppurativa in adults. It did have other Indications such as rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, and psoriatic arthritis. In May, the FDA approved a new 40 mg/0.8 mL single-dose prefilled autoinjector pen presentation Formulation. And then in July, the FDA approved this medication to have an additional Indication for the treatment of non-infectious intermediate posterior and panuveitis in adults. Since there are significant Indications, the Dosing is stratified by Indication, age, and weight, which can be found in the TCRs or the package inserts. Again, no changes to the existing Indications, and no changes to the existing Formulations here. Next, we have Amjevita. So in March of last year, the FDA approved this medication, which is a Humira biosimilar, for the treatment of moderate-to-severe hidradenitis suppurativa in adults. In August, FDA approved the following new high-concentration presentations of 20 mg/0.2 mL, 40 mg/0.4 mL, and 80 mg/0.8 mL prefilled syringe, and 40 mg/0.4 mL, and 80 mg/0.8 mL prefilled autoinjector. Again, no changes to Precautions. And with this new Indication for hidradenitis suppurativa, the Dosing was on Day one it was 160 mg given in one day or split over two consecutive days, then day 15 is 80 mg, and then day 29 in subsequent doses 40 mg every week or 80 mg every other week. Okay. Next, we have Yusimry. In March of last year, FDA approved Yusimry, a Humira biosimilar as a single-dose 40 mg/0.8 mL prefilled autoinjector pen. Previously, it was approved as a prefilled syringe. April of last year, FDA approved a new Indication for moderate-to-severe hidradenitis suppurativa. And in September of last year they approved a new Indication for non-infectious intermediate posterior and panuveitis in adults. No changes to Precautions and Formulations. In terms of Dosing, you will see very similar, if not identical dosing amongst a lot of these medications. So I won't try to repeat it for the sake of the Committee's sanity, but it's essentially the same

dosing in terms for hidradenitis, it is the same dosing as Amjevita in the previous slide. And for uveitis, it was 80 mg initial dose, followed by 40 mg every week or 80 mg every other week starting 1 week after the initial dose. Next, we have Hyrimoz. March of last year, FDA approved Hyrimoz as a high-concentration Formulation in the following presentations: 10 mg/0.1 mL and 20 mg/0.2 mL prefilled syringe, and 40 mg/0.4 mL and 80 mg/0.8 mL prefilled syringe and autoinjector. In April of last year it received a new Indication for moderate-to-severe hidradenitis suppurativa in adults, and in September of last year it was approved for noninfectious intermediate posterior and panuveitis in adults. No changes to Precautions here. Aside from the Formulation changes in March, there are no other changes. And as you can see, the Dosing is identical from its predecessors on this slide deck for hidradenitis and uveitis. Next, we have Yuflyma. May of last year FDA approved this medication, which is a biosimilar to Humira. It contains Indications for rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, plaque psoriasis, and hidradenitis suppurativa. It contains the same Precautions and Blackbox Warnings for serious infections and malignancy. Dosing is stratified by Indication. And the Formulation, you have a single-dose prefilled autoinjector and single-dose prefilled syringe with a safety guard, and [audio cuts out] a single-dose prefilled syringe without a safety guard. Okay. Next, we have Rinvoq. May of last year FDA approved for adults with moderate-to-severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers. It already contains approved Indications for a litany of other disease states here. No changes to any of its Warnings or Blackbox Warnings there. For this new disease Dosing, the recommended induction dosage is 45 mg once daily for 12 weeks. The recommended maintenance is 15 mg once daily, and a maintenance of 30 mg once daily may be considered for patients with refractory, severe, or extensive disease. And no changes to Formulations. Next, we have Hadlima. In June of last year, FDA approved for the treatment of moderate-to-severe hidradenitis suppurativa, and then in July they approved it for noninfectious intermediate posterior and panuveitis. No changes to Precautions. Identical Dosing to some of the previous medications mentioned so far, and no changes to the Formulation. All righty. In July of last year, there were some new biosimilars to hit the market. Several Humira biosimilars launched per manufacturer press releases. These commercially available biosimilars include Cyltezo, Hadlima, Hulio, Hyrimoz, Idacio, Yuflyma, and Yusimry. All products are available as low-concentration Formulations, except for Hyrimoz and Yuflyma. Hadlima, Hyrimoz, and Yuflyma are available as high-

concentration Formulations. And citrate-free Formulations include Cyltezo, Hadlima, Hulio, Hyrimoz, Idacio, Yuflyma, and Yusimry. Cyltezo is interchangeable with Humira. Next, we have Ilaris. In September of last year, FDA approved for gout flares in adults in whom NSAIDs and colchicine are contraindicated and not tolerated or do not provide an adequate response, and in whom repeated courses of corticosteroids are not appropriate. No changes to any of the Precautions. For this Dosing for gout flares, it is recommended for 150 mg sub-q. In patients who require retreatment, there should be an interval of at least 12 weeks before a new dose of Ilaris is administered. And the Formulation is 150 mg/mL solution in a single-dose vial. All righty. And I apologize to the Committee. I am going to try to pick up my cadence just to be respectful of your time and hope to finish all of this in time. Next, we have Hulio. September of last year FDA approved for the treatment of noninfectious intermediate posterior and panuveitis in adults. As you can tell, identical Dosing. No changes to Precautions or Formulations here. Then we have Entyvio. September of last year, FDA approved a single-dose prefilled syringe and a single-dose prefilled syringe in the strength of 108 mg/0.68 mL for subcutaneous self injection for ulcerative colitis. Previously, it was only available for IV injection. The IV route of administration is indicated for ulcerative colitis and Crohn's disease. After the first two IV doses at week 0 and week 2, vedolizumab may be switched to the sub-q injection at week 6. Beginning at week 6 and thereafter, the dose is 108 mg subcutaneously once every 2 weeks, and therapy should be discontinued in patients who do not show evidence of therapeutic benefit by week 14. For patients in clinical response or remission beyond week 6, vedolizumab can be switched from IV infusion to sub-q injection by administering the first sub-q dose in place of the next scheduled IV infusion and every 2 weeks thereafter. Since this is just a new route of administration, allowing a transition from one to the other. Again, no changes to the Precautions or Indications, just a new Formulation, as I mentioned. Next, we have Abrilada. June of last year received an approval for hidradenitis, August received an approval for noninfectious intermediate posterior and panuveitis, and October, it was designated by the FDA as an interchangeable biosimilar to the corresponding presentations of Humira 10 mg/0.2 mL, 20 mg/0.4 mL in prefilled syringe, 40 mg/0.8 mL prefilled glass syringe, prefilled pen and glass vial for sub-q use, and the interchangeable designation applies to all Indications: rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, psoriatic arthritis, hidradenitis suppurativa, and uveitis. Dosing is identical as we've seen for hidradenitis and uveitis here.

And no changes to Formulations. Next, we have Tofidence. October of last year FDA approved this medication as the first biosimilar to Actemra. It is an IL-6 receptor antagonist, indicated for certain adults with rheumatoid arthritis and patients two years of age or older with polyarticular juvenile idiopathic arthritis and systemic JIA. In terms of Precautions, it carries the same Blackbox Warnings as Tofidence. The Dosing is stratified by the different types of arthritis, and it is based on their weight as well. As you can see, it is stratified here. For the Formulations, it's an IV infusion injection in various concentration forms in a single-dose vial for further dilution prior to IV infusion. Then we have Enbrel. October of last year FDA approved -- my apologies, it should be Wezlana. This is a typo here. -- as an interchangeable biosimilar to Stelara. It does carry the Indication here for juvenile psoriatic arthritis two years of age or older, and it has the 0.8 mg/kg weekly with a maximum of 50 mg/ week Dose. Next slide we have been Bimzelx. FDA approved Bimzelx, a humanized interleukin-17A and F antagonist indicated for the treatment of moderate-to-severe psoriatic arthritis in adults who are candidates for systemic therapy or phototherapy. The Precautions: infections and tuberculosis, specifically patients who have active TB. The dosing here 320 mg sub-q at week 0, 4, 8, 12, and 16, and once then once we get to there, it is every 8 weeks thereafter. And for patients weighing over 120 kg, consider a dose of 320 mg every 4 weeks after week 16. And the Formulation is 160 mg/mL in a single-dose prefilled syringe. Next, we have Zymfentra. October of last year FDA approved a sub-q Formulation under the brand name Zymfentra for the maintenance treatment of adults with moderate-to-severe active ulcerative colitis or Crohn's following treatment with an IV-administered infliximab product. Maintenance treatment with Zymfentra 120 mg subcutaneous once every 2 weeks may begin at or after week 10 of IV infliximab therapy. Zymfentra is the only infliximab product that is given via subcutaneous injection and can be administered by the patient or caregiver. This carries the same Blackbox Warnings as all of infliximab. In terms of Dosing, as I mentioned earlier, it is 120 mg subcutaneous every 2 weeks but must started after week 10. In terms of Formulation, it is subcutaneous 120 mg/mL in a single-dose prefilled syringe, prefilled pain, and prefilled syringe with a needle guard. No. Marissa, I'm so sorry. Can you go back two slides where it said Enbrel? I had a typo earlier, and I misspoke for this. Emeril received an expanded Indication for juvenile psoriatic arthritis of two years of age or older. No additional changes, just please ignore line two where it says October 2023. Going back to now, we are at Wezlana. In November of 2023, FDA approved this medication as an interchangeable biosimilar to Stelara. Now, it has Indications for adult patients. It's moderate-to-severe

plaque psoriasis for candidates for phototherapy or systemic therapy, active psoriatic arthritis, moderate-to-severe active [audio cuts out] Crohn's disease, and moderate-to-severe active ulcerative colitis. For pediatric patients defined as six years of age or older, moderate-to-severe plaque psoriasis for candidates for phototherapy or systemic therapy and active psoriatic arthritis. It does carry Precautions for infections. Dosing is stratified by Indication, age, and weight, and the Formulation is a sub-q and an IV infusion. So the sub-q is 45 mg/0.5 mL or 90 mg/mL in a single-dose prefilled syringe, or 45 mg/0.5 mL solution a single-dose vial. For IV infusion, it's 130 mg/26 mL solution in a single-dose vial. Next, we have Idacio. October of last year, FDA approved for the treatment of moderate-to-severe hidradenitis. In November, it received a, approval for non-infectious intermediate posterior and panuveitis. And then January of this year, a new Formulation for 40 mg/0.8 mL single-dose vial kit for institutional use only. For those two new Indications the Dosing is identical hidradenitis and uveitis, as you can see here. Then we have Cosentyx. October of last year, FDA approved first IV Formulation IL-17A antagonist for the treatment of adults with active psoriatic arthritis, active ankylosing spondylitis, and active non-radiographic axial spondyloarthritis with objective signs of inflammation. And in November FDA approved for the treatment of moderate-to-severe hidradenitis suppurativa. As you can see, the Dosing is identical and just the IV infusion update there. Next, we have Orencia. November of last year FDA expanded the subcutaneous use of Orencia for the treatment of active psoriatic arthritis to include patients two years of age or older. No additional changes there. For that, it is still weight-based, so you stratify the dose based on the patient's weight. Then we have Simandi. We made it to 2024. March of this year, FDA approved Simlandi, a high concentration, interchangeable biosimilar to Humira. It carries the same Indications for rheumatoid arthritis, JIA, psoriatic arthritis, ankylosing spondylitis, Crohn's, UC, plaque psoriasis, hidradenitis, and uveitis. Same Warnings, Blackbox Warnings. Dosing is stratified by Indication, weight, and age, and the Formulation a 40 mg/0.4 mL single-dose autoinjector. Then we have Tyenne. In March -- last month, FDA approved Tyenne, a biosimilar to Actemra. It's approved for the following Indications: Adults with moderate-to-severe active rheumatoid arthritis who have had an inadequate response to one or more DMARD, adults with giant cell arteritis, polyarticular JIA in patients two years of age or older, systemic JIA in patients two years of age or older. In terms of Precautions, Blackbox Warning for serious infections, and to monitor signs and symptoms of hepatic injury and hepatotoxicity in patients. Dosing is stratified by Indication, weight, and age. Formulations include IV infusion injections and

subcutaneous injections. And lastly, we have Skyrizi. March of this year, Skyrizi was approved as a 90 mg/mL single-dose prefilled syringe to allow for a sub-q self-administration of maintenance dosage of treatment of moderate-to-severe active Crohn's disease in adults. The patients must be trained on a subcutaneous technique before self-injecting. And for this, the Dosing, as you can see, is 600 mg IV over at least 1 hour at week 0, 4, and 8, and then the recommended maintenance dose is 180 mg or 360 mg sub-q at week 12, and every 8 weeks thereafter. And I will pause there for the Committee while I drink a little water.

Kavita Chawla: That's marathon talk there, Umang. Well done. Questions from the Board for Umang? While the Committee is getting their thoughts together, Marissa, if we could have a look at the drug list -- the PDL list.

Marissa Tabile: Okay. This is Marissa. So this is a pretty easy class as far as preferred products. I will make a note that the Cibinqo is in its own separate class just because of the way that I believe it came to market. It was before I think some of these other products got FDA approval for atopic dermatitis. So that is really the reason why this lives in its own Atopic Dermatitis - JAK Inhibitors class. So for that reason it is preferred. There is PA on that product. There is PA on pretty much all of these products. For the Cytokine and CAMs, like I said, it is very straightforward. The only preferred product that we have in that class are preferred products I should say are brand name, Humira, and brand name, Enbrel, for those. Those are really our only two preferred products. We do have the different -- I apologize for all of the scrolling -- the different Formulations for this. The only one for Enbrel that is not preferred is the Mini, but the SureClick the syringe those are preferred. And then same thing for Humira. We have pretty much all the different Formulations of Humira preferred. There is one product I do want to call out that is preferred, but it is nuanced, and it is Spevigo. So that product we do have that preferred just because of its really specialized Indication. The Indication does slip me at this moment, but it doesn't -- it's not very similar as far as the other products that the cytokines and CAMs of the world treat, so that is why we have that one preferred because the Indication for that one is very specific. So currently, the policy that all of these live in it wasn't really appropriate, but it is still considered a cytokine and CAM, nonetheless. But just wanted to call that to your attention. And then for this one, the Simlandi, I am not sure why this is kind of separated, but it is a Cytokine and CAM Antagonist. I think this might just be some semi colon spacing maybe that got it kind of off of the other classes, but that is nonpreferred. But I do also want to call out the

adalimumab or the Humira biosimilars. We do make those nonpreferred as they do come out to the market. We do treat them like any new drug that has come out just because, right now, we are still preferring the brand name, Humira and the brand name, Enbrel, which doesn't have any biosimilar yet. But I can take any questions the Board might have regarding these agents.

Zoe Taylor: The Wezlava, is that out yet? Or was it just, like, approved, but it's not actually out yet?

Marissa Tabile: This is Marissa. So it may not be showing up. I don't see it here on our files, so it just hasn't come out yet as far as our drug database that we get approved drugs from yet.

Zoe Taylor: The Stelara is the one that I feel like I have had the most trouble with, like, even with Rheumatology writing multiple letters with inability to get it approved without trying Humira first, which I don't know the details, but Rheumatology has told me they don't think that, like, makes sense, like, science-wise. So I guess I am just really excited about the potential ability for patients to get Stelara with a biosimilar. So that's just my perspective on the ground, I guess.

Marissa Tabile: This is Marissa. Yeah, thank you so much for sharing that.

Kavita Chawla: Thank you, Zoey.

Jon MacKay: Marissa, this is Jon MacKay. Are there any JAK kinase inhibitors that are preferred at all?

Marissa Tabile: This is Marissa. Uh, no. I don't believe we have any of the JAK inhibitors preferred. Do you want me to stop at a particular -- the names of all of them escape me, [laugh] but I know that we don't have any of them preferred from what I can recall besides this Cibinqo, but that was just a caveat type of drug. I will disclaim that we are in the process of revamping our Cytokine and CAM Antagonist policy, so you will probably see that policy -- it's actually getting broken out. We are planning on breaking them out by their mechanisms of action. So right now, currently, the way that those policies are written, they are really all housed in one policy with all of the products listed. So we are working on currently breaking them out by them by their mechanism of action. You will see that policy be presented or policies, I should say, presented later this year, so that is more to come. And then we

are considering at the same time whether or not we do want to reclassify some of these drugs as far as use of their mechanisms of action, but we are still having some internal discussion on that. But this class in particular is getting very big, and there is a lot of overlap as far as the Indications, so management of it can be a little bit tricky we are coming to find.

Kevin Flynn: For all the, like, at -- I mean, you have biosimilars. Is it [cross-talk] can we just -- have you just not made any of them preferred because you are waiting on rebate negotiations compared to the brand.

Marissa Tabile: This is Marissa. Yeah, that is correct, Kevin. Right now, -- the way that we are getting -- seeing the prices for them come out, it's still just more effective or better for us to prefer the brand at this time. We are monitoring it closely to see when it is a good time that it may -- we may want to switch over to the biosimilars, but right now where we are, it's not really beneficial for us right now.

Kavita Chawla: I do know we have two stakeholders listed who had signed up to speak, so while the Committee is mulling this over, let's maybe bring them on. So I see Erin Nowak from AbbVie. Are you online? And if you are, you can unmute yourself.

Nonye Connor: I do not see Erin, but I do see Melinda here.

Kavita Chawla: Okay, great. Melinda Turkington?

Nonye Connor: Melinda, you can unmute yourself.

Melinda Turkington: Good afternoon. Can you hear me?

Kavita Chawla: Yes, we can. Go ahead.

Melinda Turkington: Wonderful. So I did fill out the form in advance on which I noted that I am not a patient or a provider. I am an employee of UCD, the manufacturer of Bimzelx. My name is Dr. Melinda Turkington, and I am a Medical Outcomes Liaison with UCD. Bimzelx or bimekizumab is the first and only FDA-approved humanized interleukin IL-17A plus F antagonist. So not only an IL-17A inhibitor but both A and F, which is a unique mechanism of action. It's indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. He went through

the dosing, but it is available as a prefilled syringe and an autoinjector for self-injection or administration by a healthcare provider. It is dosed as two syringes for a total of 320 mg every 4 weeks for 16 weeks, with that option to switch to every 8 weeks for patients weighing less than 120 kg. There were three multicenter randomized double-blind studies, which enrolled a total of 1480 subjects, which were reviewed early this morning, 18 years of age and older, with moderate-to-severe plaque psoriasis. At week 16, 85% to 91% of patients showed a PASI 90, and 84% to 93% achieved an IGA Global Score of 0 to 1. Additionally, between 59% and 68% of patients achieved a PASI 100 or completely clear skin. As it was noted in the psoriasis class review this morning, there are three head-to-head comparison trials demonstrating superiority to adalimumab, ustekinumab, and secukinumab. Bimzelx most common adverse reactions greater than 1% are upper respiratory infections, oral candidiasis, headache, injection site reactions, tinea infections, gastroenteritis, herpes simplex infections, acne, folliculitis, and other candida infections. It may increase the risk of suicidal ideation and behavior, but no causal association has been made, and it may increase the risk of infections which I already touched on. Test liver enzymes, alkaline phosphatase, and bilirubin at baseline periodically during the treatment with Bimzelx. And according to routine patient management, cases of IBD have been reported in patients with IL-17 inhibitors. And then, of course, please refer to the Prescribing Information for full Safety and Efficacy profile, or please feel free to ask me any questions as well. Thank you so much for your time and consideration of Bimzelx and our request for Bimzelx to be considered for a first-line treatment for patients suffering from moderate-to-severe plaque psoriasis. And, again, thank you for your time.

Kavita Chawla: Thank you, Melinda. Any questions for Dr. Turkington from the Board? And do you see Erin, Nonye?

Nonye Connor: No, I do not see Erin. Is Erin on the call? If you are, please raise your hand.

Kavita Chawla: And if there are any other stakeholders who would like to speak, now would be the time. Please raise your hand. No?

Nonye Connor: Nope. No one else.

Kavita Chawla: Okay. Okay. So I suppose with that, if Marissa could pull up the motion for the Board to review.

Marissa Tabile: This is Marissa. Yeah, so DUR Board, you will be making two different motions today, just because that one product lives in that one class, and then all the other cytokine and CAMs are together. So just wanted to give you all that heads up on that.

Kevin Flynn: I can make this one since it's alone. I move that all products in the Atopic Dermatitis Agents : Janus Kinase (JAK) Inhibitor - Oral 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.

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

Kavita Chawla: All those in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstained? Okay, with that the motion carries. And then the next one on CAM Antagonists.

Jon MacKay: This is Jon MacKay. I can move on. I move that all products in the Cytokine and CAM Antagonist 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 trials 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.

Kavita Chawla: All those in favor, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstained? Okay. With that the motion carries. And we are right at 4:01. Great job, Board. We covered a lot today. Nonye, Marissa, unless there is anything else, do we adjourn for today?

Nonye Connor: Yes, you can. You guys can adjourn for today. Thank you, guys, so much. I don't think there is anything. What about you, Marissa? Anything on your end?

Marissa Tabile: This is Marissa. No. We have everything that we need. So [cross-talk] thank you so much, DUR Board.

Nonye Connor: Thank you so much. [Cross-talk] --

Multiple Speakers: [Cross-talk] --

Christy Weiland: Thank you, all.

Laura Beste: Thank you.

Zoe Taylor: Thank you.

Kevin Flynn: Thank you.

Greg Hudson: Thank you.

Michael Corsilles: Thank you.

Peter Barkett: Thank you [cross-talk] --

Donna Sullivan: Thank you.

Laura Beste: Have a great day.

Kavita Chawla: Mm-hmm. Bye.

Laura Beste: Bye.

Zoe Taylor: Bye.

[end of audio]