Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
Meeting Transcription
February 28, 2024

Nonye Connor: I think we are ready, Kavita.

Kavita Chawla: All right, great. Good morning, everyone. We will now convene the P&T Committee Meeting on February 28, 2024. I am Kavita Chawla, the Chair of the P&T Committee. I will read off the names of our participating attendees. Please say "here" when I call your name. Peter Barkett.

Peter Barkett: Here.

Kavita Chawla: Laura Beste.

Laura Beste: Here.

Kavita Chawla: Michael Corsilles. Oh, he is absent today. Sorry. Dimitry Davydow.

Donna Sullivan: Dimitry is no longer able to [cross-talk] ---

Leta Evaskus: Well, hang on. He's actually going to attend this meeting. This is supposed to be [cross-talk] --

Donna Sullivan: [Cross-talk] Oh, okay.

Leta Evaskus: -- his last.

Donna Sullivan: Okay.

Leta Evaskus: It looks like he is just not on [cross-talk] --

Nonye Connor: [Cross-talk] Oh, there he is. [Cross-talk] --

Kavita Chawla: Oh, I will give him a second, and I will get to Kevin Flynn.

Kevin Flynn: Here.

Kavita Chawla: Hi, good morning.

Kevin Flynn: Hi.

Kavita Chawla: Christy Weiland.

Christy Weiland: Good morning, here.

Kavita Chawla: Good morning. Our two new members, Zoe Taylor.

Zoe Taylor: Hello.

Kavita Chawla: Hello. And Gregory Hudson.

Greg Hudson: Hello. Good to meet you all.

Kavita Chawla: Good to meet you. Do you prefer going by Greg?

Greg Hudson: Greg is fine. That is fine.

Kavita Chawla: Greg. Okay. And coming back to Dimitry Davydow.

Dimitry Davydow: Good morning.

Kavita Chawla: Good morning. All right, our Health Care Authority members.

Leta Evaskus: Kavita, can I stop you just a second? Could the new P&T members maybe just do a short introduction?

Kavita Chawla: All right. Yeah.

Zoe Taylor: Sure. I can go first. I am Dr. Zoe Taylor. I am a family doctor. I was previously at UW, and now I am at the Lummi Tribal Health Center in Bellingham on the Lummi Reservation.

Kavita Chawla: Welcome.

Greg Hudson: And I am Greg Hudson. I am a psychiatric nurse practitioner and DNP, and I am currently at Community Healthcare in Tacoma, Washington, acting as their psychiatric consultant in primary care.

Kavita Chawla: Thanks, and welcome. Is that good, Leta? Yeah? All right. Our Health Care Authority members, starting with Nonye Connor.

Nonye Connor: Hello.

Kavita Chawla: Hi. Good morning. Luke Dearden.

Luke Dearden: Good morning.

Kavita Chawla: Good morning. Leta Evaskus.

Leta Evaskus: Here.

Kavita Chawla: Amy Irwin.

Nonye Connor: She is not here today.

Kavita Chawla: Okay. Ryan Pistoresi.

Ryan Pistoresi: Hey, good morning.

Kavita Chawla: Morning. Donna Sullivan.

Donna Sullivan: Hey, good morning.

Kavita Chawla: Morning. Marissa Tabile.

Marissa Tabile: Here.

Kavita Chawla: Hi. Ryan Taketomo.

Ryan Taketomo: Morning, I am here.

Kavita Chawla: Morning. Joey Zarate.

Joey Zarate: Good morning.

Kavita Chawla: Good morning. Our L&I member, Jaymie Mai.

Jaymie Mai: Here.

Kavita Chawla: Hello. Our DERP presenters, Shannon Robalino may not be on yet. Andrea Vintro.

Leta Evaskus: They might be coming on closer to their presentation time.

Kavita Chawla: Okay. Our Magellan presenter, Umang Patel.

Umang Patel: Hi. Good morning, everyone.

Kavita Chawla: Morning. And I am going to list our Managed Care Representatives. We have got Greg Simas from Molina Healthcare, Heidi Goodrich - Molina Healthcare, Petra Eichelsdoerfer - United Healthcare, Omar Daoud - Community Health Plan of Washington, and Jeffrey Natividad from Community Health Plan of Washington. And now, Nonye will go over our meeting logistics.

Nonye Connor: Hello. This is Nonye. The P&T DUR Board Meeting logistics is as follows: 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 when presenting. Committee, please share your webcams during discussions and motion considerations. For stakeholder participation, the share will list the list -- sorry, the shareholder will read the list of stakeholder names who have pre-registered to speak. We will unmute you. After the share, we will ask if there are any other stakeholders. If there are, please raise your hand and we will 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 did not fill out a stakeholder conflict of interest form, please answer the questions as we post them on the screen. Your three minutes will start after your questions -- I am sorry, after you have answered the questions. And lastly, this meeting is being recorded, so please state your name every time you speak. Thank you.

Kavita Chawla: Thank you, Nonye. So with that, I will go to Donna Sullivan to give us a [cross-talk] --

Leta Evaskus: [Cross-talk] Actually, Kavita, I have one announcement.

Kavita Chawla: Okay.

Leta Evaskus: Sorry. [Cross-talk] --

Kavita Chawla: [Cross-talk] Please, jump in.

Leta Evaskus: [Cross-talk] This is Leta. So this is Dimitry Davydow's last meeting. He has taken a position out of state, so, unfortunately, he's ending his term early. But Dimitry, I want to thank you for all the contributions that you have made to the Committee over the last year.

Dimitry Davydow: Thank you very much, and it has been a privilege to serve on the Committee, and I appreciate having the experience.

Leta Evaskus: Great. Thank you.

Kavita Chawla: Thank you, Dimitry. All right, Donna, you are up next.

Donna Sullivan: Nonye, are you bringing up the slides? Okay. Are you going to go into presentation mode?

Nonye Connor: Sorry, I am talking while I am muted. Can you guys see the slide?

Donna Sullivan: I can, but are you going to put it into presentation mode?

Nonye Connor: Yeah, it is on presentation mode.

Donna Sullivan: It should not have the slides on the side.

Ryan Pistoresi: Yeah, it is not on our screen.

Leta Evaskus: Yeah. [Cross-talk] --

Donna Sullivan: Okay.

Ryan Pistoresi: You might be displaying the wrong screen then.

Nonye Connor: Okay. Let me do that again. Thank you. Let's see here.

Donna Sullivan: There we go. And then just start up at the first slide [laughter].

Nonye Connor: Going too far.

Donna Sullivan: Yeah.

Nonye Connor: There we go.

Donna Sullivan: Okay. Thank you.

Nonye Connor: Thank you.

Donna Sullivan: So, good morning, everybody. I am Donna Sullivan. I am the Chief Pharmacy Officer with the Washington Health Care Authority. And so I am just going to give an overview of the P&T Committee and the DUR Board process, some of the rules that we have to follow, and the origin of both of the Preferred Drug Lists that we are going to be talking about. We do this every year. Feel free to interrupt me if you have any questions. And at the end of the presentation, there are a bunch of acronyms. The state loves our acronyms, so we try to give you a data dictionary, so you can speak our language. So go ahead and go to the next slide, Nonye. Rules and responsibilities. I already introduced myself. We also have Ryan Pistoresi. He is our Assistant Chief Pharmacy Officer. He primarily manages our PEBB and SEBB Program around Policy and Benefit Design, as well as Luke Dearden, who also assists Ryan in that particular program. Ryan helps oversee with the Clinical Policy Development alongside of Marissa, who I will introduce in a minute, and then he is also our representative on the Drug Effectiveness Review Project. He is currently a former member of the Governance Board and now just participates as an attending state. We have Leta Evaskus, who is the ArrayRX Operations Manager. For those of you that might not be familiar with ArrayRX, it is the Prescription Drug Consortium that was created under Legislation, formerly known as the Northwest Prescription Drug Consortium. We have rebranded, and now we are ArrayRX. So Leta manages the P&T Committee contracts, which I believe are being transferred over to Nonye as we transition roles. She also manages the Washington Preferred Drug List for us, and she oversees the cost analysis process that we do for the Washington PDL. Nonye Connor is our Pharmacy Program Project Manager. She is taking over managing and coordinating the P&T Committee Meeting logistics. She also does a lot of project management of all things pharmacy related to HCA for us. Next slide. Amy Irwin is our Medicaid Pharmacy Operations Manager. She manages the team that runs our prior authorization clinical processes. So the operations side of the clinical policies that you guys are creating, her team is the one that implements them. We also implement the preferred and non-

preferred status and all of the credits on our prescription drugs that we fill it through our claims processing system. We have Marissa Tabile, who is a Clinical Pharmacist, and she manages the Apple Health PDL. She coordinates the agendas for all of the meetings that we have. She tracks and ensures which clinical policies that we are going to be working on for each meeting, and then when those are going to be updated and reviewed. Luke Dearden is also a Clinical Pharmacist who works with Ryan primarily on the SEBB and PEBB Program, but he does support us with assistance in helping clinical policies. Ryan Taketomo, another Clinical Pharmacist, he's our strategy and pipeline pharmacist, really looking at drugs that are coming to market and trying to figure out what we are going to do with some of these high cost drugs, primarily. Ryan also helps with the Clinical Policy Development alongside Luke and Marissa. And then Joey Zarate is our Apple Health PDL Coordinator. So he's looking at every week we get new NDCs, or new drugs come to market, and so Joe is coordinating the decision making process alongside Marissa with how those drugs are going to be positioned on the PDL, whether they require PA and all of that until they come to this group for review. So go ahead to the next slide. We also have other stakeholders or other state agencies, so Department of Labor and Industries also uses the Washington PDL. Jaymie Mai is the Pharmacy Director for Labor and Industries. Doug Tumen is a Pharmacist for the Prescription Drug Program. And then Christy Pham, also a pharmacist with the Labor and Industries is working on the PDL changes that they participate in. The next slide. Okay, so the history. June 2003, our Legislature passed a bill that established the P&T Committee and directed the Health Care Authority to create an evidence-based Prescription Drug Program, and from that we have created the Washington Preferred Drug List. The drug list is a coordinated effort between the Health Care Authority, our Uniform Medical Plan, which are our state-funded state employees, our Medicaid fee-for-service program, as well as our Labor and Industries Workers' Compensation Program. The Washington PDL has about 35 drug classes, so it is a subset of each program's overall formulary. Apple Health, we don't actually follow the Washington PDL itself anymore, but we do follow the recommendations and guidance that the P&T Committee provides for those particular drug classes that are on the Washington PDL. And the goal of the of this program as it was established was to develop the statewide evidence-based program where we are looking at drugs that are effective, looking at the safety and efficacy, and then trying to select drugs that meet the criteria of the P&T Committee's recommendations and reducing the cost to the state without reducing the quality of care. The next slide. So there are different components within the

WPDP, the Washington Prescription Drug Program. It is the P&T Committee. We have the Washington Preferred Drug List. There was an Endorsing Practitioner of Therapeutic Interchange Program that was established. We have ArrayRX, which is the Prescription Drug Purchasing Consortium, and then we have our Apple Health Pharmacy Policy Department or Program, where we are looking at clinical policies for the Apple Health Medicaid program. Next slide. The P&T Committee has 10 members on it. Membership is based on the federal requirements for the Medicaid DUR Board, and that is it can't be more than 51% pharmacist or 51% physicians. And so in order to meet those requirements we landed on a 10-member Committee of four physicians, four pharmacists, a physician's assistant, and an advanced registered nurse practitioner, and so we will fill those positions with that type of licensed provider when those vacancies open. We also try to keep a pretty good mix of different specialties, primary care, psychiatric care, mental health. We would like to keep it -- make sure that we have a broad or some depth in the specialties that the got the Board members have. The Committee meets at least quarterly. Right now we meet, and we have been meeting every other month, so the even months of the year we typically have a meeting. Of course, sometimes we do cancel those, and we will let you know when they when they do get cancelled. And then the Committee reviews drugs for inclusion on the Washington PDL. So you wear two hats. One is the P&T Committee, and we will adjourn, and you will put on your DUR Board hat, and we will go into more of that in a few minutes. The next slide. So the roles and responsibilities of the Committee, we have a Chair, and we have a Vice Chair, who are selected by the rest of the Committee members. The Chair and Vice Chair, it is a two-year term. So when the Chair leaves, I believe the Vice Chair performs -- the Vice Chair becomes the Chair, typically. But the Chair is the Executive Officer and supervises the Committee, runs the meetings. The Vice Chair will perform all the duties of the Chair when the Chair is absent. Each year, the Committee members are required to fill out the Conflict of Interest Form, the COI form, and if they have any conflicts, they have to disclose them or recuse themselves from participating in a meeting where they might have a conflict. The Committee also reviews the reports that are prepared by the Drug Effectiveness Review Project, and those are pretty extensive in-depth reports that look at the comparative efficacy of the drugs within a class, and also looking at the safety profile of drugs as well as are the individual populations that the drug may be less safe or more effective, so that we can make those considerations in our drug PDL selection. The Committee also determines which drugs are safe and efficacious, and they do that in their motion, and we will work with the

motions to reward them to the comfort of the Committee. We don't want you to make a motion of something that you are not comfortable with the words on the paper as they are written. They are not rubber stamped motions. We work on them -- we can work on them all the time, so if you want a slight change, ask questions, please, please do so. The Committee also determines the appropriateness of therapeutic interchange within a drug class on the Washington PDL. And I will go into a little bit more about what that means, I think, on the next slide. Yep. We have got a few more things. So the Committee also looks at the evidence-based review standards, so considering the overall quality of evidence, which the Drug Effectiveness Review Project will review the evidence, and they will tell you whether it is a good, fair, poor quality, low-high quality evidence. You also evaluate from your own provider and patient perspectives of your experience treating in the real world. You will produce explicit defensible recommendations based on the review of the evidence. Those are the motions that I had mentioned. You are to evaluate the drugs in a manner free of bias emphasizing the best evidence reported by DERP. And what this really means is that we do not consider evidence that has not gone through the DERP process. So the DERP process is quite rigorous for a reason, and we do have cut-off points on what evidence, which data studies get included. So if a study is a late-breaking study, it might not be in that report. However, we do not consider without evidence in the actual report that we are looking at today. Sometimes that will be brought up by stakeholders in their testimony, and we can consider updating the report in a future meeting. But we don't take that -- we don't consider that evidence that is presented outside of DERP. So we want to review the direct evidence. We like to focus more on outcomes on real health outcomes rather than intermediate outcomes whenever possible, and then you take into consideration the harms and benefits of the drugs that are reviewed. I am going to stop. Are there any questions from anybody before I keep going? Okay. I don't see any hands raised, so I am going to keep going. The Drug Effectiveness Review Project, often called DERP -- I try not to call it DERP too often because we have too many acronyms that sound similar. So it is a collaborative of 13 states. This might be a little out of date on the actual number. The states that are participating are listed below: Washington, Idaho, and/Oregon were the founding states of the Drug Effectiveness Review Project prior to 2003. We just celebrated. I forget how many years we have been in. Was it our 20-year anniversary? I think it was. So it is a pretty exciting project and collaborative that has been going on for quite a while, so I am really excited that we are still participating in that. The next slide, please. So the reviews that we get, or reports are what we call them, these

are new drugs that are eligible for inclusion on the PDL. So we talk about differences where a new drug comes to market. If it is not included in a review, it is not eligible to be preferred on the PDL, and it is not eligible, really, for inclusion on the PDL either. And the reports that we look at -- and this means that there was evidence of these drugs in the actual report will be a new class review, an update to an existing class review, a single drug addendum, or a topic brief. And the reason why we distinguish what -- which types of reports constitute whether a drug could be included or not is the evaluation of evidence. These four types of reports have some sort of consideration and evaluation of the evidence that is available on the market, where there is no -- where if there is a new drug and they are just in a surveillance report, which we do frequently for the different drug classes. The surveillance report is really just going to look at, what is the availability of new evidence in the class, what are new drugs that are in the -- that have come out that would be considered part of that class, and are there new Indications? There is no evaluation of the actual evidence itself in the surveillance reports, so those drugs are not considered reviewed, and those new Indications would not be considered reviewed if they are just in a surveillance report. So the P&T Committee will normally approve the surveillance report as adequate, or they can request an update. So if you feel like there is an overwhelming amount of new evidence in the class that warrants another report, or a new report to incorporate all of this new evidence, you can request that we do that. We do have limitations on how quickly and how many of those requested updates we can do. Usually the surveillance reports are done annually or bi-annually, and the DERP Board will -- the DERP participating states will vote collectively on whether or not those reports move forward, so sometimes it can take a while for those to get updated. Any questions about the types of reports that you are going to get or be reviewing? Okay. And I know when we dive into stuff into the actual meat of stuff, later on, when we start reviewing the classes and the reports, you might have questions, so feel free to stop and ask along the way as well.

Kavita Chawla: Hey, Donna, I think, especially for our newer members, can we call out the different terms? All right? There is the surveillance report. There is the ITR. There is topic brief -- or are we using any of those other terms, or do we just use surveillance reports now?

Donna Sullivan: So we do have new class reviews. We probably don't have as many new class reviews as we normally do because we are [audio cuts out] as drugs are coming out. There is a single drug addendum. So if let's say we have a drug

class that is on the market, that we have been reviewing, we have had reports, and a new drug comes out, and we want to be able to put that drug into the PDL, we can do like an addendum on a single drug so that it can be considered reviewed. And then the topic briefs, the ITRs, or the individual topic requests or reports that are requested by a state, so those could be -- those are generally do a deep dive into the data and would be considered reviewed for purposes of PDL selection. Ryan, I see you have your hand up.

Ryan Pistoresi: Yeah. You know, that is a great question. This is Ryan Pistoresi. So we are actually presenting a few ITRs at this meeting with our archive requests. So we did work with DERP, and this is one of the ways that we are using our state funds to develop a new product specific to our state's P&T needs. So the presentations that we will get into a little later this morning will be our use of the ITR. And as I had mentioned, some of these drugs in which you may be requesting, we go through that DERP process. So as you recall, at our last meeting with the insomnia drugs you had requested that we go back and get more information on the oxygen receptor antagonists, so that specific newer class of insomnia drugs, and so we are in the process. We did submit it for review, and at our Spring DERP Conference we will be getting the presentation and a topic brief, and if the states vote forward with it, it will be in the form of a new report. Otherwise, we would be bringing that topic brief to you as saying this is as far as we could get for that. So those are just some of the ways that these different types of reviews from DERP get presented to you and the different ways that they kind of meet our state's P&T needs.

Kavita Chawla: Thank you for that, Ryan. Yeah, it is just as he said, so many acronyms. And so each of them is just different levels of thoroughness if you will. I mean they are all thorough but like in what they are presenting changes depending on whether it is a topic brief versus a full class review. So I think our new team members -- Committee members will see that as we go on. Thank you.

Donna Sullivan: Greg, I see you have a question.

Greg Hudson: Yeah, thank you. I just wanted to use today as an example for reviewing the materials. I see an ADHD surveillance report. So this report isn't necessarily introducing new drugs that are eligible for inclusion in the PDL, but it is like a summary of the new evidence, but there is no, I guess, new ADHD drugs we are reviewing in the Committee today.

Donna Sullivan: Correct. I mean they might identify that there is a new product on the market, but it is not diving into the evidence to say this looking at the efficacy of this new drug, looking at the safety of the new drug, looking at if there is any comparative evidence between this new drug and new drugs within that class. So it is basically just saying here's what's new. There is like -- you will see the reports when you read them, it might say there were two new randomized controlled studies. There was a cohort study. There was a new indication for drug Y, and they will tell you what the indication is. There might be a BlackBox Warning. The FDA released a new BlackBox Warning that came out, so we know that there are safety considerations somewhere in the data that we might need to look at. So it is really just what we are looking at that might trigger us to want to update an existing class. And as Ryan mentioned, if it gets updated -- it gets voted upon to be updated, then it goes into our normal annual cycle of report generation. If it doesn't get voted to be updated by the project itself, what we can do is request what is called an ITR. It is an independent topic report or something like that. But that means it is just our state only is moving it forward. It is open to everybody who participates in DERP, but it is not -- sometimes it will be just a -- it won't go through the same rigor as the -- there is a pretty -- I won't say rigor -- there is a pretty good established process of what we do when we are updating reports. A topic brief is more of a smaller, faster process in order to get that done. [Cross-talk] Okay. Next slide, Nonye. So the selection process, the P&T Committee reviews the reports that we were just talking about. You will make a recommendation based on evidence. So we generally ask you to -- make a recommendation on the efficacy of the products, the safety of the products, and whether or not they are interchangeable. And when I say interchangeable, it might mean, let's say, I am going to be old school and show my age, the proton pump inhibitors. Do you really care which one they take as long as they take one? If you if you think that it doesn't matter which proton pump inhibitors somebody takes, as long as they get a proton pump inhibitor, you might say that they are equally interchangeable. And again, I will get to what that means later in the slides. So once you have made your recommendation, the Health Care Authority conducts the cost analysis with an actuary. We pool the data for Uniform Medical Plan as well as Labor and Industries, and we will look at our current PDL selection and then all of the drugs that are eligible to be preferred. And we will look at rebate offers that we get and determine following your recommendations figure out you know, what would be in the best interest of the state financially and clinically for PDL selection. We have a workgroup that reviews that cost analysis, which includes Leta, Luke, Ryan, and those from the L&I, Jamie, Doug, and Christy,

so they attend those meetings as well. It is very much a back and forth process meeting the needs of all of the agencies and making sure that we have all of our clinical bases covered on the PDL. After the workgroup makes their recommendations, the agency directors get those recommendations, and they have the final approval of what is going to move forward the changes that will be made to the PDL. The staff sends out the notice of the PDL updates to our stakeholder list, so we do notify anybody who has signed up as a stakeholder for these meetings, they get that announcement. And then the agencies will implement the changes to the PDL, and, generally, it is on the -- the implementation date would be like the first day of a quarter, depending on where we are in a given quarter. It might -- be a few months out. Next slide. So the Washington PDL, again, started in 2004. UMP, our Uniform Medical Plan and Labor and Industries are still currently using the PDL. Like I said, it is about 30 drug classes, and it is subject to the Endorsing Practitioner Interchange Program. Next slide. So, what is the Interchange Program? When the PDL was established, there was stakeholder input into the Preferred Drug List. There was concern by prescribers that they would really need to prescribe a drug that was non-preferred, and they -- we wanted to have a process where a prescriber who really needed that non-preferred drug could get the non-preferred drug without having to go through prior authorization, so the program that was developed is this Endorsing Practitioner Interchange Program. And what that really means is doctors could sign up and endorse the PDL, the Washington PDL, and by the by signing up and endorsing the list, they are allowing therapeutic interchange. So if they prescribe a non-preferred drug, they are allowing interchange to the preferred drug unless they are otherwise directed, so they are agreeing by the rules of our program. And what does that mean to interchange? So if a prescriber who has endorsed the PDL writes for -- I am going to use our proton pump inhibitors again -- Nexium was nonpreferred, and OTC Prilosec was our preferred drug. So if the prescriber wrote for Nexium, and the prescription came into the pharmacy, the pharmacist would automatically interchange the over-the-counter Prilosec for the Nexium unless the prescription -- and so we have all these drug classes that are refill protection. So, in the proton pump inhibitor example, the pharmacist would make that substitution unless the prescriber had endorsed the list and signed the blank Dispensed as Written. In that case, the pharmacist would dispense the Nexium. Otherwise, the pharmacist would dispense the over-the-counter Prilosec and then notify the prescriber of what was prescribed. That is called therapeutic interchange. There are some rules and guide rules around what a pharmacist could and couldn't interchange. So the Legislation included refill

protection for antipsychotics, antidepressants, antiepileptic drugs, chemotherapy, antiretrovirals, and immunosuppressive drugs, and drugs that treat hepatitis C, and those drugs to treat hepatitis C are actually the non-direct acting antivirals. This Legislation was passed prior to those drugs coming to market. And again, if the endorsing practitioner writes Dispensed as Written on a prescription for a non-preferred drug, then the pharmacist would dispense the non-preferred drug, assuming that there were no other clinical edits required for that drug. So if it is on prior authorization to make sure that it is being used on label or according to best practices, it would still require that prior authorization. And there are about 7200 endorsing practitioners. We always get asked this question. It is really hard to tell what percent of the total Washington prescribers are endorsing because many practitioners/providers have prescriptive authority. They might keep their Washington license current, but they may not be practicing in the State of Washington, or they might be retired, but they still choose to keep their license current. So we can we know how many are on our list, but we can't really tell what percentage of all practitioners or prescribers are endorsing. So go to the next slide. So preferred drugs therapeutic interchange does not apply. They are already preferred. And therapeutic -- you know, DAW does not override prior authorizations. So if you have something preferred and it is on prior authorization, it is still going to require prior authorization. So non-preferred drugs are subject to therapeutic interchange when they are included in the new class review, the update to the existing class, or the single-drug addendum, so those were the most reports that we were just referring to. It is not prescribed as continuation therapy of one of the refill-protected classes, and it is allowed by the P&T Committee. So that is where in your motion where you are discussing if it is interchangeable or not, you are making a decision whether or not those drugs should be allowed to be interchanged without having to get a new prescription from the prescriber, and then that would be when interchange when allowed by the endorsing practitioner. Next slide. So if it is in a PDL class but not included in a DERP report, those drugs might be covered -- or will be covered, according to the program benefit design. Therapeutic interchange does not apply. DAW does not apply. And they may or may not be preferred for the individual program. Drug classes that are not on the Washington PDL are also covered according to the program benefit design, and the therapeutic interchange doesn't apply. So those would be what we call our wrap-around drug classes where they are not even brought to the P&T Committee. They are not reviewed by DERP, but to have a comprehensive pharmacy benefit we have to rely on our vendor, Moda Health, for Uniform Medical Plan. Or Labor and Industries, you know

they manage their own Preferred Drug List outside of the Washington PDL. So those are how those programs manage what we call the wrap-around classes. And the next slide. So Ryan alluded to an archived drug class process. There are a lot of drug classes when we first started in 2003. Our budget busters were the newer beta blockers, the proton pump inhibitors, the statins, triptans, drugs that have long since gone generic, and the evidence in those drug classes is pretty stable and there is not a lot of new activity in those drug classes. And so in order to be able to manage what gets reviewed by the Committee and the reports that we are paying for, we decided to begin archiving some of those drug classes. And when we do archive those drug classes, we will request a final surveillance report of the drug class. We will ask the Committee to vote on whether the class is appropriate archive. We will determine if therapeutic interchange and the Dispensed as Written rules are appropriate to continue without continuing to review their class annually. And then we will ask you to direct us to allow us to manage these classes based on cost. If there are changes in cost within the marketplace, or if drugs leave the market or new generics come out onto the market without having to bring it back to the Committee for another full review. So the archived classes will remain on the Washington PDL, but we just won't review them unless the Committee or one of the workgroup members decides that we are going to reactivate the class. Maybe there is a new drug that is similar but not quite the same that is in the pipeline, and we want to compare that to an older class of drugs, and so we might reactivate some of those archived classes. The next slide. So DUR Board responsibilities. So generally, once the Washington P&T Committee completes the review of all of the DERP reports, we will adjourn the P&T Committee and reconvene as the Drug Utilization Review Board. It is required. The Board itself is required under Section 1927 of the Social Security Act. It is an extension of the P&T Committee in advising utilization review and prior authorization for the Apple Health Program. So the difference the main difference between the P&T Committee and the DUR Board is that the DUR Board is only taking action on Medicaid itself. And so the P&T Committee really is just looking at preferred and non-preferred status of the drug classes on the Washington PDL with your P&T Committee hats on. You are not going into clinical policy, like is this first-line, second-line compared to each other or step-therapy, where they should try something -- a different type of medication first. So that really gets relegated to the DUR Board as it pertains to the Medicaid program. So you will make recommendations and interventions based on the information that we provide. We will at times provide you with some data, utilization data. Recently, in the past year or so we have been really focusing

on getting our clinical policies up and running, and we ask the Committee to review those policies and offer modifications to those policies as you see fit. Again, these are not expected to be rubber stamped, but we would -- we do really like your feedback. And then we also at times have engaged in provider education activities where we might send out letters or try to do some sort of education activity around a safety or best practice within the organization. Next slide. So the Apple Health PDL. We started it in 2018, and we finished implementing it in 2020, so now we are just kind of in maintenance mode. The Health Care Authority also is a member of The Optimal PDL Solution, which is also known as TOPS, which is managed by Magellan, and it is a supplemental rebate pool. So we also look at cost and take cost into consideration when creating the Apple Health PDL. The next slide. So our processes you will hear from Umang from Magellan. He will review each drug class on its clinical merits relative to the other medications in the class. Those are basically based off of published peer-reviewed trials. It could also be package insert, looking at efficacy, safety, and tolerability, and then also looking at the different Indications across the different medications. Basically, Magellan presents these classes to the Board, and then the Board determines an agent's superiority, its equivalency . Similar to a motion like you do on the P&T Committee, you will make a recommendation. And we typically have a standard. If it is a non-preferred drug, you have to try and fail two preferred drugs in order -- before you can get the non-preferred, and you will see that repeated in the motions, so I am not going to keep saying that. So the next slide, please. And then the Financial Review. Twice a year Magellan will update their contracts with different drug classes that they manage, and they will give us what they call cost sheets. So they will look at our utilization and look at the net cost of the drugs net of rebate, and then make recommendations to us that we would consider if we make any changes to the preferred status of a drug. And HCA makes the final selection. So just because Magellan has a rebate offer from a manufacturer does not guarantee that that drug will be on the PDL. If we feel that there are more appropriate, less costly alternatives to that product, we might refrain from making it preferred and forego the rebate and manage it through utilization means, like prior authorization. Next slide. And here are our illustrious acronyms. And I think these are the last two slides. I am not going to read out these. I believe we are to the questions slide if there are any more questions. All right. Kavita, I will hand it back to you then.

Kavita Chawla: Excellent. Thank you, Donna, for that exhaustive kind of review of all of our processes here, and there is learning in doing so. We will now proceed to

doing some of these reviews and learning what they are all about. So I have next on my list, we have got Shannon Robalino from DERP to take us through our ADHD surveillance report.

Shannon Robalino: Hi, Kavita, can you hear me okay?

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

Shannon Robalino: Great. And I think I am doing the steering. Is that right [indistinct]?

Kavita Chawla: I am sorry. Could you repeat that?

Shannon Robalino: I think I am supposed to do the slides for this. Is that correct?

Kavita Chawla: Yes. Yes.

Shannon Robalino: Thank you. Okay. Let me just start sharing the screen. I don't use Zoom too much these days, so I got to get used to finding what I need here. Just give me a second. Closing down some items. Okay. So which screen are you seeing? You are seeing the wrong screen.

Kavita Chawla: We are seeing the meeting notes. Yeah. The speaker's notes.

Shannon Robalino: Okay. Now you should see the --

Kavita Chawla: Yes.

Shannon Robalino: Okay. Okay. Well, thank you for bearing with me, folks. I am going to run through this. This is the surveillance report. Donna has just giving you quite a overview of the kinds of products we do here at the Center. So this is a surveillance report, which means we have not gone into any depth in terms of the evidence that we have identified for this. So as it is your first presentation of the day from us, we will be going through this presentation and others in a similar format, beginning with some Background, and then we will talk through the scope of this project. That is the PICOS and the Key Questions, how we identified the evidence, what we found, and summarize that for you. Okay, so a bit of background here. ADHD affects around 10% of US children and around 5% of US adults. You can see that in children about two-thirds of them receive medications to manage their symptoms, while up to 80% of adults are receiving medications. The DSM-5 has changed the

criteria just a little bit compared to DSM-4 and other iterations of the DSM. So now to be diagnosed with ADHD you can be diagnosed at any age, but the symptoms need to have been present from the age of 12 and that those symptoms need to be present in two or more settings such as work or school or in social activities and interfere with functioning in those similar environments and not b explained by other mental health disorders. There are now three presentations of ADHD. There is the predominantly inattentive variety, the predominantly hyperactive-impulsive variety, and the combined presentation, and that combines both that inattentive and hyperactive-impulsive presentation. Psychiatric comorbidities are really common with this disorder. So this can include things like learning disabilities and anxiety, or depression and substance use disorders, depending on the age group and, likely, these can all happen and regardless of age. There are a number of treatments right now. Well, as of about six months ago when we did the surveillance reports there were 31 FDA-approved pharmacological agents. So this includes both stimulants and non-stimulants. There are, of course, behavioral interventions as well as studied specific interventions such as a workplace or school accommodation. and it is common that these therapies are combined when somebody is diagnosed with ADHD. So around 13% of Medicaid-enrolled children have an ADHD diagnosis, and this is about three times as many as the national average across insurers. Children identified as African American are less likely to receive care and more likely to disengage and discontinue their treatment. Those who are white male and living in a two-parent household kind of had the opposite, where they are more likely to be assessed and treated, especially within a medicated environment. So this is similar in adults, though males in this case and those living rurally are less likely to initiate those treatments and continue with those treatments. And the initiation of treatment across states varies quite widely with 8% initiation in New Jersey up to nearly 50% in Tennessee. Okay, so what have we done on this topic in the past? So about three years ago, now, we did an update to an earlier systematic review. This update included 70 studies. All of these were randomized controlled trials, except for -- the post hoc analysis was still a randomized controlled trial post hoc analysis. So you can see the way that those broke down on this slide. The majority of them were head-to-head comparisons. We only looked at the placebo controlled comparisons in newer drugs, and we will get to those details in a moment. So this is the PICOS, so this is the population interventions, comparators outcomes and study design. So starting out, we are interested in literally anybody of any age with ADHD of any presentation. We were looking at head-to-head comparisons as well as placebo comparisons for those newer treatments, so

those were the treatments that were approved, FDA-approved since January 2015 as well as we were going to [indistinct] take anything in individuals over the age of 18, since this group has been has not been studied very frequently in the past. We excluded studies that compared like a brand name with a generic, or compared different doses of the same medication, or explicitly included multimodal treatments. So that might be a behavioral treatment as well as a drug. If only one group, for example, if only the intervention group was receiving both of those, and the control group was maybe only receiving a placebo, and we were only interested in randomized controlled trials, so this is not going to read all of these because there are so many. You can see this is part one of four of the available treatments, pharmacological treatments for ADHD. I will just highlight those at the top. The methylphenidate hydrochloride, the dextroamphetamine, and then the amphetamine combined therapy as well as the serdexmethylphenidate and dexmethylphenidate. All of these were newer drugs since our review in 2021. So these have come on the market since then. And there are a number of them, obviously, that we included for 2015 and to 2020 in that review. I will highlight that there was one discontinuation for a brand name drug. It was an amphetamine, and that is the one here in bold, the Adzenys XR. So again, I am not going to read through this list of various stimulants and non-stimulants, but they are here on the screen and in the report so that you can have a look at those. And we have also included a few of the off-label treatments that are commonly prescribed. Okay. So what were we interested in looking at in these RCTs? We were looking at the efficacy and effectiveness, so symptom response. Were there changes in those inattention or hyperactivity symptoms? Were there changes in functional capacity and quality of life, whether that is with patient itself, or family members, caregivers, etc.? How long did it take for these treatments to become effective? And how long did they last? How long did that effectiveness last? And we are also interested in safety-related outcomes such as the tolerability. How many adverse events were there? Did folks withdrawal from their treatments due to adverse effects? And we were interested in specific adverse events such as anorexia, insomnia, and tics. And we were also looking at serious and longer-term adverse effects, so these are things over 12 months and can include cardiovascular events, suicide and suicidal behavior, as well as any misuse or diversion of these treatments. So we had four Key Questions. The first two are around the effectiveness and harms of these FDA-approved treatments. The third is around any subgroup differences and the age differences, race or ethnicity differences, presentation etc., and we also included any ongoing studies. So how we identified this evidence was we looked at a number of

different sources, including several trials registries on their FDA website to identify ongoing and published studies. We also did searches in Ovid Medline and general internet searches, or I should say Google Scholar searches, using any trial identifiers to find published RCTs, as well as looking at the FDA for any actions. We also used IPD Analytics to identify any that we may have missed through the FDA. And as I said, this is about six months out of date right now, but we did run the searches through the end of July 2023. Let's move into the findings there. This is just an overview of what we found in the new studies. So overall, we found nine new studies and 12 publications. You can see the way that they broke down in terms of comparisons. Overall, there are about 1300 new participants, and these studies had pretty short-term duration of 1 to 12 weeks. So these new studies, we will go through them. Again, this is just a really broad overview of what we found we did not do any kind of analysis of these results and just letting you know what there is out there. So we had one head-to-head study that compared atomoxetine with an oral methylphenidate, a dissolving version of that, and this was exclusively a population that had major depressive disorder. You can see that it is a small trial with about 60 participants. And then moving into the next rows of stimulants. So these -- all of those with the shading are indicating studies in individuals over the age of 18, so studies in adults. So here we have -- let me see if I can remember -- lisdexamfetamine versus placebo, that same methylphenidate versus placebo, and amphetamine versus placebo in several studies there as well as a couple more that are in children. You can see the median ages are around 10 in those children's studies. So we also found three studies in non-stimulants. These are all in adult participants. These are for atomoxetine, guanfacine, and viloxazine, and you can see that very last one there, the atomoxetine versus placebo. This was an older group of adults that all had PTSD. So, again, this is just the ongoing studies. We identified four ongoing head-to-head studies with completion dates going back to July of 2021 to December of 2027. There was one comparing two stimulants in children over the age of 6, one comparing a stimulant and non-stimulant in adult participants, and this is a larger, probably one of the largest RCTs we have seen. And these adults need to have a history of psychosis or bipolar disorder. We also found one ongoing study in children and adolescents with autism, comparing a stimulant with a non-stimulant or clonidine, and one comparing two non-stimulants with placebo in children and adolescents. In terms of those placebo controlled trials, these are for adults or in newer medications. So we found one looking at methylphenidate versus placebo in adults with or without anxiety, one comparing serdexmethylphenidate with placebo in young children from the ages of 4 to 12, and then a non-stimulant

looking at very young children aged 4 to 5, and that was viloxazine versus placebo. So the new FDA actions. What did we identify? So we have identified some new drugs and formulations. These were on that list at the top, but just so you can see here again, that there were several new formulations, methylphenidate and amphetamine-related drugs and for use over the age of 6 years. And I have already mentioned that there was this one drug that has been pulled off the market, Adzenys ER, an extended-release amphetamine. They do still have the oral disintegrating version of this on the market. We also looked at pipeline therapies and found a number of pipeline therapies in Phase III testing. One of them may have actually already been approved by now this one at the very top, this amphetamine AR19. We might see that in the upcoming pipeline report. And the remainder of them you can see there. These are all drugs that are in development, and last time we looked they were in Phase III testing. I hope you can't hear that the landscapers have arrived with their leaf blower. So what did we find in terms of New Indications, Harms, or Warnings? So these are named brands. Evekeo ODT is an amphetamine. Now, they actually removed children ages 3 to 5 from the label, so it is now only approved for use in children and adolescents 6 to 17 years. Viloxazine actually has expanded its use to individuals aged 6 and over. It was initially approved only for children and adolescents up to age 17. There is also a new Boxed Warning for the emergence or worsening of suicidal thoughts and behavior. And then the Dyanavel XR is an amphetamine/dextroamphetamine medication, and there is a Warning for clinicians to consider the potential for long-term suppression of growth. So, overall in the surveillance report what we have presented to you is new evidence since that 2021 systematic reviews. We had those nine new RCTs, one of which is a head-to-head study in adults, five placebo controlled trials comparing a stimulant to placebo, and three of those are in adults to children, three placebo controlled trials comparing a non-stimulant with placebo, all and adults. Seven ongoing studies, four of those are head-to-head, three are placebo controlled and two new Indications for viloxazine are now able to be prescribed to adults, and Evekeo, the amphetamine sulfate is no longer approved for use in those young children. In terms of the Boxed Warnings, we have just gone through these, but just a reminder that there was a Boxed Warning for viloxazine with the emergence or worsening of suicidal thoughts and behaviors. For Dyanavel XR, a Warning about long-term suppression of growth. We also identified three new stimulant drugs or formulations. The brand name, Adzenys, is no longer available in the tablet form, but the oral dissolving form is still available in five pipeline therapies all in Phase III

trials. So that wraps that up. So I am happy to take any questions that you may have. Yeah. So I will hand it back to you, Kavita.

Kavita Chawla: Thank you, Shannon. Nonye, do we have any stakeholders listed, or were there hands raised?

Nonye Connor: I don't see anyone's hands raised at this time. No.

Kavita Chawla: All right, great. Any questions from our Committee for Shannon? Otherwise, if Nonye can pull up our motion.

Nonye Connor: I see. Shannon, you are still [cross-talk] --

Shannon Robalino: Yep. I am going to stop sharing now [cross-talk].

Nonye Connor: Thank you.

Kavita Chawla: And as we review our motion if we can have our Committee members come back on video. Turn on your cameras. Thank you.

Nonye Connor: It is moving screens around. Okay, and share. Okay.

Kavita Chawla: All right, great. So this below here is the last motion that we had approved back in February of 2022. So shall we copy/paste that up above so that we can start making adjustments as needed? Okay, great. So Committee, any proposals to this motion on the basis of the new surveillance report and the new information that was proposed?

Laura Beste: This is Laura Beste. I just have one question. So serdexmethylphenidate I do not believe comes as a single ingredient medication. Does that need to have both ingredients added as a combination product?

Kavita Chawla: Good question.

Donna Sullivan: Yeah. Can you just add like a /dexmethylphenidate behind it? [Cross-talk] It is on the bottom one.

Kavita Chawla: [Cross-talk] That one?

Donna Sullivan: [Cross-talk] Right there. Yeah. Just do after serdexmethylphenidate do /dexmethylphenidate.

Nonye Connor: This is for the new people. Would you mind just explaining are the ones on the left the only ones that are on the list, or are we not being specific right now about what exact ones are on the list are off the list?

Kavita Chawla: Yeah. The ones that are on the PDL are on the left column, so those are the ones that we are approving moving forward into the PDL -- or reaffirming for the PDL.

Nonye Connor: Okay. And am I being crazy that methamphetamine is on there.

Donna Sullivan: This is Donna. It is grayed out. So if it is grayed out, they are not eligible to be part of the PDL, but we are putting it on here because it was included in the study itself, I believe. And yes, there is Desoxyn, which is methamphetamine, and we put pretty tight guardrails around it.

Kavita Chawla: Thank you. Christy, go ahead. Yeah, and this might be a better question for a letter, Donna. Considering all the shortages that are going on right now, what is -- is there anything that this Committee should consider? Or is that on the back end kind of worked out without any consideration? Just because I know that has been a struggle for a lot.

Donna Sullivan: This is Donna. We try to manage that on the back end. We will send out directions to the plans to allow like either the brand name version if there are shortages of generic products, or we might, for example, with insulins especially, we would tell them to go ahead and allow a non-preferred drug to be approved without any trial and failure, but we try not to switch the preferred statuses back and forth because doing that requires provider and patient notification. But we can always make exceptions to our nonpreferred rules to make sure that there is access to those in the time of a shortage, and if the shortage is not going to be long-term from an administrative perspective, it is just easier to instruct the plans to go ahead and make those exceptions as they occur rather than changing the preferred status on different drugs.

Christy Weiland: That makes sense. Thank you, Donna.

Donna Sullivan: You are welcome.

Kavita Chawla: And, Donna, I guess I also have a question. So you know the meds listed under off-label treatments, I know that they are listed in other drug classes as being covered agents. So is that to say that when a provider prescribes, let's say, bupropion for off-label treatment of ADHD, whether or not the medication gets covered by HCA depends on which diagnosis code they link to the prescription?

Donna Sullivan: No. I mean I think again we are putting -- including these in the class because they were included -- we are including them on this motion template because they were included in the report. Armodafinil and modafinil are not FDA-approved for ADHD; however, they are stimulants, and so they might get prescribed for that reason. They so they are on our Apple Health PDL, but they are not in this class. They are in a -- I believe they are in a different class, and so they get treated according to, I think, our narcolepsy policy that we might be that we are creating working on. Bupropion is Wellbutrin. It is an anti depressant. It is managed in our Antidepressant class, and most of those drugs are generic. They don't require prior authorization, so it doesn't matter if it gets prescribed off-label. For an adult, it would just be a filled prescription. If it is for a child, depending on other medications the child is on, we have second opinion requirements for duplicate antidepressants or antipsychotics and duplicate ADHD drugs. We also have age dose limits on ADHD drugs and antipsychotics, and we have polypharmacy second opinion as well as if a child is on more than five psychotropic medications, which Bupropion would be considered one, they require a second opinion also. So depending on what other medications a child is on, bupropion might get flagged for a second opinion, but otherwise, -- most of the generics are preferred and don't require prior authorization.

Kavita Chawla: Right. So I guess, first, Committee, if we can have a motion to accept the surveillance as adequate. Any concerns about that? Or if not, you could propose a motion one of our Committee members.

Zoe Taylor: Can I just ask one more thing? Sorry, just because I'm new?

Kavita Chawla: Yeah, of course [cross-talk] --

Zoe Taylor: If there was a new medication that was just reviewed, is this the time that we would add it to this list? Or is that separate from this process?

Ryan Pistoresi: So this is Ryan Pistoresi. So if we were doing a topic brief or a report, we would have one of the new drugs in bold to be included [cross-talk] on the left. And if you actually scroll down, in the last notion we had in 2022, we did have a couple of new drugs. It looks like there are two in bold there for that motion. But because today is a surveillance report, we are not able to add [cross-talk] drugs. But that is typically where you would see the new drugs being added.

Zoe Taylor: Okay, and nothing about approving this motion like precludes next quarter or the quarter afterwards doing that process to -- like, it doesn't have to be two years until the next review where we would add a drug?

Ryan Pistoresi: It depends. So going back to Donna's earlier presentation, we, as the states, will vote for different drug topics that we want to move forward [cross-talk] depending on how the states see this drug class we may or may not be moving forward. [Cross-talk] We will likely know more at our June P&T DUR Meeting because that will be after our Spring DERP Meeting, and we can then provide a bit of an update on what we see as the next year's list of reports that will be developed.

Zoe Taylor: Okay. Thank you.

Ryan Pistoresi: Thank you for the clarifications, Ryan. Okay. So coming back to a motion for approving the surveillance report as adequate.

Christy Weiland: Christy Weiland, I motion to approve the surveillance as adequate at this time.

Peter Barkett: Peter Barkett, I will second the motion.

Kavita Chawla: All in favor?

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

Kavita Chawla: [Cross-talk] Any [cross-talk] or abstain? Okay, great. And then shall we read through this if anybody wants to propose a motion that is in front of us, and then as needed we can wordsmith it. Okay. So are there any concerns about the motion? Or are we ready to move forward? Any comments from the Committee about the motion? No? I see shaking heads. Great. So are we ready to reiterate the prior motion from 2022?

Laura Beste: This is Laura Beste. I make a motion that after considering the evidence of safety efficacy and special populations for the treatment of Attention Deficit Hyperactivity Disorder, I move that methylphenidate-based and amphetamine-based agents of both long- and short-acting formulations are safe and efficacious. A long- and short-acting formulation of each stimulant should be preferred drugs in the Washington State Preferred Drug List. No single stimulant medication is associated with fewer adverse events in special populations. Stimulants listed above shall not be subject to therapeutic interchange in the Washington Preferred Drug List. After considering the evidence of safety efficacy and special populations for the treatment of ADHD, I move that at least one non-stimulant that is not an alpha agonist that is safe and efficacious for ADHD will be included as a preferred drug on the Washington State Preferred Drug List. After considering the evidence of safety efficacy and special populations for the treatment of Attention Deficit Hyperactivity Disorder, I move that the alpha agonists, clonidine and guanfacine, are safe and efficacious and that both of these agents should be included as a preferred drug on the Washington State Preferred Drug List.

Dimitry Davydow: This is Dimitry Davydow. I second.

Kavita Chawla: All in favor.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstained. All right, the motion passes. Next on our list is archiving the Anticoagulant drug class. And I see Andrea Vintro from DERP will be sharing the slides with us.

Andrea Vintro: Hi, everyone.

Kavita Chawla: Hi, Andrea.

Andrea Vintro: So you can hear me and see me. Great. Let me share my screen. Let's see here. Share screen. Okay. Are we seeing [cross-talk] --

Kavita Chawla: [Cross-talk] Yes.

Andrea Vintro: -- up there? Great. Okay. So I will just dive in if that works for you all. [Cross-talk] Okay, great. So yes, thank you. My name is Andre of intro. I am a Research Associate here at the Center. So welcome to the first of seven presentation reports for the nine drug classes of interest for this Washington Drug Archive Project. So today we will be reporting on four drug classes in three presentations, so we are going to double up on the last one, and then the remaining five drug classes will be presented in June. This first presentation is entitled Direct-Acting Oral Anticoagulants, or they will be called from this point forward, DOACs. The aim of this work is for the Drug Effectiveness Review Project, better known as DERP, to develop and present information to the Washington State Pharmacy and Therapeutics Committee on nine drug classes that are candidates to be archived from active review by the Committee. And you can see the list of drug classes that are included in this project at the bottom of the slide, and, of course, that class of anticoagulants is highlighted in green for this presentation. So this presentation will review the topics in the darker green boxes on this slide in order from left to right. So starting on the far left, I will first define the health condition of interest that this drug class is intended to address and then summarize the general epidemiology and treatments for the condition. Then I will review key information in the most recent DERP reports for this drug class, including the PICOS Key Questions, high-level-summary of the Key Findings of that report, and then general findings of any surveillance that was done after that last systematic review. And then I will move to any new actions by the FDA for the drug class since the last report, including any new drugs, any new Boxed Warnings or serious Warnings, and also any new Indications, where I will also present the current FDA-approved Indications for all of the drugs of interest. And then moving on, I will report on any new pipeline drug findings and also discuss the generic status of existing FDA-approved drugs. And then, finally, I will provide a high-level summary of relevant clinical practice guidelines for the condition, which includes information about how and where these drugs are used along the treatment pathway, and then we will follow up with questions and discussion. Okay. So our condition of interest here is thrombosis, which is defined as the inappropriate clotting of the blood. So it is the formation of a blood clot within the blood vessels that have either partially or completely blocked the natural flow of blood, resulting in some clinical complications. This thrombosis can occur in both the venous and arterial systems. So venous thrombosis or venous thromboembolism is when the clot forms in a vein, which carries blood from the body back to the heart. Clots that develop in these deeper veins are usually occurring in the legs, and those are called

Deep vein thrombotic events, which result in pain or swelling. A pulmonary embolism is a clot that also typically develops in a vein and then travels to the lungs, where it blocks the blood flow of the artery of the lungs. Symptoms for that include chest pain, shortness of breath, and dizziness. So major risk factors for venous thrombosis include cancer, longer-term immobilization, such as during long plane flights or after major orthopedic surgery where you are not moving much. Also, pregnancy is a risk factor. Also oral contraceptives, smoking, obesity, as well as being older than 60 years of age. An unprovoked venous thrombosis is when there is no identifiable provoking event or risk factor, and then a provoked venous thrombosis is when there are risk factors that have been identified prior to the event, such as after surgery or with estrogen treatment. Arterial thrombosis is less common, but it is considered more lethal. This is when a blood clot develops in an artery, which can block the blood flow to vital organs, including the heart and brain. This can cause a full stroke or transient ischemic attacks, which are mini strokes as well as heart attacks. Major risk factors include a family history nonvalvular atrial fibrillation (AFib), atherosclerosis, smoking, also among other factors that are similar to those for venous thrombosis. So the Center for Disease Control and Prevention estimates that close to about a million individuals are likely affected by venous thrombosis annually, and up to 100,000 individuals die from this condition. So it is a common disease and comes with a substantial disease burden because of the risk for longer-term complications. At least half of all strokes are considered caused by thrombosis, -- and about one-third of all sudden cardiac deaths are thought to be caused by thrombotic events. So incidences of venous thrombosis were steady over the past 10 year period ending in 2013, and there was no more recent data that was analyzed over time to present today. There is evidence of disparities around this condition. So in the US, black individuals have higher rates of venous thrombosis compared to white individuals, and one study showed that being of African American, Hispanic, or Pacific Islander race, or a female gender, those are predictors of mortality for individuals who were hospitalized because of venous thrombosis. So I will direct your eyes first to the bottom of this slide so you can see that the nonpharmacological interventions include healthy lifestyle behaviors and physical activity and healthy diet, and those are recommended to reduce risk for thrombosis as are compression devices or stockings if you are at high risk, including after surgery, and these recommendations typically continued should pharmacological agents be recommended later on. So back to the top of the slide, for pharmacologic treatment, both anticoagulant and antiplatelet drugs can be considered with thrombosis as they work at different places in

the coagulation system, and the type of drug treatment depends on whether the thrombosis is considered provoked or unprovoked and also whether the embolism is a first or a subsequent event. Clinicians often consider three stages of treatment. The initial or acute stage is typically up to the first seven days after the event. The chronic or long-term phase is seven days to three months post event, and then extended stages or if treatment is needed after that three-month period. So when a patient first presents with thrombosis, anticoagulants are often given intravenously. So either this is unfractionated heparin or low-molecular weight heparins, and these drugs provide this quick response to avoid that progression of the condition and to reduce mortality. During the chronic or longer-term phase, patients can be transitioned to oral medications such as warfarin, which is that vitamin K agonist, or DOACs, and then these drugs can be prescribed for a longer-term as needed during that extended phase of treatment. Okay. So moving on to DERP reports. The last DERP Systematic Review for DOACs was completed and presented in May of 2016, so that is about seven and a half years ago. The sources were searched through mid-September of 2015 for that report. DERP conducted two surveillance reports, or scans as they were called back then, since that last report with that last surveillance presented in April of 2018, and sources were searched through February of 2018 for that last surveillance. So the next three slides list the PICOS for the DERP products for the reports on DOACs. The population included adults for the treatment of deep vein thrombosis or pulmonary embolism and for the prevention of subsequent thrombotic events in patients with increased risks. The comparators were other included drugs or any head-to-head studies. Also other anticoagulants which could be oral or injectable agents, also placebo as the sole comparator if that were allowed for studies that looked at prevention. Study designs included randomized controlled trials, comparative effectiveness systematic reviews, and also non-randomized studies. So this table lists the DOAC agents that were included in that last report, and they are in alphabetical order. So we have at the top apixaban, with the brand name Eliquis, which was approved in 2012, dabigatran with brand name Pradaxa, which was the first approved drug in this class in 2010, edoxaban with brand name Savaysa was approved in 2015, and then rivaroxaban or Xarelto was approved in 2011. And they are all Direct Factor Xa inhibitors, except for the dabigatran, which is a direct thrombin or Factor IIa inhibitor. So outcomes for the last report included mortality, thrombotic events, cardiovascular events like heart attacks, functional capacity, quality of life, and several measures for adverse events. There were four Key Questions in the most recent report, and they asked about the evidence for

effectiveness and harms of the included agents only in adults for treatment of a thrombotic event, extended treatment for the prevention of a recurring event, prevention of events in people with atrial fibrillation, and/or after orthopedic surgery, and then how did those outcomes differ by patient characteristics, including by people of different ages, racial groups, gender, among other factors. So now for a very high-level summary of the findings in that most recent report. So overall, the report included 53 studies that compare to DOACs with warfarin, heparins, aspirin, and placebo. 44 of those were randomized controlled trials, four were observational studies, and five systematic reviews were also included. So importantly, as you can see, in that first bullet point, there were no head-to-head comparison trials identified for this last report. However, the report authors did conduct some network metanalyses and included pre-existing network metanalyses into the findings. So in general, again, these are very high-level findings, and so please feel free to go back to the report and dig in as you need. The authors found some evidence for apixaban and rivaroxaban as having lower risks of venous thrombosis and mortality in orthopedic patients compared with the higher doses of dabigatran. In studies of individuals with atrial fibrillation, a higher risk of stroke or embolism was found with 30 mg edoxaban doses compared with apixaban, and rivaroxaban had higher risks of stroke or embolism compared with the higher doses a dabigatran. And that fourth bullet point there, we see that they found no differences in effectiveness among the included agents for initial or extended treatment phases in people with venous thrombosis. And they also mentioned that there was no evidence for extended treatments with edoxaban. Next, they compared these studies indirectly, not via any head-to-head studies or network metanalyses. They found that apixaban, edoxaban, and lower dose dabigatran demonstrated lower rates of major bleeding compared with other DOACs. And lastly, they mentioned that there was insufficient evidence for all other comparisons and outcomes. So surveillance after the most recent DERP report was through February of 2018, and they found one new drug called betrixaban with a brand name Bevyxxa, I think. No new Indications or Boxed Warnings were identified, and then they found 11 new eligible studies. One was a new systematic review on the prevention of venous thrombosis in people who experienced major orthopedic surgery, and 11 were new head-to-head trials. So finally comparative studies were published. Seven were for atrial fibrillation, two were for orthopedic surgery, one was for pulmonary embolism, and one was for venous thrombosis in cancer patients. So now we switch over to new FDA actions since the most recent DERP report. The new drug listed here was the one found during the prior surveillance, betrixaban,

which was indicated for the prevention of thrombosis in at-risk hospitalized patients. That was actually discontinued, and it was on the market for only three years, so that was discontinued in 2020. For new Indications in 2021, the FDA expanded the use of dabigatran to include pediatric patients 8 years and older for the treatment of thrombosis after at least five days of intravenous anticoagulant treatment and for the prevention of recurring thrombosis. In 2018, rivaroxaban was approved to be used in combination with aspirin to reduce major cardiovascular events in adults with coronary or peripheral artery disease and to reduce events after revascularization procedures performed for peripheral artery disease. So here are the FDA-approved Indications for the DOACs of interest as of October 2023. So at the top there we show betrixaban as discontinued in 2020. All of the remaining drugs, so apixaban, dabigatran, edoxaban, and rivaroxaban are indicated for the prevention of stroke in individuals with nonvalvular atrial fibrillation and for the treatment of deep vein thrombosis and pulmonary embolism, and you can see that with those checkmarks in the second and third columns there. All of these drugs, except for edoxaban are then further indicated for the prevention of recurrent thrombosis, including after total knee or hip replacement, which you can see in that fourth and fifth columns. And then only rivaroxaban is indicated for two additional conditions. Those are listed in the last two columns. So we have prevention of thromboembolisms in hospitalized patients and for the prevention of major cardiovascular events in patients with chronic coronary or peripheral artery disease. Since the last report, there have been no new Boxed Warnings that were identified. However, we did find one new Contraindication we thought might be important to report here that was added in 2018 for apixaban, dabigatran, and edoxaban, and that contraindication is for people with triple positive antiphospholipid syndrome, which from what I understand is an autoimmune disorder. So pipeline therapies were identified via the IPD Analytics Database, and we only included those that were either in Phase III trials or had a listed PDUFA date. So we found three pipeline oral anticoagulants; however, these were not listed under the DOAC sub header in IBD analytics but rather under Other Anticoagulants, but we thought it was important to report them here for completeness. All three are undergoing Phase III trials. We have tecarfarin, which is a noncompetitive inhibitor of vitamin K epoxide reductase. It is being studied for the prevention of thromboembolism with end-stage renal disease and atrial fibrillation. It is described as being similar to warfarin but not a vitamin K antagonist. So next, we have Milvexian, which is an oral Factor X1a inhibitor. It is reported to be similar to apixaban and rivaroxaban, but with potentially lower risks for

bleeding. And then at the bottom is BAY24334. This is also a Factor X1a inhibitor, and the end the Phase III trials are studying this drug for the prevention of thrombosis. So for generic status, as of end of October 2023, only dabigatran was available as a generic product in this class, and it became available in 2016, so since the last report. The earliest estimated date possible of generic launch for apixaban is April of 2028, and then for rivaroxaban, that date is March of 2025. And while it appears that there are applications into the FDA for generic manufacturing for edoxaban, it was quite unclear as to when generic options may actually become available according to IBD Analytics and the FDA. On the next six slides, we are providing a very general summary of clinical practice guideline recommendations for the treatment of thrombosis including how and when DOACs are used along the treatment pathways. So for this section, we began with information from the up-to-date clinical decision support online resource and then cross referenced that information with key practice guidelines from professional medical associations, and those are listed at the end of the slide deck. So with initial presentation of thrombosis, oral or subcutaneous anticoagulation therapy is recommended, and the options include low-molecular-weight heparins or fondaparinux, which are both delivered via subcutaneous injections, or DOAC agents are the other options, and decisions around which is best should be based on patient risks for bleeding, any patient comorbidities, and patient preferences. So low-molecular-weight heparin is preferred for patients with cancer, individuals who are pregnant, those with absorption issues, and also individuals who plan on using warfarin, dabigatran, or edoxaban for later long-term use. And finally, intravenous unfractionated heparin is only recommended as first-line treatment in patients with renal failure, and it can also be an option for those with poor gut absorption. So far for thrombosis prevention, the guidelines recommend apixaban or rivaroxaban in patients who are receiving thrombotic anti-cancer therapy, mostly because there is just more evidence for this patient population with those drugs. After discharge to up to 12 months post event, which is also termed as the extended or chronic phase of prevention treatment, the guidelines recommend any of the DOACs, except in people who are pregnant or having renal insufficiency. For pregnancy, actually, observation is preferred over any pharmacotherapy until delivery. And after major orthopedic surgery, except for hip fracture surgery, DOACs and low-molecular-weight heparins are options. Rivaroxaban and apixaban were preferred over dabigatran or edoxaban mostly again because there is more evidence available for those former two agents for that post-surgery population. For individuals at high risks for an event recurrence, the

guidelines generally recommended the continuation of anticoagulation therapy for an extended time, and it was generally recommended that patients continue with those same agents that they were on before if they were well-tolerated and they appear to be working. On the next two slides, we have a little bit more detailed guidelines for the specific types of venous thrombotic events. So here, we have deep vein thrombosis. Initial treatment recommendations are based on the clots locations in the body and on bleeding risk of the patient. So proximal clots are closer to the central core of the body and considered more likely to cause major problems, so if the individual has low bleeding risks, they are treated as was mentioned in the prior slide. But if there is a higher bleeding risk, anticoagulation therapy is recommended after the placement of an inferior vena cava filter. Distal clots are typically located below the knee, and if the patient has a high risk for embolism recurrence but low bleeding risks, they are treated with anticoagulants, as mentioned. But if they have lower risks for a recurring event or high bleeding risks, it is recommended that they forego pharmacologic anticoagulant therapy and should only be monitored by ultrasound. And then as you can see in that green box at the bottom to prevent a recurrence of these events, anticoagulants can be initiated or continued for at least three months. So for pulmonary embolism, after the patient has been stabilized with treatments with anticoagulation therapy is recommended for patients with low bleeding risks only. The inferior vena cava filter is recommended to be placed first in patients with high bleeding risks before anticoagulation therapy. If they remain unstable, reperfusion therapy is recommended first, which is typically fibrinolytic agents that can dissolve that clot. And then similarly as with the vein thrombosis, in the green box at the bottom, DOACs or other anticoagulant agents can be initiated or continued for at least three months for prophylaxis. Finally, for arterial thrombosis with acute coronary syndrome, where the blood flow to the heart is suddenly reduced because of a clot, a triple-drug treatment is recommended to reduce risks of recurrence in those patients who don't undergo a percutaneous coronary intervention (PCI) This includes the DOAC rivaroxaban, plus an antiplatelet drug, as well as aspirin. So the dual antiplatelet therapy or DAPT regimen or a mix of those latter two components. Rivaroxaban was also the recommended agent to be used for antiplatelet therapy. For arterial fibrillation, longer-term therapy with anticoagulants is recommended, and DOACs are the preferred agents. There were no specifics about one type of drug being preferred over another. And then for ischemic stroke, it was mentioned that DOACs actually play a very limited role, if any, immediately after stroke, but recommendations for the

prevention of a recurring stroke are similar to those for the recurrence of arterial fibrillation. So on this slide, we list those relevant key clinical practice guidelines, which are also a reference for the guideline section. They are in alphabetical order of the author or association, and the dates of publication or guideline updates range from 2018 to 2023. And so that is it for this first presentation. Thank you for your attention.

Kavita Chawla: Excellent. Thank you, Andrea. Committee, any questions for Andrea? And if not, Nonye [cross-talk] --

Laura Beste: [Cross-talk] Okay. This is Laura Beste. So I just have one question. So this is an archive presentation. So just to confirm that means that we are reviewing this data, and then this drug class will be archived indefinitely until there is either a new medication that is added to the class or further studies to show difference?

Ryan Pistoresi: Hi, this is Ryan. So when we archive a drug class, that means that we are typically not getting updated reports from DERP, and we are not getting updated surveillance documents. So this means that states have typically voted to not update these drug classes because they are focusing on other newer drug classes. And so the purpose for us is that when we archive a drug class, we are able to do cost analyses and update the preferred and non-preferred status, we just continue to use the same motion that was approved as the last motion. So we continue to carry forward your last recommendation, but we are able to do these cost analyses as the agencies see fit. So a good example is that we did one for the NSAIDs a couple of years ago, even though that drug class has been archived for almost 10 years now. So we could have an updated report in the future in case that there is a major evidence discovery or that there is a new type of drug class in which these are being compared to, but typically, we archive drug classes because we are not expecting any updated evidence products in the near future.

Laura Beste: Thank you.

Kavita Chawla: Other questions from the Committee? I have a question. I don't know if it is for Andrea or for our [indistinct] team. But as we are looking at these DOACs there are also Indications to use DOACs for superficial vein thrombosis depending on the size and location. And I know that that wasn't a specific indication that was covered, but when we approve these medications or

DOACs to go on to the PDL, is it understood that they can also be covered when prescribed for superficial thrombophlebitis?

Ryan Pistoresi: So this is Ryan. And yes, they can be. So typically what you are doing here as the P&T Committee is approving how we should structure the PDL between preferred and non-preferred. When these drugs are being prescribed, it depends on the agency's policy. So for example, when it is an Apple Health client, there may be PA Criteria 4 them, and so that is usually when that is applied. Not necessarily here at the P&T part, but we do cover it for those conditions in our different health plans. It is just that your motion that you are making today doesn't really have an impact on that since that is something that is downstream of the motion and the decision that you are making as part of the P&T Committee. For the DUR Board, right, you know the latter half of these meetings, if we were to make a policy, that is typically where you would see that level of criteria, but we would have to check with Marissa. I don't believe we are bringing a DOAC Policy today.

Kavita Chawla Okay. That is helpful. Any other questions from the Committee? Thank you, Ryan. And if not, Nonye, do we have any stakeholders?

Nonye Connor: No. No stakeholders have their hands raised at this time.

Kavita Chawla: Great. So if we can have you please put up the motion.

Nonye Connor: Okay.

Kavita Chawla: I guess, Andrea, we will have you stop sharing your screen. It should be in that same area where it said share screen. Do you see? Oh, Nonye got it.

Nonye Connor: Yeah, I got it.

Kavita Chawla: Thank you. Okay, so we last reviewed this in 2018. I guess, again, we can use the same template as a starting point.

Laura Beste: This is Laura Beste. I have a question or comment, I suppose, regarding that these are subject to therapeutic interchange. So there are certain populations that have renal insufficiency or geriatric patients, that one of these agents might be preferred over the other, so I would question whether they can just be an automatic therapeutic interchange.

Ryan Pistoresi: This is Ryan. And yes, that is what the P&T Committee decided back in 2018. If you feel that that should not be in the motion today, based off of the report that was just presented, you can amend that section.

Kavita Chawla: That is a great point, Laura. Christy, go ahead.

Christy Weiland: Yeah. I think similar to Laura. I have concerns specifically about rivaroxaban and its increased risk of bleeding and the therapeutic interchange around that as presented by the data today and other associations that have also identified that, like the [indistinct] list and various things.

Kavita Chawla: Yeah, great point. And also on the basis of the presentation today, I see, like, edoxaban, for example, does not have the same Indications as apixaban does. And so, yeah, better safety profile overall for apixaban. So, Committee, how would we like to rewrite, or should we just remove that part of the motion?

Ryan Pistoresi: So this is Ryan. And just for clarity, given that we have typically had therapeutic interchange in this drug class in the past, I would recommend amending it to say these are not subject to therapeutic interchange rather than just deleting it because of maybe [cross-talk] we would carry that language forward. So historical sake, I would say that the best way to amend that if you do not want therapeutic interchange going forward is to specifically state that in this motion.

Kavita Chawla: Okay. Should we say like, instead of listing out just -- or calling out just apixaban, edoxaban, and rivaroxaban, should we just say these agents are not subject -- so, like, the ones that are just listed above the four agents, these agents are not subject to therapeutic interchange? What does the Committee think?

Ryan Pistoresi: This is Ryan. So in the past, the last time that we looked at this class, the P&T Committee did specifically take out dabigatran and left apixaban, edoxaban, and rivaroxaban as the ones that could be. So within this class, dabigatran does not have therapeutic interchange but the other three do. So if you wanted to make sure that none of them -- none of these four drugs -- you could amend to say, the four drugs in the anticoagulant class are not subject to therapeutic interchange, or you could add in dabigatran into that list and just say apixaban, dabigatran, and so on are not subject to, so you have a few options, and either of those would be clearer for our staff when updating the PDL.

Greg Hudson: This is Greg Hudson. Is there any information on the frequency of therapeutic interchange with any of these agents we are discussing? I am just curious before we make this change, if it this would be a major change of practice moving forward. That is [cross-talk] --

Donna Sullivan: I agree.

Greg Hudson: Oh, go ahead, Donna.

Donna Sullivan: This is Donna. I was just going to jump in and say it is probably rarely ever done anymore. In a retail setting. A lot of the chain drugstores won't allow their pharmacists to make these interchanges without getting a new prescription anyways. So it is kind of still a requirement because of the Legislation, but I don't think in practice it is done that often unless you have maybe an independent pharmacy working with a provider's office where they already had a collaborative practice agreement or something of that nature in place, but I think it is pretty infrequent.

Kavita Chawla: That is helpful. With that information, what does the Committee think about updating the language?

Laura Beste: This is Laura Beste. I liked Ryan's suggestion. The four medications within this class. Or was it the four anticoagulants listed within this class that cannot be subject to therapeutic interchange.

Kavita Chawla: Okay.

Ryan Pistoresi: So this is Ryan. And I would just clarify that for this class, just given that warfarin is another anticoagulant, and it is outside this class, so just making it clear that it is these four that were reviewed today in case that there are new anticoagulants included in this class in the future.

Kavita Chawla: Yeah, Kavita here. So I think Ryan said, too, just add dabigatran to that list. [cross-talk] I think, Nonye, that is what you were starting to do.

Ryan Pistoresi: Yeah. So that would fit in right there. Yeah.

Kavita Chawla: And then we will say cannot. I guess, make that one word if we can/cannot. Okay. All right. What does the Committee think of that? It looks okay. Other comments or edits?

Dimitry Davydow: I think it just needs an Oxford comma after edoxaban.

Nonye Connor: Oh, thank you.

Dimitry Davydow: We are good.

Kavita Chawla: We need this -- we need it to be grammatically correct as well. All right. Any other comments, or are we ready to proceed with the motion?

Dimitry Davydow: This is Dimitry Davydow. I am ready to proceed with the motion. After considering the evidence of safety efficacy and special populations for direct-acting anticoagulant drugs for their FDA-approved Indications, I move that apixaban, dabigatran, edoxaban, and rivaroxaban are safe and efficacious for their approved Indications. Apixaban, dabigatran, edoxaban, and rivaroxaban cannot be subject to the therapeutic interchange in the Washington Preferred Drug List.

Peter Barkett: 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 abstain? And the motion carries. All right. So per the schedule in front of me, I think we are running about eight minutes behind. Nonye, is this a good time to take a break?

Nonye Connor: Sure. Not a problem. Do we want to come back at 11:10? I think that is 10 minutes, right?

Kavita Chawla: Yes. Sounds good. All right. We will see the Committee back in 10 minutes at 11:10.

[break]

Kavita Chawla: Forum? Yep, I see a forum. Okay. We are ready to move forward. Andrea, back to you covering the Antiplatelet drug class.

Andrea Vintro: Great. Okay, hopefully that is up there. Great. Okay, again, my name is Andrea Vintro. Let me see here. You can all hear me, correct?

Kavita Chawla: Yes.

Andrea Vintro: Great. So I am a Research Associate here at the Center for Evidence-Based Policy. And just as a reminder for those of you that were with me for the previous presentation for this drug archiving project, I will be repeating all the topics for this in the final report because there may be new audience members that we are recognizing for each of these different reports, so including topics like the aim of the project overview of the presentation, etc., so bear with me. So this is the second of seven presentation reports for the nine drug classes of interest for this Washington Drug Archive Project. Today, we are reporting on four drug classes in three presentations, and the remaining five will be presented in June. So this is the second presentation for this project today, and it is titled Newer Antiplatelet Drugs. The aim of this work is for the Drug Effectiveness Review Project, also known as DERP, to develop and present information to the Washington State Pharmacy and Therapeutics Committee on nine drug classes that are candidates to be archived from active review by the Committee. And you can see that list of drug classes that are included in the project at the bottom of this slide, and that class of antiplatelets is highlighted in green for this presentation. So this report will have you review the items in the darker green boxes on the slide for the drug class of newer antiplatelet drugs, and that is in order from left to right. So we will start with the left. I will first define the health conditions of interest that this drug class is intended to address, then summarize the general epidemiology and treatments for the condition, and then I will review key information in the most recent DERP reports for this drug class, including the PICOS and Key Questions, a high-level summary of the Key Findings in that report, and then General Findings of any surveillance that was completed after that last systematic review. Then I will move to any new actions by the FDA since the last report, including any new drugs, new Boxed or Serious Warnings, any new Indications, and there, I will also present the current FDA-approved Indications for all of the drugs of interest. Then I will move on to report any current pipeline -- current drugs in the pipeline and then also the generic status of existing FDA-approved drugs. And then, finally, I will provide this high-level summary of relevant clinical practice

guidelines for this condition, which includes information about how and where these drugs are used along the treatment pathway. And then we will answer any questions you have, and that will be followed by discussion. So our conditions of interest are complications of atherosclerosis. So in other words, any cardiac or cerebrovascular event that is caused by atherosclerosis, which is that narrowing or hardening of the arteries, typically caused by the buildup of plaque, which is composed of fatty-like substances of cholesterol, cellular waste products, calcium, as well as fibrin, which is that clotting material in the blood. So while the conditions treated by this drug class appear similar to the conditions for thrombosis, which was the condition of interest for the for the last report on anticoagulants, it is different because here we are talking more about the secondary prevention of vascular events, where the blood flow is not blocked by blood clots but rather because of atherosclerosis. So the three primary subgroups of atherosclerosis are ischemic, coronary artery disease, cerebrovascular disease, which affects blood flow to the brain, and also, peripheral artery disease, which is when the atherosclerosis is happening usually in the legs or extremities. And with these conditions, there are risks for vascular events where there is this lack of oxygen to the tissues and can result in myocardial infarction or heart attack or stroke, also an injury to the arms or legs. So risk factors for atherosclerosis include unhealthy lifestyle behaviors, such as having a poor diet or inactivity. Also medical conditions such as hypertension, diabetes, excess body weight or obesity, also having Polycystic Ovarian Ovary Syndrome or PCOS among other conditions that are listed there. Also having a family history of atherosclerosis increases risks as well as being of advanced age. In fact, the risk increases after age 45 in men and at after 55 in women. The prevalence of cardiovascular disease in the US is quite high at nearly 50% of all US adults, according to NHANES data, and in 2020 100,000 individuals died of heart disease and stroke. Cardiovascular disease is the leading cause of death in adults in the US. Risk of death is highest in Black and Asian populations. The MESA study, which is an acronym for multiethnic study of atherosclerosis, was a large prospective observational study that was conducted in the US, and it found black participants had a 34% higher mortality risk compared with white participants. And CDC data show that about one in four deaths in males and one in five deaths in females are due to heart disease alone. While we do recognize that interventions for primary atherosclerosis and associated conditions can indirectly reduce cardiovascular events, these interventions are out of scope for this presentation, and that is mentioned at the bottom. So these would be interventions like healthy lifestyle behaviors or drugs for

high blood pressure or diabetes medications for example. This report again focuses on those agents for the treatment and prevention of the complications of atherosclerosis, which include cardiovascular events. So treatments are mostly pharmaceutical in nature, and those include nitrates, which dilate the arteries and can relieve or prevent angina, which is the pain around the heart or pressure in the chest. Intravenous antiplatelet agents, like glycoprotein IIb/IIIa inhibitors are commonly used in the acute phases of poor initiation of therapy. Aspirin has been considered the standard blood thinning agent for many years, but in the past decade, newer antiplatelet agents have been developed as substitutes for or in combination with aspirin in certain clinical situations, and this is commonly referred to as the dual antiplatelet therapy (DAPT). And the mechanisms of these newer antiplatelet therapies include adenosine reuptake inhibitors, P2Y12 receptor blockers or inhibitors, and also protease-activated receptor- antagonist or PAR 1 antagonist, and these antiplatelet agents, they decrease platelet aggregation and inhibit thrombosis formation, and they are effective in the arterial circulation where the sort of classical vitamin K antagonist anticoagulants don't have much of an effect. So the last DERP Systematic Review that was titled Newer Antiplatelet Drugs was completed and presented in August of 2017. The sources for that report were searched through mid-April of that year. DERP conducted one surveillance report since that 2017 report, and that was presented in July of 2018, and the sources for that report were searched through June 22, 2018. So the next three slides list the PICOS for the DERP products for this drug class report. The population included adults with at least one of the following conditions: acute coronary syndrome, recent or ongoing coronary revascularization by stenting or CABG, prior ischemic stroke or transient ischemic attack, and symptomatic peripheral artery disease. So comparators included Other Oral Antiplatelet Drugs, so any head-to-head trial, also placebo or aspirin, only if there were no head-to-head studies found for a particular drug. Study designs included randomized control trials, retrospective observational studies, and systematic reviews. This table lists the interventions that were included in the last report, and they are in alphabetical order by generic name. And just to point out something fun here a fun coincidence, they are also in order of FDA approval. And I do want to mention that in the report the intravenous drugs of ticlopidine and cangrelor were specifically excluded, so all of these agents listed here are delivered orally only. So we have clopidogrel at the top with brand name Plavix, which was approved in 1997, and you can see that notation of the letter B there indicates that this drug is to be taken alone or in combination with aspirin. Next, we have dipyridamole with brand name

Persantine, approved in 1998. That notation C there indicates this drug has been approved only in combination with aspirin. Next is Aggrenox, approved in 1999. It is a combination fixed-dose drug of dipyridamole and aspirin. And then Prasugrel, brand Effient was approved in 2009. And then ticagrelor, with brand named Brilinta was approved in 2011. And finally at the bottom, the most recently approved anticoagulant, Vorapaxar or Zontivity, was approved in 2014. This drug is the only PAR-1 reversible antagonist of the bunch. In the far right column, you can see also that three of these agents utilize the mechanism of P2Y12 inhibitor. So outcomes for the last report included all cause mortality, cardiovascular mortality, heart attack, stroke, and failure of an invasive Vascular Procedure and that was for the efficacy, efficacy and effectiveness outcomes. On the right there we have the safety outcomes, which included overall adverse events, withdrawals due to adverse events, serious and specific adverse events, as well as withdrawals due to adverse events. The four Key Questions in this last report asked about the difference in effectiveness and harms of these agents in the populations of interest. As you can see in Key Questions 1. and 2. Key Question 3. asked about differences in outcomes across patients' subgroups. And then Key Question 4. asked about differences in outcomes depending on the duration of the therapy. So this is a brief summary of the findings of that last report. And as you can see, by the superscript letter A there that notation at the top, it was somewhat unclear as to the actual total number of studies included in that final report versus those that were newly added to the update because we have since changed how we report the methods and included studies. So, for example, how many were primary trials versus ancillary publications or assistant public publications? So that was sort of difficult to discern. So this is our best estimate. We believe that there were 48 studies included overall with 44 randomized controlled trials, three cohort studies in one pooled analysis. For Key Findings, they found that there were few differences in cardiovascular benefits across all of the comparisons that were included of the antiplatelet drugs, and then any benefits that were there were small and likely not clinically meaningful. They also found that vorapaxar as an add-on treatment to existing antiplatelet therapy compared with placebo showed no additional benefits in people with atherosclerosis but did show small benefit in patients with a history of heart attack or coronary artery disease, although major bleeding was increased in all of these populations. So continuing on with Key Findings, they also found that in individuals with acute coronary syndrome or a prior MI, they found that compared with ticagrelor, there were no differences in effectiveness or harms with prasugrel. More cardiovascular events but fewer adverse events, withdrawals with

clopidogrel, and then more cardiovascular events but fewer or less bleeding and fewer adverse events withdrawals with aspirin compared with prasugrel, clopidogrel resulted in more major cardiovascular events but fewer major bleeding events. And then in individuals with peripheral artery disease those randomized to clopidogrel experienced more strokes but fewer withdrawals due to adverse events compared with ticagrelor. And then finally, in stroke or transient ischemic attacks, those who were randomized to clopidogrel. So compared to clopidogrel, they found no differences in effectiveness or major bleeding, but more overall adverse events compared with the combined product of the dipyridamole extended-release plus aspirin. And then compared with aspirin alone, there were no differences in effectiveness and major bleeding but more overall adverse events with ticagrelor and, again, this is compared with clopidogrel. For the surveillance -- it is the last report -- they found no new drugs, no new formulations or Indications or serious harms. There was one new systematic review of ticagrelor compared with other antiplatelet agents and placebo for stroke prevention. They also found four new head-to-head studies, three were for ticagrelor compared with clopidogrel, and one compared ticagrelor prasugrel in people with myocardial infarction. For new FDA-approved drugs and action since the most recent report, I did list here Yosprala here as a new drug for completeness. Again, it was discontinued in 2018, so there is not much else to say other than it was a fixed-dose combination drug of aspirin and omeprazole. There were two new Indications for ticagrelor. In 2020, the FDA expanded its approval for the prevention of heart attack and stroke in people without prior events but are with high risk because of existing coronary artery disease, and also for risk reduction of recurring stroke and people with a history of stroke or in those who have had high-risk transient ischemic attacks (TIAs). So on this slide, we have the FDA-approved Indications for the antiplatelet agents of interest in this report. So walking across the Indications. In that top green header row we see that clopidogrel and ticagrelor, those are listed there in the second row from the bottom are both indicated for reducing risk for heart attack, stroke, and/or death due to cardiovascular events in patients with acute coronary syndrome, and in column three there in patients with a history of heart attack or stroke if they have peripheral artery disease, so a lot of conditions. And as you can see, vorapaxar in the bottom row there is also indicated for that lateral population. In the fourth column we have an indication of reducing risk of from thrombosis in people who received cardiac valve replacement, and only dipyridamole is approved for that specific indication. Moving over to the next column we see that the fixed combination dose drug of extended-release

dipyridamole plus aspirin, however, is indicated for reducing the risk of stroke in people with a history of stroke. And ticagrelor, again, in that second row from the bottom also has an indication. In the sixth column, we can see that prasugrel and vorapaxar -- I might need to take a sip of water here -- are indicated for reducing risk of thrombotic cardiovascular events in people with stents. That final indication listed is for the prevention of the first stroke, not just a recurring stroke, in individuals with high risk of stroke. And then ticagrelor is the only drug included here with that indication. So that last column on the far right highlights that most of the drugs are indicated to be used in combination with aspirin, so as dual therapy agents. Since the last report, we found no new Boxed Warnings, but there were two new contraindications for ticagrelor and vorapaxar in 2019. These drugs are not recommended for individuals who are breastfeeding, and only vorapaxar listed a new contraindication for individuals who are pregnant. And we found no current oral antiplatelet pipeline agents. And again, we are only looking for those agents or drugs that are either in Phase III trials or that have a pending PDUFA date. So next, we will move on to generic status of the use drugs. So as of the first of November 2023, three drugs have become newly available as generic since the most recent report. Those are clopidogrel, the fixed-dose combination product of dipyridamole plus aspirin and prasugrel. Dipyridamole was also available was already available as a generic with the last report. And then at the bottom we can see that neither ticagrelor nor vorapaxar are available as generics. And again, according to IPD Analytics, the earliest possible generic launch that they have identified for ticagrelor is May of 2025. And then the patent for vorapaxar was reported to expire in December of 2027, so probably around that time as well. On the next six slides, we provide a very general summary of clinical practice guideline recommendations for select complications of atherosclerosis in the populations of interest, including how and when these included oral drugs are used along the treatment pathways, the oral antiplatelet drugs of interest. So for this section, we began with the information from the up-to-date clinical decision support online resource and then cross-referenced that information with key practice guidelines from professional and medical associations, which are which are listed in the last slide of this slide deck. So we begin with the complication of myocardial infarction, which is defined as cell death that damages or destroys heart tissue. And we also recognize that there are many clinical categories for types of MI, so just understand that these are very general recommendations. We have them listed here under either acute ST-elevation on this slide and the non-ST-elevation on the next. So acute ST-elevation MI is when there is complete blockage of the artery, so

initial management is with mechanical stenting and/or intravenous treatment for fibrinolysis, as you can see in that first bullet point there, which is then followed by a recommendation to initiate dual antiplatelet therapy or DAPT as early as possible, and this includes the antiplatelet drugs in this report in addition to aspirin. The types of antiplatelet drugs depend on the reperfusion strategy, but only the P2Y12 drugs are recommended here. So if the individual has a stent placed, guidelines typically recommend starting with ticagrelor or prasugrel. If they start with fibrinolysis treatment, they recommend a loading dose of clopidogrel. No antiplatelet drugs are recommended if the patient is preparing for a CABG procedure, and then to start with, they recommend starting with ticagrelor if patients are not undergoing reperfusion. And this dual antiplatelet therapy can last for at least 12 months unless there is high risk for bleeding. Then for partial blockage or non-ST-elevation coronary syndrome, the guidelines mention that most patients should receive dual antiplatelet therapy if they do have a stent placed or undergo other invasive procedures. They should -- it is recommended that they receive ticagrelor if there is ample time between identification of the condition and surgery, and then after the procedure ticagrelor or prasugrel were recommended. If the invasive procedures are not done, the more conservative ischemia-guided strategy includes starting ticagrelor as soon as possible, and then dual antiplatelet therapy is to be continued for at least 12 months, again, depending on bleeding risk. So on this slide we have the summary of guidelines for individuals with coronary artery disease who have undergone a PCI and are at risk for another cardiovascular event. So for the first year they recommend initiating a triple therapy of oral anticoagulant, a P2Y12 inhibitor, and aspirin therapy, and then after one week consider dropping the aspirin. For patients with stable coronary artery disease, clopidogrel is recommended over prasugrel or ticagrelor. And then for acute coronary syndrome, clopidogrel or ticagrelor are recommended, but, again, that will depend on bleeding risk. In the same population, we move to what the guidelines say that longer-term therapy. Anticoagulants are recommended with or without oral antiplatelet agents as needed. Clopidogrel is preferred over prasugrel or ticagrelor for the more stable patients that require DAPT. These two drugs are considered more potent P2Y12 inhibitors, which is often why they are preferred over clopidogrel in patients with acute coronary syndrome. And then finally, patients are typically on this dual antiplatelet therapy for 6 to 12 months, depending on risks for bleeding and on risk for recurring events. And now we are moving on to complication for stroke. So for acute treatment, aspirin is typically the first-line treatment alone or with clopidogrel, and timing

depends on other treatments or procedures with stroke. And then for longer-term prevention, aspirin alone or clopidogrel alone are recommended as best options. And in some cases the extended-release dipyridamole plus aspirin can be indicated, but it was reported that DAPT is generally not recommended because of the lack of evidence in this population, and it comes with an increased risk of bleeding. So finally, we have the summary of recommendations for the prevention of secondary cardiovascular events in individuals with peripheral artery disease. So long-term antiplatelet therapy is recommended for patients with symptomatic lower extremity peripheral artery disease, and aspirin and clopidogrel were examples of drugs that were recommended. Finally, since it wasn't commonly mentioned, I did want to search for the drug vorapaxar. It included guidelines. Interestingly, they indicated vorapaxar was typically reserved only for patients with very high risks for these secondary events because of the high bleeding risks with this drug. So it was either not mentioned in the guidelines or just as an option for oral antiplatelet agents, and again, for patients with peripheral artery disease only, even though the FDA indication is for the prevention of events and individuals with history of MI, stroke, as well as peripheral artery disease. So here is the final slide where we list the relevant key clinical practice guidelines that were also referenced for this guideline section. Again, they are in alphabetical order of author or professional or organization, and the dates of publication or the guideline update ranged from 2014 to 2013 -- excuse me, through 2023. Let's end it with it being correct. That is it for this presentation. And I can pass it back to you all.

Kavita Chawla: Thank you, Andrea. Excellent exhaustive review there. Any questions from the Committee for Andrea? Okay, hearing none. Nonye, do we have any stakeholders?

Nonye Connor: No, not that I see at this time. No.

Kavita Chawla: Okay. We can pull up our motion. Great. You are on it. All right, so we will use -- okay, I see that we -- yeah. So there are two motions. One is for ACS and the other is for stroke it looks like. Am I reading that right? Okay. So let's start with that as our big -- oh, you did already. Okay. So it is interesting. I wonder, maybe, if Ryan can speak to it why we have that last sentence. It is "at this time vorapaxar is included on PDL as a nonpreferred drug? Is there a reason that needs to be part of the motion?

Ryan Pistoresi: So this is Ryan Pistoresi. That is a good question. I think I would need a bit of time to research and see what the discussion was from the P&T Committee at the time this was last reviewed. Nonye, if you can scroll down just a bit onto the second page. Yeah. So it was back in 2018. I probably wouldn't be able to research it between now and the time that this meeting is over, but I think it was based off of the discussion that the Committee had, and they felt that vorapaxar should not be a preferred drug and that we should have some of the other drugs be eligible to be preferred. So essentially, that line there just says that vorapaxar is not eligible to be preferred. It can still be accessed, but it just means that patients and providers would need to try preferred alternatives first before being allowed access to vorapaxar.

Kavita Chawla: I see. Okay, that is helpful.

Zoe Taylor: Can I ask? We don't review any like class data at this meeting, so how is that decided if not based on costs? Like, I assumed that like all those preferred things are all based on costs as a clinician.

Ryan Pistoresi: Yes. Yeah. So this is Ryan again. So the way that this P&T is structured is you are reviewing the safety and efficacy and effectiveness of the drugs as presented by our third-party Drug Effectiveness Review Project. Once we have your motions about how our PDL should be structured, we will go back and work with the actuaries that Donna had mentioned earlier, and we look at the rebate opportunities and how we could structure our PDL. So after this meeting, our teams work together to create these stakeholder memos and agency director memos that then update and share what the final results are after we do those analyses. But because of the way that this is set up, we don't actually review any of that cost data here within a P&T meeting. Thank you, Ryan. Go ahead, Donna.

Donna Sullivan: Yeah. So I just wanted to add, I mean, we are trying to shield the Committee from [cross-talk] --

Zoe Taylor: [Cross-talk] That makes sense.

Donna Sullivan: -- we are trying to shield the Committee from having to make sometimes those costs decisions that you are really here to look at the data and see, are there any drugs that really stand out that you might say, "This one has to be preferred," just as the Committee back in 2018 said, "this one should not be preferred." But generally, we don't have you make those recommendations

because you are not looking at the cost, and if they are relatively equally efficacious and equally safe, then let's choose the lowest cost product. With Medicaid, it becomes a challenge because the costs are in proprietary. We can't disclose publicly what the net of rebate costs are, and so that makes it extremely difficult to try to share that information with the DUR Board because we are required to have open public meetings. And so that is another reason why that we don't share that information for the Committee.

Zoe Taylor: So if we decide that vorapaxar is non-preferred, does that mean that we are deciding that it is a less good drug, clinically? [Cross-talk] but we are not like neurologists, and so like shouldn't the neurologists decide that, and we should just say, like, because there is a huge burden, if there is a patient where for some reason that we don't understand that is the best drug for them, or they have tried all the other ones and they are allergic. And I guess, like there is a balance between trusting the neurologists that they are not going to use something that is not as good unless it is really needed and us putting up barriers to them doing so, if they are not based on cost considerations [cross-talk] --

Donna Sullivan: [Cross-talk] And this Donna [cross-talk] --

Zoe Taylor: [Cross-talk] And as a new member, that is what I am just trying to, like, grapple with.

Donna Sullivan: Yeah. I mean, you could say that for any drug that is considered non-preferred [cross-talk] --

Zoe Taylor: [Cross-talk] Right.

Donna Sullivan: -- so there is there is a process. If their neurologist feels that this drug is the one that is appropriate for this patient and that they shouldn't have to try a preferred drug, they are able to submit an authorization request [cross-talk] and document that medical necessity, and those get reviewed on a case by case basis.

Zoe Taylor: Yeah.

Donna Sullivan: So there is access, but it is just, we, the Committee, like Ryan said, for whichever reason, you can just strike. If you no longer agree with that sentence, you are more than welcome to strike that from your current

motion. You don't have to reiterate that piece of the motion if you disagree with it. but there is a process kind of behind the scenes to get the non-preferred drugs when medically necessary.

Zoe Taylor: I understand. Just as a primary care doctor who has to do that process, I am very sensitive to the fact that, like, it takes a lot of time, and we should be trying, when reasonable I think, to minimize those barriers. I have never heard of vorapaxar, so I have no opinion either way. I just think the attention is, like, are we purporting to know more than the provider who would be prescribing this? Anyway, it looks like Kevin has his hand up.

Kavita Chawla: Go ahead, Kevin. [Cross-talk] --

Kevin Flynn: [Cross-talk] Oh, sorry. My only comment is that ticlopidine was discontinued. And I know we sometimes leave it on there for because like we are waiting for like Medi Span or something like those updates, but it has been several years. Can we remove it now?

Kavita Chawla: Kavita here. I would agree with that, unless any Committee members have comments or -- Donna, go ahead.

Donna Sullivan: No, that is fine with me. So, Nonye, could you just gray it out?

Ryan Pistoresi: Yeah. This is Ryan. So typically, we do leave them on there to show that, yes, this was a drug that we reviewed, and even though it is no longer on the market, it can't be accessed. And I think in the upper left, you will also need to gray it out in that reviewed list to the left that [cross-talk] --

Donna Sullivan: It doesn't appear unless [cross-talk] --

Ryan Pistoresi: Oh, no. Right.

Kavita Chawla: Yeah, it is not on there.

Donna Sullivan: [Cross-talk] Can you just delete the sentence? I don't want to delete the sentence in a former motion, but if this is for today's motion, then [cross-talk] go ahead and delete that I move ticlopidine products not be included due to safety concerns because it is no longer relevant, which basically means you just can't reiterate the motion. You have to say it over again.

Kavita Chawla: And Kavita here. Going back to the initial comment about the vorapaxar, I imagine that the previous Committee maybe included and they are calling it out as a non-preferred agent because it just compellingly looks like all of the other agents are so much more effective than vorapaxar, but that is -- I will say that this is one of the rare times that I have seen that being included in the motion. So with that, what does the Committee think about leaving that last sentence as is versus removing it or rewriting it?

Laura Beste: This is Laura Beste. I feel it should be removed for consistency reasons as the other motions that we make don't call out which medications are preferred and not preferred within the motion.

Ryan Pistoresi: So this is Ryan, and in the past if you feel that certain drugs on the PDL must be preferred, you can make that as part of your motion, just like you are able to say certain drugs are not eligible to be preferred. So if there are certain drugs in which you understand the safety and efficacy feels superior to other ones, you can make that recommendation for certain drugs to be preferred, like with the ADHD motion from earlier with some of those non-stimulants that were included in that motion.

Kavita Chawla: Thank you, Ryan. That is helpful for the Committee. Go ahead, Christy.

Christy Weiland: Yeah. So to kind of piggyback off of that, so would it be more appropriate than to state one of the preferred agents should be clopidogrel, prasugrel, or ticagrelor? Is that a more clear? Like, Laura, does that offset the line that you wanted to remove? Or what do you guys think about that, then, identifying which one should be preferred by giving those options and just making sure that the only preferred agent wasn't the vorapaxar?

Kavita Chawla: Kavita here. It seems to me that majority of the time most clinicians are not going to pick vorapaxar anyway, so I think we might be wordsmithing but without maybe any clinical implications. And so I think to Laura's point, just to be consistent across our motions, if we don't really have strong feelings about it, we just eliminate that sentence, then I think [cross-talk] --

Laura Beste: [Cross-talk] So this is Laura Beste. [Cross-talk] --

Kavita here: Yeah, go ahead.

Laura Beste: What is odd is that it specifically lists that clopidogrel, ticagrelor, and prasugrel are safe and efficacious, but it doesn't mentioned the vorapaxar as being safe and efficacious.

Kavita here: Yeah.

Laura Beste: So I think that is why they probably added that? But I don't know that we have reviewed enough data to state that it is not safe and efficacious. It just has higher risks than the other agents.

Kavita Chawla: And along those lines, I also don't see dipyridamole listed on there. I don't know if it -- oh, that is just listed [cross-talk] --

Laura Beste: [Cross-talk] Down below --

Kavita here: -- on the screen section. Yeah, that makes sense. Okay, so what are the thoughts of the Committee to remove the last line or addend as Christy proposed? We would like some votes so we can move forward. So I will vote to maybe just remove the last line. Any other thoughts?

Ryan Pistoresi: So this is Ryan. So if you do remove the last line on vorapaxar, you will want to include something about your decision on vorapaxar within the motion, so if you feel that it is safe and efficacious based off of the information that you saw today, you could delete that line and then move it into the sentence before -- or two sentences before, I guess, otherwise, you will want to leave that line as is to show that you did not feel that there was enough evidence to determine that it is safe and efficacious and should not be preferred.

Kavita here: If I can follow up, at least one of these antiplatelet agents will be always preferred? Is that correct? For every class, is there always at least one preferred drug?

Ryan Pistoresi: This is Ryan. Yes. In my experience, anytime that we have had one of these P&T classes, we have always had at least one preferred.

Kavita Chawla: Okay. Okay, so that is helpful. And it already states on here that the antiplatelets cannot be subject to therapeutic interchange. So that also takes care of any concerns about vorapaxar being prescribed inappropriately or dispensed inappropriately. So other comments from the Committee?

Kevin Flynn: I just think because it is "less good," maybe we just leave it because I doubt many people are prescribing it anyway.

Kavita Chawla: Okay.

Kevin Flynn: The top three are basically what everyone chooses between and what the guidelines talk about.

Kavita Chawla: Okay. Any other comments? Okay. Does anybody want to proceed with a -- oh, I guess we should also look at the Stroke/TIA section. Any addendums there or edits? If not, we are ready to entertain the motion whenever the Committee is ready.

Kevin Flynn: This is Kevin Flynn. I move after considering the events of safety, efficacy and special populations for the treatment of acute coronary syndrome, percutaneous coronary intervention, and peripheral vascular disease, I move that clopidogrel, ticagrelor, and prasugrel are safe and efficacious for the treatment of their approved Indications. The antiplatelets cannot be subjected to therapeutic interchange in the Washington Preferred Drug List. At this time, vorapaxar is included on the PDL as a non-preferred drug, and after considering the evidence of safety, efficacy and special populations in the treatment of stroke and transient ischemic attack, I move that extended-release dipyridamole, aspirin, and [audio cuts out] are safe and efficacious. The extended-release dipyridamole, aspirin, and clopidogrel can not be subject to therapeutic interchange in the Washington Preferred Drug List for the treatment of stroke and transient ischemic attack.

Dimitry Davydow: This is Dimitry Davydow. 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. And we will bring Andrea back to review the statins and PCSK-9 drug class.

Andrea Vintro: One more time with me. Okay. Let me share my screen again. Okay. We shall get started. Once again, Andrea Vintro here. I am a research associate at the Center of Evidence-Based Policy. Just another reminder for those of you who were with me for at least one of my last two presentations for this drug

archive project, I will be repeating all of the topics for this final report today because there may be new audience members, meaning I will repeat the aim, overview of the presentation, etc., so bear with me. So this is the third of seven presentation reports for the nine drug classes of interest for this archive project. This is the last set in the series to be presented today. We continue with the theme of medications for cardiovascular conditions. So this presentation is a combined report of two drug classes because of the significant overlap in the Indications for these drugs. So this final presentation is instant as titled HMG-CoA reductase inhibitors (statins), and PCSK-9 inhibitors. I won't even attempt to try to say the full term out loud for all of your sake. Okay. So the aim of this work is for the Drug Effectiveness Review Project, also known as DERP, to develop and present information to the Washington State Pharmacy and Therapeutics Committee on nine drug classes that are candidates to be archived from active review by the Committee. So you can see the list of the classes that are included in this project at the bottom of the slide with the two drug classes to be presented in this report, highlighted in green. So this presentation will review the topics in the dark green boxes on this slide. So in order from left to right, starting on the left -- yes, on the far left I will first define the health condition of interest that these drugs are intended to address, then summarize the general epidemiology and treatments for the condition, and then for each of the drug classes I will review the key information in the most recent DERP reports. So for both of those drug classes, I will include the reports for the information for the PICOS, Key Questions, a high-level summary of the Key Findings for the reports, then General Findings of any surveillance that was completed after that last systematic review. Also any new FDA drugs or Indications or actions since the last report, and also any relevant pipeline agents, and then the generic status of the included drugs of interest. And finally, I will provide a high-level summary of relevant clinical practice guidelines for the condition, which should include information about how and when these drugs are used along the treatment pathway. And then we will follow up with questions and a discussion. Because of the larger volume of text in these slides, particularly because this is a large, combined drug class report, we thought it would be best to provide only abbreviated terms in the PowerPoint for readability, and those are only for the terms that are commonly abbreviated in the clinical literature, so this slide is then here for your reference as the key to those abbreviations. So the condition of interest for the two drug classes in this presentation is high blood cholesterol, specifically low density lipoprotein or LDL cholesterol, which is a relatively dense molecule in the blood consisting of lipids, cholesterol, and proteins,

including apolipoprotein B, and it appears to be one of the better predictors of risks for atherosclerosis and cardiovascular disease compared to the other lipid proteins in the blood, like HDL, high-density lipoprotein cholesterol or VLDL cholesterol are also even blood triglycerides. There's a decent volume of research out there that indicates elevated LDL cholesterol is a major cause of coronary heart disease, and with the progression of atherosclerosis, risks for heart attack and stroke also increase. High blood LDL cholesterol is attributed to a number of factors including genetics, poor lifestyle habits, like smoking, poor diet, being inactive, and also there are higher risks in older individuals, and they are more likely to have elevated HDL. On the right side of the slide we also have the cutoff values for LDL cholesterol risk classification. According to the National Cholesterol Education Program (NCEP), normal or optimal LDL cholesterol levels are considered to be below 100 mg/dL, high LDL cholesterol is considered from 160 to 189 mg/dL, and an LDL of 190 mg/dL or higher is classified as very high-levels. So approximately 40% of all US adults have elevated total blood cholesterol, so that includes the LDL and HDL cholesterol as well as a portion of blood triglyceride levels. But the CDC also noted that this number could be greater than 40% because many individuals don't experience other symptoms, so they might be unaware that they have the condition. Familial hypercholesterolemia affects about 1:250 individuals in the US. This is a genetic condition caused by a chromosomal defect, so the heterozygous form is more common, but the homozygous form is more rare, however, it is more serious and can result in heart attacks during childhood. With high LDL cholesterol comes the increased risk of cardiovascular events, including stroke and heart attack, especially in older individuals. Evidence also shows that when LDL is lowered, the risks for those events decrease. Although the available demographic data showed that white and Hispanic adults have higher rates of elevated total cholesterol than black compared with black individuals. The numbers show that black adults have both a higher prevalence of cardiovascular disease, and they have a higher rate of mortality due to cardiovascular disease. The next three slides show some common treatments for high blood cholesterol. So we are starting with the common pharmaceutical agents on this page. So here we have four of the eight antihyperlipidemic drug classes that are options to treat elevated blood cholesterol and triglyceride levels. So the rows in blue are the drug classes that are included in this presentation. The leftmost column lists the class of drugs followed by the mechanism of action and then in the far right column, we list the common primary indication for that drug class. So starting with statins, they work by inhibiting the HMG-CoA reductase enzyme which

reduces the synthesis of cholesterol in the liver. And then if you look in the right column, you can see that they are considered as first-line treatments for high blood cholesterol. Next is as ezetimibe, which is a selective cholesterol absorption inhibitor, which limits absorption in the gut. And then we have PCSK-9 inhibitors, which limit the breakdown of LDL receptors on the surface of liver cells so that more LDL can be cleared from the bloodstream, lowering blood cholesterol levels. And that bottom row we have prescription Omega-3 fatty acid esters, so at those higher doses these agents help to reduce the synthesis of LDL cholesterol and triglycerides in the liver, leading to low lower blood cholesterol and this agent is as most commonly used for people with high triglyceride levels. These are the remaining four common pharmacological agents typically used for lowering blood cholesterol. So fibrotic acid derivatives target the LDL cholesterol molecule. It is more often recommended for people with hypertriglyceridemia, but it also demonstrates a moderate decrease in LDL cholesterol as well as increases in the good HDL cholesterol. In the next or third row, we have bile acids sequestrants. They work in the gut to reduce absorption of dietary cholesterol. And then we list also higher prescription doses of nicotinic acids, which are also good for people with primary hypertriglyceridemia because they affect the production of VLDL and triglycerides from the liver. And then in that bottom row, we have adenosine triphosphate-citrate lyase (ACL) inhibitors. These are newer agents of bempedoic acid. These drugs inhibit ATP citrate lyase, which lies sort of two steps upstream from HMG-CoA reductase in the cholesterol synthesis pathway. So here we list common nonprescription treatments for hypercholesterolemia. They include lower doses of Omege-3 fatty acids, polyunsaturated fatty acids, and also niacin, which can be found in dietary supplements. And as we all know, these can be purchased over-the-counter, but they are not regulated by the FDA. Although healthy lifestyle behaviors are listed here, you are likely aware that these are first-line interventions for improving blood cholesterol. And they are also typically recommended concomitantly with pharmaceutical agents, and those include a healthy low-cholesterol and high -fiber diet, increased physical activity, weight -- achieving a healthy body weight, and then also avoiding smoking. And then combining all of these treatments, so combining drugs from within and across different classes in addition to healthy lifestyle behaviors have been shown to help lower cholesterol in people with very high-levels and in people with more statin-resistant conditions, so doing all of those at once. So now we will focus on the drug class of Statins. So the last DERP Systematic Review for statins was completed and presented in November of 2009, so over 14 years ago. This report was entitled HMG-CoA reductase inhibitors or

statins and fixed-dose combination products containing a statin. The search dates for that report were through May of 2009. DERP then conducted six surveillance reports since that last report, and they were, as mentioned, called scans back then. So with the last surveillance presented in March of 2018, those sources were searched -- the evidence resources were searched through February of 2018. So the next three slides list the PICOS for the DERP reports for statins. So three populations were included. The first was for outpatients of any age with risks for primary or secondary coronary heart disease or noncoronary atherosclerosis, with or without hypercholesterolemia. The second population was inpatient, so hospitalized patients with acute coronary syndrome or those who are undergoing revascularization procedures. And then that third population included people with familial hypercholesterolemia. The comparators of interest were another listed intervention, so any head-to-head comparisons or another medication that is used to lower blood cholesterol. Only randomized controlled trials and comparative effectiveness systematic reviews were included study designs for this report. So the interventions included in that last report are listed here in alphabetical order by generic name. All of them are HMG-CoA reductase inhibitors, of course, as statins, and they are all delivered orally. So we have atorvastatin, also known as Lipitor at the top. Then fluvastatin as regular and extended-release formulations. Lovastatin is next, which was the first drug of its class approved by the FDA in 1987, and it also is available -- was available as regular and extended-release formulations for that report. Then we have pravastatin, rosuvastatin, and simvastatin, and rosuvastatin was the most recently approved statin in 2003. And to note that there were fixed-dose combination products included in that last systematic review such as statin plus ezetimibe or plus niacin, but they were excluded here because they were not of interest for this drug archive report. So outcomes for the 2009 report included changes in LDL and HDL cholesterol levels, also cardiovascular events with the need for revascularization, mortality, and also several measures for adverse events. So the six Key Questions for that most recent report asked about statins and fixed-dose combination products as requested. We are not including those drugs in this review but did keep the original question just for completeness and continuity. And so the question asks about the effectiveness of statins to reduce LDL cholesterol, also to raise HDL cholesterol, the good cholesterol, and then to reduce the risks of cardiovascular events. Also the need for procedures and reduce the risk of death. They also asked about differences in effectiveness across patient subgroups with different comorbid conditions and differences in harms, if any, across individuals with different age groups

and/or other special populations. And again, the text in red is there just to identify the part of the Key Question that is not included in this report but was in the in the original report. The 2009 report was quite large. It covered a lot of territory, there were a total of 347 studies included a cumulatively across all the report updates for systematic review, in that last original -- since the last since the original report, way back when. So it is not clear again, if those were all individual trials or if they included some ancillary or sister publications. But of those studies that were reported there, 102 were head-to-head trials, 123 were other randomized controlled trials, 80 were observational studies, 21 were systematic reviews, and then there were 21 other studies which included post hoc studies, pooled analyses, and also dose range studies. So we start off with a very high-level summary of the findings in adults. Again, we marked any information relating to the combined products in red, so while not directly of interest for this report, but the points of the Key Findings are there. So in adults, all of the statins were found to be to be effective for patients with a goal of reducing LDL cholesterol up to 35%. High-dose rosuvastatin appeared to have greater LDL cholesterol lowering and HDL cholesterol raising effects compared with high-dose atorvastatin. So continuing on with the Key Findings in adults for statins, there was no head-to-head evidence for outcomes relating to the frequency of cardiovascular events. It was demonstrated that statins were equally effective across the populations of men, women, and older individuals, and rates of adverse events were not different across these groups at maximum doses of simvastatin and lovastatin. We could skip the bullet point in red there, and next we can say that they found people with diabetes did not have higher rates of adverse events with statins compared with other drugs used to lower cholesterol. In regard to the Key Question about drug interactions, it was found that there were some serious drug interactions between statins and agents known to inhibit cytochrome CYP3A4 and 2C9 inhibitors. For sake of time I won't go into detail about those agents. So moving on to the Findings in the last report for children and adolescents, they found that studies in children were mostly in individuals with familial hypercholesterolemia, so not in other populations of interest. Overall, LDL cholesterol improved with statins studied in children, but there was no difference between the drugs, nor were there improvements in HDL cholesterol compared with placebo. Moving past the text in red, they also reported that they found no evidence for any head-to-head comparisons for outcomes relating to cardiovascular morbidity and mortality, nor did they find any studies comparing differences in children with diabetes or obesity. And it was also noted that adverse events were poorly reported in studies of children. And of the existing

evidence, there were no clinically meaningful elevations in liver or kidney function tests, so safety issue tests here with statins that were tested and studied. So surveillance after the most recent report was through February of 2018, and those reports found one new drug, no new Indications or serious harms, and 55 new head-to-head trials. The studies included 16 trials comparing monotherapy with fixed-dose combination products. So not sure if those are of interest to you, but they are mentioned here for completeness. Two studies that compared also found two study that compared three drugs. So that was atorvastatin, pitavastatin, and rosuvastatin. There were no new comparative studies that included the drugs fluvastatin extended-release or lovastatin, and there were 37 new comparative trials for monotherapies. So the combinations can be seen here in the matrix below. So the two sides across that darker green horizontal box are identical. So, for example, if we look at that second column, we can see that they identified six trials of pitavastatin compared with atorvastatin and so on. So four new FDA-approved drugs and actions. The only new statin drug identified since the last report was pitavastatin with brand name Livalo, which was the drug identified in the surveillance reports, and it was approved way back in 2009. There were no new Indications or Boxed Warnings for these drugs. There was one new Warning of Precaution for all of the statins that I thought was worth reporting. This Warning became active in September 2020, and it was for a rare condition known as immune-mediated necrotizing myopathy. And then in December of 2022, a Warning for central nervous system toxicity or hemorrhagic stroke was actually removed for atorvastatin in patients without coronary heart disease. So here on the slide, we have the FDA-approved Indications for the statins of interest. In the top row, you can see that most of these drugs are indicated as adjunct with healthy dietary interventions. The drugs are listed in alphabetical order on down the far left column. I will walk across the Indications in green at the top. So the first two columns of Indications only differ by whether individuals are at risk for coronary heart disease -- so in the first column, or are with established coronary heart disease or atherosclerosis, so that is the second column. So atorvastatin, lovastatin, pravastatin, and rosuvastatin are indicated for reducing risk of cardiovascular events and procedures for both of those populations. Fluvastatin is indicated only for those with established disease, and then simvastatin is only indicated for those with risk of coronary heart disease. And then as you can see in that fourth column, all of the included drugs are indicated for -- reducing LDL cholesterol in pediatric patients with heterozygous familial hypercholesterolemia. And all but fluvastatin are indicated to reduce cholesterol in adults with primary hyperlipidemia. In that

fifth column, we go down the line go down the column, so atorvastatin, fluvastatin, rosuvastatin, and simvastatin are indicated for the homozygous familial hypercholesterolemia. And then in the far right column, we have the indication for adults with primary dysbetalipoproteinemia, which is a rare genetic condition that leads to elevated blood triglycerides. So for that indication, the drugs atorvastatin, pravastatin, rosuvastatin, and simvastatin are FDA-approved. So for generic status, all the drugs except for pitavastatin are available as generics. In fact, all of these appear to have been available as generic options since 2009, so with the last report, however, there may be some formulations under some of the drugs that may not be available as generic. For example, at the bottom, there is the oral suspension for simvastatin that does not appear to be available as a generic. And I have included on this slide as well now some brands and formulations that have been discontinued just for completeness. Like the Lipitor brand of atorvastatin appears to have been discontinued. You are all probably more aware of what's going on in that space. At the bottom bullet point there, you can see that we did not identify any new HMG-CoA reductase inhibitors as pipeline agents for elevated cholesterol. So let's pivot to the PCSK-9 inhibitors. So for the last report for this drug class, it was presented in December of 2018, and resources were searched through July of 2018. There was one DERP surveillance report since that last review, which was presented in February of 2020, and the sources for that surveillance were searched through December of 2019. The next few slides are of the PICOS for those DERP products. So the populations included adults and youth with heterogeneous or homozygous familial hypercholesterolemia or individuals with non-familial hypercholesterolemia who were intolerant to or unsuccessful with statin therapy. There were two interventions of interest, alirocumab with a brand name Praluent, and of a evolocumab, with brand named Repatha. So both were approved in 2015, and both are delivered via injection, either bi-weekly or monthly. So for comparators, they included any head-to-head trial of included interventions. Also active pharmacological treatments like statins, including trials of add-on therapy that provide comparative data on included drug versus other active treatment, and then also placebo if the study included asked outcomes associated with cardiovascular disease. For outcomes, they included health events like heart attacks, mortality, change in blood cholesterol levels, and also a variety of measures for adverse events. Randomized controlled trials and systematic reviews were eligible study designs for this report. So five Key Questions were included in this most recent report, and they asked about the comparative effectiveness and harms of the PCSK-9 inhibitors in patients

with familial hypercholesterolemia, high cholesterol levels in individuals who are unable to take statins, and in individuals with non-familial hypercholesterolemia who were not successful with other treatments. And then Key Question four asked about effectiveness of these drugs as monotherapy or together with other agents or non-pharmacological treatments like statins with or without ezetimibe or healthy diet on looking at cardiovascular risk, and then Key Question five asked about differences in effectiveness or harms across patients with different characteristics. So on this slide, we have a summary of the findings from the most recent report for this drug class. So we identified 13 randomized controlled trials, one systematic review, and two publications of pooled analyses. So in summary, that report found that PCSK-9 inhibitors were more effective than other lipid-lowering therapies at reducing LDL cholesterol levels in various populations with familial and non-familial hypercholesterolemia. Those with statin intolerance had substantial reductions in LDL cholesterol levels, and also in general incidences of adverse events are relatively similar between PCSK-9 inhibitors and other lipid-lowering agents. So continuing on with Key Findings in the most recent report. In individuals with non-familial hypercholesterolemia, alirocumab or evolocumab demonstrated significant reductions in cardiovascular risks compared with placebo during follow-up periods of at least two years, and these findings in individuals who are also on statin background therapy. It was also reported that the absolute risk productions in number of events were small, and the incidences of all-cause mortality was lower for alirocumab and evolocumab compared with placebo after 34 and 26 months, respectively, but only significantly different with evolocumab. So this is the summary of findings for the surveillance since the last report with sources again searched through December of 2019. There were no new drugs identified. One new indication was identified for the alirocumab. This was for the approval, so the approval was expanded to include adults who were hospitalized with established cardiovascular disease in order to help reduce risk of heart attack, stroke, and unstable angina. There were no new serious Harms. And there were two new randomized controlled trials identified. One was for alirocumab compared with standard of care in patients with acute coronary syndrome, and one trial was for evolocumab compared with ezetimibe in statin-intolerant patients. So next we have new FDA drugs Indications since the last report. We found one new drug. So inclisiran, with the brand name Leqvio, which was approved in December of 2021. So inclisiran is delivered via injection, and it is indicated to be used like an adjunct to diet and to statin therapy for treatment of heterozygous familial hypercholesterolemia or atherosclerotic

cardiovascular disease that requires further LDL cholesterol lowering in patients who have allergic responses to both of the other two PCSK-9 inhibitor drugs or in patients who have difficulty using a pen injector because of arthritis or weakness of the hands. There were three new Indications for the two drugs. So alirocumab was expanded to include hospitalized patients with cardiovascular disease in April of 2019, and it was expanded to include patients with homozygous familial hypercholesterolemia in April of 2021. The indication for evolocumab was expanded to include younger pediatric patients at least 10 years of age for homozygous familial hypercholesterolemia, and so this was lowered from the age of 13 years before that, and that was done in February of 2021, and this was also expanded in patients with heterozygous familial hypercholesterolemia. So this is a table of the Indications for PCSK-9 inhibitors that were in this last report as well as the one new drug that was identified since then. The three drugs are in the lefthand column. So moving to the next column you can see that all of the drugs are indicated for reducing LDL cholesterol in adults with primary hypercholesterolemia or heterozygous familial hypercholesterolemia as adjunct to diet or with other cholesterol-lowering therapies. All drugs are also indicated for reducing the risk of cardiovascular events or procedures in adults with cardiovascular disease, as you can see that in that fourth column. And then in the third column or second column of Indications there is alirocumab and evolocumab are also indicated for adults with homozygous familial hypercholesterolemia. And then in the final column, we can see that only evolocumab is indicated in pediatric patients with familial hyperlipidemia who are ages 10 and older. I might have messed up the columns there. There were no new Boxed Warnings for PCSK-9 inhibitors since the last report. There was only one new Warning of hypersensitivity listed in 2021 for alirocumab and evolocumab. There were two new pipeline PCSK-9 inhibitors identified. Both are in Phase III trials. We found lerodalcibep, which is delivered subcutaneously, and it is for patients with familial hypercholesterolemia as well as those with atherosclerosis due to hypercholesterolemia. And we have MK-0616, which is taken orally, and it is also for patients with familial hypercholesterolemia and for the reduction of cardiovascular events in patients with elevated lipoprotein a. At the bottom there you can see that regarding generic drug status, none of these drugs are available as generics at this time. So I also wanted to include these two other drugs that are new since the presentation of either of the PCSK-9 inhibitors and also for statin drugs. We were not sure if they were of interest but wanted to report them here for completeness. So the first drug is icosapent ethyl, which is Vascepa. So this new indication is not specifically to

lower LDL cholesterol, but it is now indicated to be used in combination with statins for the reduction of cardiovascular events and hospitalized adults with established cardiovascular disease or with diabetes and have high risk for cardiovascular disease. And then we do have the Bempedoic acid with brand names Nexletol. So Nexlizet is bempedoic acid plus ezetimibe. The drug was approved in February of 2020 for adults with heterozygous familial hypercholesterolemia and in adults with established atherosclerotic cardiovascular disease, who require additional lowering of LDL cholesterol. So on the next six slides, we are providing a very general summary of clinical practice guideline recommendations for high blood cholesterol in the populations of interest. And this will include of course, how and when the two drug classes of interest here are used along the treatment pathway. For this section, we began again with information from up-to-date clinical decision support online resource, and then we cross-referenced that information with key practice guidelines from professional medical associations, which are listed at as the last slide of this in this slide deck. So on this slide, we have the treatment of hypercholesterolemia as primary prevention for cardiovascular disease. First line of treatment is counseling. All patients on healthy lifestyle behaviors, not surprising. And further treatment then depends on LDL cholesterol levels after that and a calculated risk for cardiovascular disease over a 10-year period. So if an individual has a very high blood LDL cholesterol alone, or if it is lower but they are at high risk for cardiovascular disease, they can start on a high-dose statin, immediately atorvastatin and rosuvastatin were listed in the guidelines, primarily because there is more existing evidence for those drugs. And then if they are at intermediate risk, it should depend on patient preference. According to the guidelines and if low risk then there is likely a recommendation for no statin therapy. The guidelines also recommended that PCSK-9 inhibitors can be considered if there is intolerance to statins or if LDL cholesterol low goals were not achieved. But this class is typically limited to patients with existing atherosclerotic cardiovascular disease or familial hypercholesterolemia or individuals with statin-resistant hyper cholesterol, like high-level, high cholesterol. And importantly, so the Veterans Affairs or VA, the Department of Defense guidelines strongly recommend against using PCSK-9s for primary prevention because of the lack of evidence that they found for long-term safety and also inconclusive evidence for any benefit as well as the higher costs. Among lower lipid-lowering drugs, statins were considered the cornerstone of therapy across all guidelines that were reviewed. And of course, this was in combination with healthy lifestyle behaviors or interventions. And I thought this might be a useful table with

information. This is from the 2018 Guidelines from the American Heart Association and the American College of Cardiology, which divides the intensity of the statin therapies into these three categories, so high-, moderate-, and low-intensity therapy that is needed. So high-intensity statin therapy typically lowers blood LDL cholesterol levels by at least 50%, moderate-intensity by 30% to 49%, low-intensity statin therapy by less than 30%. So higher-dose atorvastatin and rosuvastatin are considered higher intensity agents, and all drugs at the respective doses shown here are found to have moderate-intensity capabilities, and then with lower doses -- the four statins on the right there -- can be used for lower-intensity therapy. The US Preventive Services Task Force included age cutoff values in their key recommendations for cardiovascular disease prevention with statins, so statins are recommended for all adults 40 to 75 years with at least one risk factor and a 10-year risk for cardiovascular events of 10% or higher. And then they recommend to selectively offer statins to those with at least one cardiovascular risk factor at a 10-year risk of an event between 7.5% and 10%, so depending with a clinician various factors, and they also state that because of insufficient evidence they don't recommend statins for adults over 75 years, and this is again for the primary prevention of cardiovascular disease. Next, we will transition to what the guidelines say about familial hypercholesterolemia. So the first point here is that the guidelines recognize that intense LDL cholesterol lipid-lowering treatment does reduce the risk for heart disease, heart attack, and all-cause mortality, and should also always include lifestyle behavioral counseling. So for patients with homozygous familial hypercholesterolemia, they recommend the more aggressive and intense doses of atorvastatin and rosuvastatin plus ezetimibe for many patients. So for those who are likely not responding at rates that are preferred or their goal reached -- or not reaching their goals. PCSK-9 inhibitor could also be added for patients with heterozygous familial hypercholesterolemia. Again, high-dose statin therapy is recommended. And then only if LDL levels are not at the target goal do they recommend adding ezetimibe. And then PCSK-9 inhibitors are considered as a third-line therapy to add in this patient population. Also to mention NICE Guidelines from the UK do recommend them off the bat, depending on the PCSK-9 inhibitors, depending on patients' initial LDL cholesterol levels. And then the guidelines also recognized individualized LDL goals may not be attainable, but aggressive lipid-lowering therapy is still important, even for those with the highest risks for cardiovascular events. So for children and adolescents with familial hypercholesterolemia, the recommendations are similar to those for adults, perhaps with a bit more caution. If considering the addition of a PCSK-

9 inhibitor for adults with existing atherosclerotic cardiovascular disease, for the treatment of high cholesterol as secondary prevention of cardiovascular events, statin therapy is indicated for all adults, and then the decision to include -- whether to include PCSK-9 inhibitors depend on a variety of factors listed here, including the risk of future events. High- and very high-risk might increase the recommendation high-levels of LDL cholesterol levels, for example, greater than 190 mg/dL. Also familial hypercholesterolemia, diabetes status, statin-resistance and/or statin intolerance. And then we continue with this population. So ezetimibe is typically recommended as the initial non-statin therapy for the patient who is on the highest dose, the highest tolerable dose of statins, and then PCSK-9s are next in line for recommendations. And an example of this treatment path could be, for example, a patient with atherosclerotic cardiovascular disease and an LDL cholesterol level of at least 70 mg/dL, so it is recommended that this individual be placed on the highest tolerable dose of statin therapy. And then ezetimibe would be initiated if the patient would not achieve the target cholesterol within a given timeframe, and then a PCSK-9 inhibitor would also be included if that patient is considered very high risk. Okay, so this is our final content slide for this report and for today. This is for the two drug classes, Statins and PCSK-9 inhibitors were listing the relevant clinical practice guidelines for the treatment of hypercholesterolemia, again, which were also referenced for this guidelines section, there is an alphabetical order of the author or professional organization, and the date ranges for these updates or publications are from 2018 to 2022. So that is it for this presentation. Thank you all for your attention.

Kavita Chawla: Excellent, Andrea. Thank you. Questions from the Committee for Andrea? Okay. I do see one stakeholder listed. We have got Josh Wageman. Are you online?

Nonye Connor: Josh, you can unmute yourself.

Josh Wageman: Okay. Can you hear me?

Kavita Chawla: Yes, we can. Thank you, Josh. And we did receive your conflict of interest, so thank you for filling that out ahead of time.

Josh Wageman: Thank you [cross-talk] --

Nonye Connor: [Cross-talk] Give me a quick second so I can share my screen.

Josh Wageman: Okay. Perfect.

Nonye Connor: Thank you.

Josh Wageman: All right. [Cross-talk] -- and we will have Nonye put up the timer, and as soon as we have that up there, we will get you started.

Josh Wageman: All right. And you can hear me okay, correct?

Kavita Chawla: Yes, we can. [Cross-talk] --

Josh Wageman: [Cross-talk] All right. Um, I wish you could see me. My camera apparently isn't working or something. That's okay.

Kavita Chawla: Okay.

Josh Wageman: All right. So thank you all for having me. My name is Josh. I am a Lipid Specialist. I used to practice in Endocrinology, and now I am a Medical Science Liaison for Amgen. I always like to say that every LDL particle is potentially a criminal that can invade your vascular neighborhood, and you and I don't want to get broken into. However, for the people who have been broken into, as evidenced for by atherosclerotic vascular disease, we would prefer to have them living in a safer gated community rather than the same neighborhood that gotten broken into in the first place, and so that is where a lipid panel comes into play. And so the policy really has some good stuff there. The one update I wanted to inform everyone of was the 2022 ECDP, which means Expert Consensus Decision-making Pathway on behalf of the American College of Cardiology regarding the actual step-through process as far as ezetimibe first then PCSK-9 inhibition for the high-risk and very high-risk population with established disease. And so according to that guidance, the very high-risk folks should be at an LDL cholesterol less than 55. Whereas if the person has established disease but only one enriching factor or has not had multiple events and still remains less than 70. And I have the criteria if you need a cheat sheet there. There are all of these different factors there. However, the guidance there was that if the patient needs 25% or more additional LDL cholesterol lowering on top of their maximally-tolerated statin to get them to target, they recommend just skipping the ezetimibe step and going straight to a PCSK-9 inhibitor monoclonal antibody. For instance, let's say you had a patient who is on maximally-tolerated statin, who has had

a heart attack and who has two enriching criteria, such as diabetes and hypertension, and their LDL cholesterol is 100 mg/dL on atorvastatin AD. Well, their target would be less than 55 based on the 2022 update. And if you just went to ezetimibe, you would only get them maybe to 75 or so, and then you would still need the monoclonal antibody afterwards. And so the recommendation from that document on behalf of the ACC ECDP is to just skip the ezetimibe step and go straight to the monoclonal antibody, just because they need to be living in a safer neighborhood anybody anyway , and ezetimibe, although a great drug, and I used to prescribe it a lot, is a great drug. It is just not as potent as the monoclonal antibodies for the very high-risk folks. And so, basically, I will leave you with this -- if somebody is living in a rough neighborhood, where there are lots of criminals, we want them living in a safer-gated community now rather than waiting around because the cost of inertia often is a recurrent event. Thanks for your time.

Kavita Chawla: Thank you, Josh. Any questions for Josh from the Committee? Okay. Any other stakeholders, Nonye?

Nonye Connor: No one else has their hands up.

Kavita Chawla: Okay, great. We shall proceed to the motion for both agents, statins and PCSK-9 inhibitors.

Nonye Connor: Okay, and we can start with the statins.

Kavita Chawla: Okay great. We can copy what we had last time, and then we can start wordsmithing.

Nonye Connor: Sure. No problem.

Kavita Chawla: Thank you. It is interesting wording there that the PDL must include at least one high-potency option, and it must include pravastatin. I would propose that we should -- the PDL must include at least one high-potency option as a preferred agent. What does the Committee think about that as having [cross-talk] --

Zoe Taylor: [Cross-talk] Can you explain the difference?

Ryan Pistoresi: So this is Ryan. And when it says the PDL must include at least one high-potency option, that meant that one of them had to be preferred. As you can

see, a lot of the motions that have been brought forward from the past may have some of the more outdated language, so we could update it so that way so it is even more clear, but when we read this, to us, as the agency, it meant that we must have at least one high-potency option as preferred as well as the -- pravastatin. Sorry. So yeah, that is again, language from, like, 2009 that has just been carried forward over and over and over again.

Kavita Chawla: I see. Thank you, Ryan.

Peter Barkett: This is Peter Barkett. Is there any reason we wouldn't want to have both high-potency options on the Preferred Drug List? They are both generic now. And depending on the way that we use our Preferred Drug List, sometimes we require that people go through two preferred options, right? In order to get to non-preferred options? Am I correct there?

Ryan Pistoresi: So this is Ryan. And yes, that is typically true for the Apple Health PDL. We typically require two preferred options. Again this is older, and so in the past there were rebates in this space before everything became generic. And so we were typically looking at one or the other as preferred. If you feel that you would like to have both preferred, you can amend the motion to remove that OR and say it must include both high-potency options.

Peter Barkett: I would suggest that we include both high-potency options.

Zoe Taylor: I agree. Is there any way to know, like, which ones are on the Preferred Drug List right now?

Ryan Pistoresi: Yes, this Is Ryan. So we do have a copy of the Preferred Drug List. Let me see. I don't know if it is in the attachments or not. I am going [cross-talk] --

Zoe Taylor: [Cross-talk] Just because so many people have statin intolerance, and it is really helpful to be able to try a bunch of different ones and try like lowest dose possible. It just doesn't seem like there is reason not to just have all of them be available.

Ryan Pistoresi: Yeah. So just looking at the list, we have atorvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin. So [cross-talk] we already are --

Zoe Taylor: [Cross-talk] Okay. That's another I would recommend. Perfect.

Ryan Pistoresi: Yeah, so we already are including both atorvastatin and rosuvastatin, so [cross-talk] --

Zoe Taylor: And so can we just say that we want to keep it the same? Like we want to have all five of those on the Preferred Drug List. Is that within our power?

Ryan Pistoresi: Typically, we would do the cost analysis, and we may choose to add or remove depending on what the market is. This class has been stable since 2018, so it is unlikely that we would be adding or removing one of these, I think, given the way this class has been stable for so long [cross-talk] --

Zoe Taylor: [Cross-talk] Got it. Okay. --

Ryan Pistoresi: -- it is likely that it would stay like this.

Zoe Taylor: And then in a case like Martin Shkreli, buys one of them, and then it gets really expensive, then you guys are protected against having to keep that one on the list [cross-talk] --

Ryan Pistoresi: [Cross-talk] Yeah, this is Ryan again. [cross-talk] --

Zoe Taylor: [Cross-talk] if you don't call it out?

Ryan Pistoresi: Yeah [cross-talk] --

Zoe Taylor: [Cross-talk] Yeah, okay, [cross-talk] --

Ryan Pistoresi: [Cross-talk] So in that case, [cross-talk] --

Zoe Taylor: [Cross-talk] That makes sense.

Ryan Pistoresi: -- there are usually many manufacturers, and so in that example there would have to be only one generic manufacturer in case of a monopoly situation [cross-talk] added. In that case we would have a plan in place to help manage our patients so that way they did have access to cost-effective medications.

Kavita Chawla: Kavita here. So to reiterate, I see on a list atorvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin. Those are the five preferred agents on the Washington PDL. So how does the Committee feel about editing the current motion to include those five that they should continue to remain preferred,

as Zoe suggested, or should we leave the motion as is? What other comments do we have? Go ahead, Donna.

Donna Sullivan: Hi, Kavita. This is Donna. I mean they are currently preferred today, but if you leave the motion as it is, it provides us with the flexibility to make changes as the market changes. There is -- traditionally, we don't have you say make these all preferred. [cross-talk] Especially if we make more guidelines around like a high-potency option or a pediatric option, or an injectable option, but let us decide on the actual products.

Kavita Chawla: Got it.

Zoe Taylor: So in that case, I think Peter's suggestion that we say that there needs to be maybe at least two high-potency options, and then we could say there needs to be at least two other options as well including pravastatin. That way we are kind of leaving it open, but it is still a little bit more protected than it is now.

Donna Sullivan: There is -- this is Donna again. There is really no need for that. I mean, you can if you want. Most of the time we do prefer like all generics when stuff goes generic, so I don't see the need for it. It will just make our life more complicated trying to make sure that we have exactly the number [cross-talk] --

Zoe Taylor: [Cross-talk] Okay.

Donna Sullivan: -- that you that you have dictated in the motion.

Ryan Pistoresi: [Cross-talk] And this is Ryan, so [cross-talk] --

Zoe Taylor: [Cross-talk] I totally get that. Yeah.

Ryan Pistoresi: Yeah. And this is Ryan. Again, we prefer the flexibility. so that way when we are doing our cost analyses and modeling, not necessarily just for this class but for other classes, it can get pretty complicated and can also then eliminate our ability to select certain rebates that are offered to either UMP or Apple Health. So again [cross-talk] --

Zoe Taylor: Yeah, I understand, I guess. Not to be like the new kid causing trouble, but as a primary care doctor, like, I also prefer the flexibility. Right? To be able to

keep patients on a medicine that is working for them that they are tolerant to. So there is, like, always going to be this tension of, like, whose convenience is more important, and so I am totally, like, I am not trying to, like, make waves or anything. We can keep it the same, but do you understand that, like, the flexibility to keep someone on pravastatin, even if it is a little bit more expensive, is really important from, like, a patient care perspective sometimes, too. So, like, there is obviously this tension.

Ryan Pistoresi: Yeah, and this is Ryan. So I think you are thinking more on the policy aspect, rather than kind of the preferred aspect, and so someone were already on the medication. We typically allow continuation. I say typically because we are talking about 36 different drug classes on the Washington PDL, but it is really up to the plans to create those different policies. So this is really more on what should be preferred and what patients should be starting on. So if someone is already on a non-preferred drug, we do have pathways for a continuation of coverage.

Donna Sullivan: Yep. Pravastatin -- This is Donna. Pravastatin is currently preferred for Medicaid, and I don't see it changing anytime soon.

Peter Barkett: But I am fine. This is Peter Barkett again. I am fine with keeping the motion really simple. The one thing that I would like to call out in the motion is that I do think rosuvastatin should be specifically mentioned that it has to be included on the Preferred Drug List because it has better efficacy data, it is the most effective statin and, currently, it is on the Preferred Drug List, but there is nothing in the motion that would keep it there if say, like, we want to use atorvastatin instead of rosuvastatin, and I know this is kind of a very hypothetical situation, but I just think rosuvastatin should always be on there, and I would like to have it in the motion.

Zoe Taylor: I agree.

Kavita Chawla: Kavita here. So I guess going back to the sentence there, "the PDL must include the high-potency options of atorvastatin and rosuvastatin. And the reason that I would propose also leaving atorvastatin on there is because we are like kind of the whole area of statins and diabetes, and there was a trial that was recent that showed that maybe rosuvastatin tended to have more patients transition to diabetes compared to atorvastatin. So there is always going to be this kind of back and forth, so having both of those agents exactly as Donna said, they are both generic, so they are likely to remain preferred. If

you can just call out both high-strength options and then have pravastatin also on their available as an alternative. Does the Committee agree with that? Or any other comments about that? [Cross-talk] -- I am fine with that.

Kavita Chawla: Okay.

Laura Beste: This is Laura Beste. I agree.

Kavita Chawla: All right, great. So, Nonye, we will have your help here. So the PDL must include, and then you can remove the one high-potency option.

Nonye Connor: This one line? This?

Kavita Chawla: Yeah, that phrase, exactly, and then we will open the parent -- yeah, remove the parentheses and say atorvastatin and rosuvastatin. I guess we should also remove it at least. The PDL must include at least -- oh no. I guess not. At least it's fine. So PDL must include at least atorvastatin and rosuvastatin, and PDL must include pravastatin as an alternative. So as preferred options, we want to put that on there. Where should that go? At the end?

Ryan Pistoresi: Yeah. So this is Ryan. So typically the way that this sentence and older motions that include this language that the PDL must include, we have always interpreted that to mean that they must be preferred. So you could add that to the motion, but it is not necessary at this point. We understand that those three are going to be preferred in every iteration or scenario that we model with our actuaries.

Kevin Flynn: Okay. Can we simplify and just say the PDL must include atorvastatin, rosuvastatin, and pravastatin? Or do we [cross-talk] --

Kavita Chawla: Yeah, that sounds good.

Nonye Connor: So remove the at least?

Kavita Chawla: At least is fine, but we would just [cross-talk] -- yeah, it must include at least atorvastatin, rosuvastatin, and pravastatin as preferred agents. I guess I like having the preferred agents verbiage there just so that nothing is left to interpretation. You know? If there are leadership changes or something like that, we are just very clear in our motion, if that is okay with the Committee.

Does that sound okay to call out as preferred agents? Okay. And pravastatin. Yeah.

Nonye Connor: Okay. This is Nonye. Remove the PDL must include?

Kavita Chawla: Yes.

Nonye Connor: Okay, thank you.

Kavita Chawla: Thank you. Pravastatin as preferred agents.

Nonye Connor: Did you want me [cross-talk] --

Kavita Chawla: Yeah, all of that can go.

Nonye Connor: Okay.

Kavita Chawla: And then the next sentence, I prefer not -- I move not to include combination products. They are not really listed in the left column, so do we need that sentence in there?

Ryan Pistoresi: So this is Ryan, and that was more of a historical aspect of this class. So in the past we had a separate motion for combination products, but we did find that those were typically much, much higher priced than taking the drugs individually, and we worked with the P&T Committee back in, I think, 2016 2017 to remove the combination products from the motion and to recommend that patients take each individual ingredient separately because around that time is when we saw a lot more generic entry in this space, whereas the combinations were all brand and, therefore, a lot pricier. So that is the historical context for that sentence. And a reason that we keep it moving forward is that this drug class typically does include evidence around the combination products.

Kavita Chawla: I see. Kavita here. So it would be beneficial to leave it on there for HCA?

Ryan Pistoresi: Yeah, so this is Ryan. Yeah. I would recommend keeping that line in there just because we have carried it forward for so many years.

Kevin Flynn: Okay, almost all those generic now and like, they are, they were all combinations of bid rates, right? And those are not the guidelines anymore. I don't think a lot of people are prescribing them like that.

Ryan Pistoresi: So yeah. This is Ryan [cross-talk] --

Kevin Flynn: [Cross-talk] Kind of like old -- kind of like old knowledge, right? Like our old way of thinking and we kind of come around to it doesn't really help, except in certain --

Ryan Pistoresi: So yeah. So this is Ryan. And I think the last time that I looked at this class, it has been a while. The combination products are still more costly than the two individual products themselves. Again, we could look at that when we do a cost analysis for this class again, but we have typically just said that they are not part of the PDL. They can be preferred when we are doing our cost analysis, but we have typically just removed them from this motion and focused just on the safety and efficacy of the individual ingredients.

Kavita Chawla: Okay. Kavita here. I think the reason there is confusion is because it is not really -- I mean, it literally says it is individual status, and so it seems like we are commenting in the motion about something that is not being reviewed. But I am happy to leave it on there if it helps simplify HCA's work a little bit. So with that any other edits Committee? Or are we ready to proceed with the motion?

Peter Barkett: I think it looks good. I will make the motion. This is Peter Barkett. After considering the evidence of safety, efficacy and special populations. I move that the following statins are safe and efficacious. Pitavastatin, atorvastatin, fluvastatin, fluvastatin ER, lovastatin, lovastatin ER, pravastatin, rosuvastatin, and simvastatin all forms and can be subjected to therapeutic interchange in the Washington Preferred Drug List, and the PDL must include at least atorvastatin or rosuvastatin and pravastatin as preferred agents. I move to not include the combination products as part of the statin drug class on the PDL.

Laura Beste: [Cross-talk] This is Laura Beste. [Cross-talk] --

Dimitry Davydow: [Cross-talk] This is Dimitry Davydow. I second. Oh.

Kavita Chawla: I think I heard Davydow second. All in favor please say aye.

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

Kavita Chawla: Any opposed or abstained? Great. With that the motion carries. And we shall them move on to the PCSK-9 inhibitors motion.

Peter Barkett: This is Peter Barkett. I have a question about this motion because I think on the agenda it was slotted for archiving. Are we still talking about archiving? And would there be any kind of negative impact of archiving when we are expecting two new agents to come out, including one with possibly a new indication and a new route of administration?

Ryan Pistoresi: So this is Ryan, and no, it would not. So what we could do is as these drugs are getting closer to approval and we are able to get evidence, states can reconsider this, and we can bring that forward at a DERP meeting. You could also make a motion to direct the agency to request this the next time topic nomination comes up. I would just say that for the topic nomination process, this was back in December. And we did use your direction for the Insomnia class, and so that is still going forward. But for the purposes of this class, you can see that we have not got any new products since 2019. The reason that we were wanting to bring this forward for an archive is that then we could then do our cost analysis as this class continues to evolve, but we wouldn't need to continue to commission these reports as an ITR and then be able to do a cost analysis. So for that flexibility for the agency to be current in this class, we are recommending archiving today.

Kavita Chawla: Okay. Kavita here. And I see inclisiran was added to the list. I guess, Nonye, if you could please start with just copying the motion [cross-talk] --

Nonye Connor: [Cross-talk] Of course.

Kavita Chawla: -- and then [cross-talk]. Thank you. Let's edit. So I will lean on our Committee here, especially our pharmacists to tell us if we include inclisiran on this list, whether we can do that therapeutic interchange. Does that still apply?

Ryan Pistoresi: So this is Ryan. And reading it as is, you would want to add the inclisiran up above in the safe and efficacious. And if that were the case then, the way that I am reading it is that all three would be subject to therapeutic interchange [cross-talk] with the language as written.

Kavita Chawla: Right. Yes. Thank you, Ryan. And so I guess my question is, clinically, with the evidence that we were presented and with your experience and with your expertise, whether our PharmD's on the Committee will also agree that inclisiran is therapeutically equivalent with the other two?

Peter Barkett: This is Peter Barkett. I would suggest that we keep inclisiran out of the therapeutic interchange. The mechanism of by which it works is different. And at least, initially, there were concerns around siRNA technology in, I think, causing liver problems. I would leave the monoclonal antibodies as therapeutically interchangeable, and I am fine with having inclisiran included in a safe and efficacious category up above, but I would suggest that we keep alirocumab and evolocumab as therapeutically interchangeable but leave inclisiran out of the TI statement.

Laura Beste: This is Laura Beste. I agree with Peter's assessment. They are different mechanisms, and I don't think there is enough data to support that.

Kevin Flynn: I think functionally it doesn't matter either because all of these are going to go to a specialty pharmacy for the most part, and I doubt they are therapeutically interchanging them.

Kavita Chawla: Okay. Kavita here. So what I am hearing is that eventually it may not matter, but for the sake of the, I guess, integrity of the motion, we want to call out that just the evolocumab and alirocumab are subject with therapeutic interchange, like we call those two out. Is that fair? Okay. That is some fun typing for you, or you can copy/paste there, Nonye, those two drugs. Yeah, just those two are subject to therapeutic interchange. Should we say therapeutic interchange with each other? Or that is extra words.

Ryan Pistoresi: Uh, typically, we would say that those two drugs are within therapeutic interchange with each other and then on that PDL, so the document that I linked to you when it says subject to therapeutic interchange, we would have the note in that class. And then for the new drug it would say No TIP.

Kavita Chawla: Okay, got it. So yeah, so interchange with each other, Nonye, please. Okay. Any other edits or comments, Committee?

Zoe Taylor: Does this what we are doing now have an effect on whether, like, a prior authorization is required to prescribe one of these?

Ryan Pistoresi: So this is Ryan, and no. This is not going to impact PAs. S

Zoe Taylor: So even if we say they are [cross-talk] if we say they are safe and efficacious and should be on, I guess we are not saying they should be on the PRL, or --

Kavita Chawla: We are saying they are on the PDL [cross-talk] --

Zoe Taylor: Okay, awesome.

Kavita Chawla: Yeah, yeah, we [cross-talk] can get it to be authorization, yeah.

Ryan Pistoresi: Yeah. So this is Ryan. So, again, for the PDL some preferred drugs will have PA, and some prefer drugs will not have PA. That is up for the individual programs to decide and not part of this PDL. So when we get into the DUR portion, you will get into more of those policy concepts, and those are going to be applicable to just the Apple Health Program. So, for example, these decisions are going to apply to Uniform Medical Plan Labor and Industries, and so those plans will create their own utilization management strategies as a result of these motions and these decisions.

Zoe Taylor: And if something is on the PDL, then you can't make people try other drugs first? Or you still can?

Ryan Pistoresi: And so this is Ryan, and you can. So, for example, with these classes, we could require someone to use a statin unless contraindicated. So if someone had statin intolerance or another issue [cross-talk] we could check for that and a PA, and then if they have one reason or another that they can't take a high-potency statin, they could then be approved.

Zoe Taylor: So then what does Preferred Drug List mean? Is it just the list of all the drugs that could possibly be covered?

Ryan Pistoresi: So this is Ryan, and that is a great question. So when we are making a decision on what is preferred, we are looking at the drug that we would want to be kind of the first in class. So, for example, today for Uniform Medical Plan, Repatha is preferred and Praluent is not. And so if the provider were to try to write for Repatha, there would be a PA in place that asks the questions: Are they able to take statins? Are they on the highest dose statin? Do they have familial hypercholesterolemia? Whatever that policy is. And if they meet

that, then they would go to Repatha. If they were to do it to Praluent, it would say, Have you tried Repatha first? And is Repatha ineffective, contraindicated, or are there other issues? So, when we are making this decision of saying both of these drugs could be preferred on the Preferred Drug List, we then go back and look at: What is the best value for the health plans? Where are the rebates? How do we structure this, and how do we create this program to not only allow access to these drugs but help to manage our costs and our premiums. [cross-talk] So that is really where this preferred decision comes into place and why it doesn't necessarily impact prior authorization or other utilization management.

Zoe Taylor: So within this class we can say at least one of these needs to be on the Preferred Drug List, but then it could still be that like statins are preferred to this whole class, basically.

Donna Sullivan: [Cross-talk] So this is Donna. [cross-talk] been here for a minute.

Zoe Taylor: Sorry.

Donna Sullivan: I think we are kind of getting out of scope here.

Zoe Taylor: Okay. I will stop.

Donna Sullivan: The purpose of this is to really not name a drug to be preferred. It is not necessarily -- the purpose of us reviewing this is, yes, at least one will be preferred unless the Committee says none of them should be preferred. So I think there is a little overthinking. So we will select one of them to be preferred. And we don't -- the Committee does not get into decisions about should statins be used first- or second-line? Or should these be first or second-line behind statins? That is out of the scope of the Committee, and we take care of that for our Medicaid Program in the DUR portion. Today, we are not reviewing the PCSK-9 policy. And then for Uniform Medical Plan, we have a clinical team with our carrier, Moda Health, who administers the benefit for us, that really works on the policies, and they have their own P&T Committee that works on clinical policies, but they do have to follow our PDL decisions that the Health Care Authority makes. So does that help?

Zoe Taylor: Yeah. I am sure I will understand it more just with more experience. [cross-talk] --

Donna Sullivan: [Cross-talk] And there is a lot that goes into creating a Preferred Drug List and why it is going to matter where we will push back on you about saying "they all have to be preferred" type of decisions is that oftentimes our rebate offers are predicated on the drug is positioned preference in front of its competitors, and so the fewer preferred drugs not including generics -- usually they are excluded from this --but if you have two brand name drugs in a class, like we traditionally did, if you have them both preferred, oftentimes, manufacturers are not willing to give you a discount on their drug because there is nothing that is going to make -- provide more access for their own product. And so that is all of the -- we are trying to take you out of having to deal with that, but those are things that we take into consideration, and -- when we push back on when we have very few drugs within a class, we might be pushing back on, we don't really want to say they all have to be preferred in some instances unless there is a really good clinical reason to do so.

Kavita Chawla: Thank you for that explanation, Donna. Other comments or questions from the Committee? Edits? Or shall we move forward with this motion?

Peter Barkett: This is Peter Barkett. I think it looks good, and I am ready to make a motion.

Kavita Chawla: Go ahead.

Peter Barkett: So after considering the evidence of safety, efficacy and special populations for the treatment of hypercholesterolemia, I move that alirocumab, evolocumab, and inclisiran are safe and efficacious for the treatment of their approved Indications. Alirocumab and evolocumab can be subject to therapeutic interchange with each other in Washington Preferred Drug List.

Christy Weiland: Christy Weiland, I second.

Kavita Chawla: All in motion, please say aye.

Multiple Speakers: Aye. Aye. Aye. Aye.

Kavita Chawla: Any opposed or abstain? All right. With that, the motion passes. And that gets us to our lunch break for 30 minutes. Nonye, what time should we be getting back?

Nonye Connor: Okay. Um, looking at the clock. Thirty minutes from now will be [cross-talk] --

Kavita Chawla: 1:41?

Nonye Connor: Yes. Thank you. [laughter]

Kavita Chawla: Sounds good. We shall see you back in 30 minutes, 1:41.

Nonye Connor: Thank you.

Kavita Chawla: Thank you, Nonye. Just got to make sure we have a quorum. Yes, we do. All right, everybody, welcome back. Hope you had a good lunch. So before we adjourn the PNT Committee and go into our DUR Business, I did want to make sure that we have this motion to archive those four drug classes that we reviewed with Andrea. So thank you, Nonye, for bringing it up. Let's review together, and if there are any edits from the Committee, please bring them forward. Any comments on the verbiage there?

Ryan Pistoresi: Hi. So this is Ryan Pistoresi. I think this was an oversight on my part, but I think given that we just reviewed the updated reports and made motions today, I think we can update those four dates in there to the actual date of today rather than the old date.

Kavita Chawla: Thank you.

Nonye Connor: No problem.

Kavita Chawla: Committee, any comments? Or are we ready to proceed with this motion?

Kevin Flynn: I can make the motion. So after considering the archived reports presented today, I moved to archive the following drug classes from further regular review by the P&T Committee: Anticoagulants. Antiplatelets. Statins, and PCSK-9 inhibitors. The drug classes will remain on the PDL, and the Committee's last motion will remain in effect until changed by the Committee. The agencies may conduct updated cost analysis of these drug classes without additional Committee approval so long as any resulting changes in the preferred status of the drug remain consistent with the Committee's last motion for the drug class. The Committee may review the

archive status of the drug class upon its own initiative or by request of the participating agencies at any time.

Kavita Chawla: Kavita here. It is actually PCSK-9, not PS, so I think those two letters do need to be flipped there. S and C.

Nonye Connor: Thank you.

Kavita Chawla: Is that okay, Kevin, with your motion?

Kevin Flynn: Yes. Sorry.

Kavita Chawla: Thank you.

Kevin Flynn: [Cross-talk] wait, that's weird.

Kavita Chawla: And it is PCSK-9 inhibitors if we want to be accurate. PCSK-9 inhibitors.

Laura Beste: This is Laura Beste. I will second the motion.

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

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

Kavita Chawla: Any opposed or abstain? All right, great. With that the motion carries.

Peter Barkett: And just really quick.

Kavita Chawla: Yeah, please.

Peter Barkett: Do we want to do we want to change that on the left side under drug classes too?

Kavita Chawla: Oh, yes. Thank you for calling that out.

Nonye Connor: You said on the website?

Kavita Chawla: Yeah. In the left column.

Peter Barkett: On the left under Drug Classes.

Nonye Connor: Oh, thank you. Thank you.

Peter Barkett: On the left side.

Kavita Chawla: PCSK-9 inhibitor. Yeah.

Nonye Connor: Yeah, and also removing the "s" after the 9.

Kavita Chawla: Yes. Beautiful. Thank you, Nonye.

Nonye Connor: Yeah. No problem.

Kavita Chawla: All right, wonderful. So with that, we adjourn our P&T Committee, and we convene our DUR Board [cross-talk] --

Nonye Connor: [Cross-talk] Before -- I am so sorry. [Cross-talk] Before we go on, I did want to remind everyone, please say your name before you make a comment. That way it can be recorded because this is being recorded, and it just helps keep track, especially when we are transcribing. Thank you.

Kavita Chawla: Thank you for the reminder, Nonye. Okay, so with that, I hand it over to Ryan Taketomo.

Marissa Tabile: This is Marissa. So, actually, DUR Board, we are going to switch two of the policies. So we are going to have Luke go first, and then Ryan will go after the [indistinct] policy just because of the timing and everything.

Kavita Chawla: Okay.

Marissa Tabile: So just wanted to throw that out there. So we will be doing the Tepezza policy first. Let me go ahead and get that teed up for you, Luke, and then you should be ready to go. So, hopefully, you can see the screen, and it is ready whenever you are.

Luke Dearden: Great. Thank you, Marissa. My name is Luke Dearden, for the record. So I will be summarizing the Apple Health Policy for Tepezza or teprotumumab. A little bit of just a really brief Background to start off with. Tepezza is indicated to treat thyroid eye disease, which is an autoimmune condition, occurring most frequently in the setting of Grave's disease. Patients with

thyroid eye disease can present with a variety of symptoms ranging from more minor symptoms like excessive tearing to eye discomfort, proptosis, diplopia, and then also loss of vision in severe cases. Tepezza has demonstrated the ability to decrease proptosis and reduce overall symptoms in the setting of thyroid eye disease. So going through the criteria here you will see on the left-hand side, the indication which is thyroid eye disease. So Tepezza may be approved when all of the following are met: 1.) Patient must be 18 years or older, and 2.) prescribed by a specialist, so in Ophthalmology or Endocrinology, and 3.) patient's thyroid levels are being controlled prior to starting therapy with Tepezza, and that is defined as T4 and T3 are within normal limits for the laboratory specifications, or T4 and T3 levels are within 50% of normal limits per laboratory specifications, and 4.) they must have an appropriate diagnosis of thyroid eye disease that is related to Grave's disease, and 5.) they must have a thyroid eye disease clinical activity score of 4 or greater. That clinical activity score is an assessment of symptoms. It was an inclusion criterion in the clinical trials, and that is out of 7, so 7 is the maximum. So they must have a score of 4 or greater, and 6.) they must meet one of the following criteria, and this follows consensus guidelines -- the American Thyroid and European Thyroid Association Consensus Guidelines for use of Tepezza. So they must have one of the following precedence of diplopia or there is significant proptosis, which is defined as 3 mm or greater than the upper limit of normal, or proptosis that significantly affects daily life, and there are some examples of what that might look like -- or c., patient has had an inadequate response in tolerance or contraindication to IV glucocorticoids. And there is some Dosing down there as well that represents an appropriate dose of glucocorticoid steroids. And then an inadequate response is defined as still meeting Criteria 5, so still having the clinical activity score of 4 or greater after a six-week trial of these glucocorticosteroids or corticoids. This is a one-time treatment, so it is a maximum of eight doses. Under this policy, it can't be reauthorized, so there are no reauthorization criteria. And then these are the usual Dosing and Quantity Limits. And the Background, which I already summarized. And then, Marissa, if you would like to pull up the form document as well. So this is the form that helps facilitate the prior authorization process that a provider would see when requesting a prior authorization for this product. So I will invite the Committee to look it over. And I am happy to answer any questions as well.

Kevin Flynn: So just for clarification, though, you are going to authorize all eight doses all at once, right? Because that is typically what [cross-talk] --

Luke Dearden: [Cross-talk] That is correct.

Kevin Flynn: -- in treatment course?

Luke Dearden: Yeah. So it is a one-time authorization for the full course of treatment.

Kevin Flynn: Okay. Thank you.

Luke Dearden: And I believe it was within 12 months, so it kind of gives them some grace if they get a late dose or something like that.

Kevin Flynn: That that would be helpful because I have seen it get delayed sometimes due to just patients coordinating their visits.

Kavita Chawla: Kavita here. Are there any age restrictions on this?

Luke Dearden: Yeah. The first of the criteria was 18 or older.

Kavita Chawla: Oh, okay. Thanks.

Luke Dearden: Was that your question?

Kavita Chawla: Yes, that is my question. I didn't know if that needed to be on this form that the providers fill out.

Luke Dearden: I don't believe so because I think the age is captured [cross-talk] --

Kavita Chawla: [Cross-talk] Oh, yeah, it is with their demographics.

Luke Dearden: -- as part of the request.

Kavita Chawla: Yeah.

Luke Dearden: Yeah, date of birth. There you go.

Kavita Chawla: Okay.

Greg Hudson: This is Greg Hudson. I just have a question on 1.) there. Given that this is a one-time treatment with eight doses, is this question necessary, or would it confuse the treatment process at all?

Luke Dearden: Yeah. That is a great question. The only time I can think that this question may be useful is if, for example, they were a new patient to Apple Health, and they were in the middle of their eight doses. So this could help our team know that -- they are currently undergoing their course of treatment. [Cross-talk] But, yeah, that's a good call out.

Kavita Chawla: Kavita here. So the approval would be like a ruling 12-month interval, right? Not calendar year.

Luke Dearden: That is correct. So let me just verify the -- yeah, it is 12 months. So yeah, it is 12 months from the time of approval [cross-talk] and that is standard across all of the Apple Health policies. [Cross-talk] The 12 months isn't necessarily standard, but from the time that it is approved.

Kavita Chawla: Kavita here. I do see -- I don't have a question for Marissa or Nonye, but I do see two stakeholders also listed on the agenda. When is the right time to invite them to provide their testimony?

Marissa Tabile: This is Marissa. Um, I would say if the DUR Board doesn't have any additional questions, we can do the stakeholder input now, if you guys are okay with that.

Kavita Chawla: Kavita here. Let's leave this up here, and then let's have our stakeholders come forward, and then that way we can also ask more questions after they are done.

Nonye Connor: Lisa, I just unmuted you.

Marissa Tabile: This is Marissa. Hold on just one second. I am going to pull up the Conflict of Interest Form and the timer as well.

Kavita Chawla: Kavita here. Thank you. So I do see Lisa Carman and Alice Jackson listed here, and we did receive COI forms for both of them, so thank you for sending that ahead of time. Are we hearing from Lisa Carman first?

Nonye Connor: Yes, Lisa Carman. This is Nonya. Lisa Carmen, you are first.

Lisa Carman: Okay. I was responding to the Zoeller review. Do you want me to do that now? The Zoeller review?

Marissa Tabile: This is Marissa. No. You would do your Zoeller at the next policy.

Lisa Carman: Okay. Okay. Do you want to take me off for this one?

Marissa Tabile: Uh, yeah.

Nonye Connor: Yeah. That's okay. No problem.

Lisa Carman: Okay. Thing is just mixed up.

Nonye Connor: This is Nonye. Alice, sorry, I just unmuted you.

Alice Jackson: Hi, I am present.

Kavita Chawla: Great, Alice. Thank you. You can go ahead whenever you are ready.

Alice Jackson: Hi. Thank you for the opportunity to provide testimony. I am Alice Wise-Jackson, Regional Medical Director for Amgen, and I am going to provide a brief overview of Tepezza. Tepezza is the first and only FDA-approved therapy indicated for the treatment of thyroid eye disease, regardless of disease duration or activity. Thyroid eye disease, also known as TED, is a rare, serious, and vision-threatening autoimmune disease. People living with TED often experienced long-term functional, psychological, and financial burdens, including inability to work and perform activities of daily living. Approved in 2022, Tepezza is a fully human monoclonal antibody against the IGF-1 receptor, the primary receptor involved in TED. Blocking this receptor reverses the disease pathology, including proptosis, which is eye bulging, diplopia, or double vision and, of course, the inflammatory symptoms. Prior to Tepezza, TED was typically treated with steroids or surgery. Steroid requirements raise many serious clinical concerns, specifically, oral or IV corticosteroids are not FDA-approved treatments for TED and have not been shown to be effective in improving proptosis or diplopia. Steroids only treat symptoms caused by TED, not the root cause. TED is a progressive disease, which means that patients with TED can experience worsening symptoms and even blindness if their treatment is delayed. And of course, high-dose steroids carry significant risks including liver failure, diabetes, insomnia,

psychological changes, and even death. In 2022, the ATA and ETA published a consensus statement on diagnosis and management, stating that Tepezza is recommended as preferred or first-line treatment for active moderate-to-severe thyroid eye disease patients with proptosis, diplopia, and [indistinct] disorders. Therefore, we request consideration of language that would allow physicians to determine the best dose and duration of steroid treatment and failure. In April 2023, the FDA-approved new indication language to state Tepezza is indicated for the treatment of thyroid eye disease regardless of thyroid eye disease activity or duration. Additionally, positive data from the Phase IV clinical trials in patients with chronic TED and showed that patients treated with Tepezza achieved statistically significant reduction in proptosis from baseline compared to placebo, emphasizing the patients with proptosis regardless of the clinical activity score can benefit from Tepezza. In summary, Tepezza is the only FDA-approved treatment for TED. It is the only treatment with data supported improvements in proptosis, double vision, information, and quality of life. As such, Amgen respectfully requests the State of Washington consider amending their Tepezza medical coverage policy to be consistent with the FDA indication for patients with thyroid eye disease regardless of disease duration or activity. So thank you very much for the opportunity to present. And I am very happy to answer any questions.

Kavita Chawla: Thank you, Alice. Any questions from the Committee for Alice?

Peter Barkett: Hi. This is Peter Barkett. I have a question for Alice. Alice, you mentioned that steroids are not FDA-approved for the indication of thyroid disease, which is correct, but my understanding is that for many years that was kind of all we had before Tepezza was around. And you also mentioned that Tepezza was studied against placebo. Has Amgen done any studies comparing Tepezza to high doses of steroids to demonstrate superiority?

Alice Jackson: We haven't compared them in a phased clinical trial, no. There is data out there that we have looked at comparing all of the studies that have used steroids to the data that we have for Tepezza and, of course, we show superiority for proptosis response, which is the primary outcome of Tepezza.

Peter Barkett: And so you are referring to comparing studies that looked at efficacy of steroids and studies that looked at the efficacy of Tepezza and inferring what a head-to-head study might look like? Is that -- do I have that correct?

Alice Jackson: Yes -- the outcomes of our Phase III trial were looking at clinical activity score and proptosis reduction. We know from the studies in the literature that proptosis isn't affected by steroids, not significantly.

Kavita Chawla: Great discussion. Thank you for the question, Peter, and your responses, Alice. Any other questions from the Committee for Alice?

Peter Barkett: This is Peter Barkett again. One other question for Alice. And what we are trying to do with this policy is balance affordability against high standards of quality medical care, and we are talking about diplopia and proptosis. And for me, it would be helpful to understand. What does Tepezza cost? What does Amgen bill for Tepezza?

Alice Jackson: I am afraid I cannot answer that. It obviously depends on the patient's plan.

Peter Barkett: I have got a ballpark figure, which I think is accurate, is it is in the six figure range. Is that correct?

Alice Jackson: That is likely correct. Yes.

Kavita Chawla: Thank you for that discussion. Additional questions? All right. Kavita here. So, Nonye, do we have any other stakeholders?

Nonye Connor: This is Nonye. No. There are no other stakeholders, and I don't see anyone else's hands raised up.

Kavita Chawla: Okay, great. Thank you. So with that, we can go back to our policy and look at any edits or proposals that the Committee might have. So I invite the Committee to come back on their cameras so if there is any additional discussion or give us a cue on whether we should move forward on the motion.

Peter Barkett: This is Peter Barkett, again. I was just kind of comparing notes against another policy I was involved with on this particular medication. And I think that policy is very reasonable for the cost of this medication. It is a very high cost medication, and it is not -- there is benefit to it, but this is not a life-saving medication, and so I think utilization management is appropriate, and I think that this policy has been well crafted. Well, great, thank you for that feedback, Peter, with that experience. Any other comments from the Committee?

Zoe Taylor: Just a quick question. So is this a medicine that is currently not covered by Apple Health, and this is the first time that it would be based on this policy?

Marissa Tabile: This is Marissa. So I can answer that question. So we do cover this medication. However, at this time, we don't have a clinical policy for it, so we don't [cross-talk] have that criteria that we would use in our clinical reviews. And the approval, if you are approved this policy, would be the criteria that we would use in our clinical reviews.

Zoe Taylor: Okay. And it sounds like the sticking point is like that clinical activity score issue, and it sounds like because it is so expensive, we are kind of that is like kind of the main thing to decide on.

Kavita Chawla: Kavita here. It sounds like Luke also mentioned that the criteria were on the basis of what was used in the clinical trials itself.

Zoe Taylor: [Cross-talk] Right.

Kavita Chawla: So that is reasonable to leave the language in there. Any opposed on the Committee or any on the Committee want to edit point number five or anything else, really. All right. And if not, Marissa, do we have a motion that we sign off on?

Marissa Tabile: This is Marissa. Yeah. Let me go ahead and pull that motion up for you all.

Kavita Chawla: Thank you.

Marissa Tabile: All right. And it is ready when you all are.

Laura Beste: This is Laura Beste. I am going to make a motion that I move that the Apple Health Medicaid Program implement the clinical criteria listed on Policy 30.19.20.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? Okay, with that the motion carries. Thank you. Marissa, I look to you to which motion or which policy we should review next.

Marissa Tabile: This is Marissa. Yep. We are going to go ahead and move on to the Xolair policy. So let me just exit out of my many windows and get the policy teed up. I will actually be the point person for this one, so that works out very well. Okay, let me turn on my camera. All right. You should be able to see the Xolair policy. If not, just go ahead and yell at me if it is not showing. So this policy that I will be presenting to you all today is our Xolair, or we call it our Anti-IGE Antibody Policy. Just a little bit of history on this policy. We do currently have one that is posted online that we do use. And I think it is hasn't been updated in quite some time, so really, the reason why we are bringing this policy to you all is a policy refresh. There is an indication that is on our current policy listed online that is not listed, so this one is just adding that new indication to this policy and then refreshing any of the criteria as we see fit. So I will just go ahead and get straight into the policy itself. So I believe right now, the policy that we have only includes the Indications of moderate-to-severe persistent allergic asthma and then also the chronic idiopathic urticaria. It doesn't include the chronic rye new site use rhinosinusitis with nasal polyps indication. So that is what you will see is a little bit different than what we currently use. And then also some of the criteria have changed a little bit. I will try to know exactly which criteria have been changed or added just that then you can kind of compare and contrast what we currently use to what this future policy will look like once approved by you all. So getting into the severe persistent allergic asthma, moderate-to-severe persistent allergic asthma indication. The first is the age indication used in 6 years of age or older. I don't believe that has changed from the current policy. The second criteria is requirement of a specialist. So we got a little bit more specific in these criteria, so we kind of laid out which specialists we would be looking for, so Allergy, Pulmonology, Immunology, or ENT. In the current policy it is not specific, so we just kind of made that a little clearer for our providers. The third criteria are it is not just in combination with another monoclonal antibody indicated for the treatment of asthma. So those monoclonal antibodies such as benralizumab, dupilumab, mepolizumab, reslizumab. So this list should include most of the FDA-approved monoclonal antibodies used for asthma, but if we are missing some, it is still kind of included in that, or as new products get approved Indications for asthma, those would apply to this policy. Four, the patient has a confirmed allergy showing reactivity to a perennial arrow allergen, so really what we would be

looking for is like a confirmed allergy test. Five, the patient has a serum total IGE level measured before the start of treatment of either -- so if you are older than 12 years old, we will be looking for serum IGE levels between -- so greater than 30 and less than 700 IU/mL, and then if you are less than 12 years old, so between 6 to 12 years old, your IGE levels that we would be looking for is greater than 30 or less than 1300 IU/mL. And that really just goes off of the labeling of the product and the Dosing because the Dosing is weight-based and also based off IgE, which I will show you at the end of this policy. You will see a table. Six, this is so if the patient has moderate asthma, they will need documentation, or it will be defined as one of the following. We kind of split this up so it is a little bit clearer to understand, and we updated these particular Criteria 2 match what is defined as moderate or severe asthma per the GINA Guidelines. So if a patient has moderate asthma, they will follow these, or it would be defined as one of these: a.) Documentation of functional impairment due to poor asthma control or exacerbations. So that would show a limitation of activities of daily living. nighttime awakenings greater than one time a week but not nightly, or b.) SABA, short-acting beta agonist used for symptom control occurrence daily, so you would see a patient using their rescue inhaler every day, or c.) Lung function would be the percent predicted FEV1 is greater than 60% but less than 80%. Or if a patient has severe asthma, they would be defined as one of these, and that would follow: a.) Documentation of functional impairment due to poor asthma control or exacerbations, so kind of the same as above. Limitations of activities of daily living, but where it really differs between moderate and severe is the nighttime awakenings. So for severe asthma, the nighttime awakenings would occur at least seven times a week, or b.) Their SABA use or their rescue inhaler, for their symptom control occurs multiple times a day instead of in moderate it would be daily, they are using it maybe one, two, three, hopefully not four times a day, or c.) Their lung function, their FEV1, would be less than 60%. So patients would either fall into the moderate or severe bucket, depending on kind of what we see. So we just laid that out there to be consistent with guidelines and also a little bit clearer, so they would either have six or seven. And then eight, the patient remains uncontrolled with either of the following medications used separately or simultaneously within the last year. So they could be on, they would start like an ICS, for example, and then add-on a LABA, or they could be on those combination inhalers that are commercially available, but we just wanted to call that out. So they would need to meet either A, B or C. So the first one is a maximally-tolerated inhaled corticosteroid in a LABA. Like I said, it can be used separately or in a combination product, and we have listed some

examples there -- or they could be on an inhaled corticosteroid or a LAMA, so a long-acting muscarinic agent. An example is the tiotropium, or they could be on inhaled corticosteroid and a leukotriene receptor antagonist, so something like Montelukast. So if they meet all of these Criteria 4 this indication, the request will be authorized for 12 months, and then for the reauthorization criteria, we would want to make sure that Criteria #3, which is the provider attests that it is not going to be used in combination with another monoclonal antibody, that that is continued to be met. The patient will continue maintenance asthma therapy. So whether they are on an ICS/LABA, ICS LAMA, ICS leukotriene receptor antagonists. We want to make sure that they are still adhering to their asthma control plan. And three, documentation is submitted, showing improvement or stability of disease symptoms. So anything that shows there are reduced asthma exacerbations or FEV1 measurements, any notes of reduced hospitalizations. And if they meet all of these criteria, then it will be reauthorized for another 12 months. So moving into the chronic spontaneous urticaria indication. For this one, the age indication, I believe, is still the same at 12 years of age or older. It is still prescribed by a specialist, which is the same as above. It is not used in combination with another monoclonal antibody indicated for the treatment of urticaria. 00:33:43 The underlying cause of the patient's condition is not considered to be any other allergic conditions or other forms of urticaria. So really ruling out anything that may cause -- that is, I guess, not chronic spontaneous urticaria. We just want to make sure that all of the avenues have kind of been researched as far as the patient's condition and making sure it is really not any other underlying cause. Five, the provider attests that the patient has been evaluated for triggers and is being managed to avoid those triggers, so whether they have allergies to NSAIDS, psychological stress that could cause this condition, dietary habits, or avoiding foods that might cause an allergic reaction. We just want to make sure that patients have counseled or talked to their patients about avoiding those triggers. Six, baseline assessments using one of the following assessment tools are completed and we will accept any of these: So it can be an urticaria activity score, angioedema activity score, dermatology life quality index, angioedema, quality of life, or chronic urticaria quality of life questionnaire. Those, we did not specify in our current policy that we have online, so we did get a little bit more specific in this policy just so that then for the reauthorization, the reviewers know kind of what clinical measures they should be looking for or comparing when they do get requests like this because it is a little hard. We wanted something that is more of an objective measure rather than a subjective measure. So as long as that is included in there, we will accept

those. The patient has had an inadequate response to a second-generation H1-antihistamine product, and the anti histamines are listed at the bottom of the policy. That has not changed from our current policy. That is still the same. And then criteria eight, the patient had an inadequate response to at least one of the following unless contraindicated, and we would really call response at least one month, so they have to have tried it for at least one month, and then if it didn't work, they would be eligible. These criteria have not changed from our current. It is still the same. So we will be looking for a dose increase of a second-generation H1-antihistamine at the maximally-tolerated dose, or the provider did add-on therapy with a leukotriene antagonist, so something like Montelukast, or they did an add-on therapy with another H1-antihistamine, or they did another add-on therapy with an H2-antagonists. So one of those that the provider has tried, or the patient has gone through, we would be looking for that. Same authorization duration as above, 12 months. And then for our reauthorization, we are still looking for about the same as the asthma indication, so as long as the provider attests that the patient is not going to be taking this with another monoclonal antibody, and then documentation is submitting showing reassessment of baseline measurements, so that is the baseline assessments in number six, and that shows either disease stability or positive clinical response, it will be reauthorized for another 12 months. And then for the last indication for this product, this is not currently on our policy right now. It is the chronic rhinosinusitis with nasal polyposis. For this one, the age indication is 18 years of age or older. And mind you this is new criteria, so like I said, not in the current policy, so this is brand new criteria. For this one, it would be -- the second criteria is the same specialist that we will be looking for as the ones above. Three, it is not used in combination with another monoclonal antibody. Four, there is a diagnosis of bilateral sinonasal polyposis as evidenced by either an endoscopy, rhinoscopy, or computed tomography (CT). And five, the patient has had at least two of the following symptoms. So they would need a combination of whatever these could be a. or b., b. or c., what have you, the possibilities are endless, so we will be looking for either symptoms of a nasal blockage, obstruction, or congestion, purulent nasal discharge, facial pain or pressure, or reduction or loss of smell. And six, we will be looking for documentation of current persistent symptomatic nasal polyps despite maximal treatment with all of the following within the last year, unless it is not effective, not tolerated, or contraindicated. So the patient would have to have tried some type of intranasal corticosteroid and also an oral systemic corticosteroid within the last year. And seven, intranasal corticosteroid will be continued with the use of Xolair unless it is

contraindicated, so making sure that the patient is still continuing to use their inhaled nasal corticosteroid. Same approval duration as the above, 12 months. For the reauthorization, it is still the same as the other one, so not used in combination with a monoclonal antibody and that they continue to use their intranasal corticosteroid, and there is documentation submitted showing improvement or stability of disease symptoms, so looking for things in the clinic notes such as improvement in nasal congestion, obstruction, severity reduction, and nasal polyps. And then the reauthorization will be for 12 months. Getting into the Dosage and Quantity Limits, these are each for their FDA-approved Indications. We have the dosage forms here. I did realize that the Quantity Limits are actually not listed, so I will make sure I get that updated after this meeting. Then we have some background, and then here are the appendices just listing, like I was talking about before, the H1-antihistamine products, and then the dose recommendations for -- based off of the IGE labs that we received. Then I will go ahead and show the form. Kind of the same as the last policy, so I will go ahead and stop there and welcome any questions from the Board.

Kavita Chawla: Thank you, Marissa. I guess my question is -- a couple of questions. One also applied to the prior policy. At the top it said it goes into effect as of date. So will the date be today's date if we do approve it?

Marissa Tabile: This is Marissa. So we determine -- let me actually just show so everyone knows what we are talking about. So this effective date gets determined by our team internally, so kind of based off whether this gets approved or denied, we usually pick the first of whatever month we decide. I will caveat that by saying we do contractually have to let our MCOs know that we want this policy to go live on a certain date, and that date can -- usually it is 90 days. Sometimes it can be sooner but usually. So if you guys are all approving this today, most likely you won't see it implemented tomorrow. Most likely, you will probably see it be implemented maybe two to three months from today. So just wanted to let you know. Yeah.

Kavita Chawla: Okay. And then a second question. Kavita again. You probably heard. So a couple of weeks ago, Xolair also got the FDA approval for food allergies. And so with that FDA approval, does that mean that the policy will be looked at again? Because I understand that it is like not enough time to review that and include it for today's agenda. So how does that come about with that new FDA approval?

Marissa Tabile: This is Marissa. So it wouldn't affect the approval that you all put in today. So what would happen is you guys would approve it, and then from there we would determine -- most likely we probably won't have time to add that indication just because it is so fresh and new [cross-talk] and we would want to get these -- you know we try to stay very current with our policies as much as we can, but due to time constraints and FDA approvals that happen, so I would like to think we would probably incorporate it, hopefully, sometime within this year, but that may get a little tricky. So probably next, maybe next year you might. So yeah, we will have to have a conversation internally on what that process would look like with that new indication because then that kind of adds a little bit more time for our timeline. Yeah. But if we do get -- I do want to caveat that by saying if we do get cases for that new indication, they are reviewed for medical necessity per the labeling. So we still do have kind of a way to review those cases if they do come.

Kavita Chawla: Got it. Okay. Kavita here again. So I think this was Zoe's question earlier, too. So because it does have an FDA approval for food allergies, if you were to get a request for that, you would just rely on that.

Marissa Tabile: Yeah. We would have to [cross-talk] yeah, like medical. This is Marissa. We would have to use just the labeling and review it for medical necessity. None of the criteria that you saw today would apply for that indication because [cross-talk].

Kavita Chawla: Right. Okay. Great. Other questions from the Committee for Marissa?

Peter Barkett: This is Peter Barkett. I have a question. So my understanding is that omalizumab can be paid for under the medical benefit or the pharmacy benefit, and the medical benefit often ends up being a bit more expensive because patients need to come in for those injections and, you know it is several hundred dollars each injection every month for a year. Does this policy apply to both the medical benefit and the pharmacy benefit as in -- or is there any separate policy that would prefer, say, like the pharmacy benefit over the medical benefit for payment of omalizumab?

Marissa Tabile: This is Marissa. I apologize, I don't know this information off the top of my head. It depends on whether or not we allow it through the medical benefit because we can still steer patients to just use, you know, bill things through our providers to bill it through pharmacy. If it is through medical, the policy would still apply. It is just the trial of nonpreferred would not apply to those

cases. So the clinical criteria will still be very much used in those cases, but I believe Xolair is preferred, but if this was non-preferred, then it wouldn't be subject to any non-preferred use before they could get that, if that makes sense. And Donna, it looks like you have your hand up.

Donna Sullivan: I hit my camera and not my mute button. We would actually require nonpreferred use for a drug if it is under the medical benefit, and it does require prior authorization on the Medical benefit as well, and we do use the same policy. We don't want providers to be able to get around our policy criteria by routing it through a different avenue of either the pharmacy or a physician-administered process, and so we try to close it on both ends.

Kavita Chawla: Go ahead, Kevin.

Kevin Flynn: This is Kevin Flynn. Just on Page 2 under where you say ICS or leukotriene receptor agonist. Theophylline is not a leukotriene receptor antagonist. I would just delete those.

Marissa Tabile: This is Marissa. Okay, I can go ahead and remove that.

Kavita Chawla: Good catch, Kevin. Thank you. Go ahead, Zoe.

Zoe Taylor: This is Zoe. So if a patient had ICS contraindicated, for example, for point eight, would that just be in that case the doctor would just, like, write a letter explaining that instead because the patient wouldn't meet the criteria? Sometimes I feel like it has, like, an option, like, or these are contraindicated, and sometimes it doesn't. So just, like, practically speaking, I imagine that patient could still eventually get it.

Marissa Tabile: This is Marissa. Yes. So if the patient had some type of contraindication -- I am trying to look -- there should be somewhere on this form where that is marked, and we would take that into consideration [cross-talk] and do that on a case by case basis. Yeah. [cross-talk] --

Zoe Taylor: [Cross-talk] Yeah, it looks like maybe the other specify thing for the -- yeah, okay. [cross-talk] --

Marissa Tabile: [Cross-talk] Yeah. [Cross-talk] --

Zoe Taylor: [Cross-talk] That makes sense. [Cross-talk] --

Marissa Tabile: [Cross-talk] We do [cross-talk] --

Zoe Taylor: [Cross-talk] They could put it there.

Marissa Tabile: This is Marissa. We do allow for that flexibility, so if -- cases are reviewed on a case by case basis, so if for some special extenuating circumstances patients really can't use some of these agents that are listed in the clinical criteria, we would just want to make sure that that is noted either in the clinical notes, in the forms, the authorization forms, so then we can really take a look at that, and the clinical reviewers can take a look at that holistically and just make sure that this treatment is still appropriate for the patient, and then they can make that decision.

Kavita Chawla: Thank you, Marissa. Other questions from the Committee? Okay. And I do see one stakeholder listed, Lisa Carman, and we can have -- and we did receive your COIs, so thank you for sending that along earlier.

Nonye Connor: This is Nonye. I am so sorry. Yes. [cross-talk] Lisa, you are good to go.

Kavita Chawla: Lisa Carman? I do see her online.

Lisa Carman: Okay. Hi, this is Lisa. Can you hear me now?

Kavita Chawla: Yes, we can.

Lisa Carman: All right. It popped up a different mute button this time.

Kavita Chawla: No worries.

Lisa Carman: Well, a lot that I had planned to say, Marissa, you already covered, so that is exciting. But again, I wanted to hit just a couple additional points. Again, Lisa Carman from Genentech. I am Medical Affairs here to talk about Xolair, and I wanted to respond to the one issue you were just talking about, the medical and pharmacy benefit. In the package insert we now have language that says initiate therapy in a healthcare setting, and once it has been safely established may determine whether self-administer can be appropriate. So, generally, patients get their very first potential three injections in the office, and then they can go to home use. So if that has any bearing on what we were just talking about. And I wanted to additionally talk about, and it includes in

the package insert that says if it by using a prefilled syringe or an auto injector. And just to let you know, we do hope to get approval from the FDA in March for the largest strength prefilled syringe of Xolair 300 as well as an auto injector, which is a new device and would be available pending approval for all of the different doses. And that is particularly important for that change of being able to do it at home now as well as the new indication that you guys were just talking around, food allergy. And I was going to mention the rhinosinusitis, but you already covered that, so I will just focus on a couple of things around the food allergy for potential future considerations of updated policy. Again, we just got approval on February 16th. This was an NIH-funded study that we did get breakthrough therapy designation in 2018. The New England Journal of Medicine that has the Phase III OUtMATCH trial has just been released this week, as you can see. And a few things I wanted to mention just around there are really no other treatment options for patients with food allergy, with the exception of the Palforzia, which is oral immunotherapy, essentially introducing the allergen to the patient. So Xolair, our indication is down to patients one year of age, so very appropriate treatment population for Apple Health. And it is for any food allergy in accordance with food avoidance. And a couple of things I just wanted to mention is children from lower income families are eight times less likely to have an EpiPen device versus higher income children as well as African American and Hispanic children with food allergy have higher rates of ER visits for food allergy: 18% white, 40% Hispanic, and 43% African American. So what we know is due to accidental ingestion of an allergen, they have less access to specialty care, allergenic foods, and Epi injectors. So I just wanted to mention that additional kind of sub-patient population information.

Kavita Chawla: Thank you, Lisa. Does the Committee have any questions for Lisa? Yes, Lisa, I did have a question about this latest trial. And I realized that is not on the policy, but just real quick. Is there going to be any follow up to the current trial population to see how long it is going to be safe to continue to use Xolair? Because oftentimes kids outgrow some of these allergies.

Lisa Carman: Yes. That is a very important question. I am glad you asked it, and I can follow up with additional data. But I did want to mention the OUtMATCH trial you refer to had 168 patients, 165 were children, and they took the first 60 patients after the initial results, which they were on drug or placebo food challenge. They took the first 60 and they sent them into an open-label extension. So we did get to see the durability if you stay -- if you went on Xolair for more, 24 to 28 weeks, and they did have higher response rates of

less dose-limiting symptoms, but additionally to your question, they took the 60 and sent them to an open label. They took the remaining patients, and they have sent them to what we call Stage 2 and Stage 3. So I don't have the data readout on those yet. We haven't -- it hasn't gotten to that point, but we hope to answer that question. And in Stage 2, what they did is they took patients and put them on -- kept them on Xolair and initiated OIT, so that means if it is peanut or whatever the allergy, they slowly start to expose them to that allergen, and then they take them off the Xolair, and then there is a period of time where they are just doing the allergen, and they get food challenged to see the result. The other arm in that Stage 2 looks at patients who are on Xolair and no OIT. So basically, it is going to have two arms, one that we maintain on Xolair and one that did not and look at those rates. And then Stage 3 has additional groups, those patients will go on to Stage 3 that looks at patients who continue to do the OIT, which is small amounts on a regular basis, and patients who do food avoidance as well as patients who totally incorporate into their diet and actually eat those foods. So I hope to have that data later this year or early next year, but that would help define the duration of Xolair therapy.

Kavita Chawla: Great. Thank you, Lisa. All right, Committee, back to our motion then. Unless there are other questions for Lisa, we are ready to proceed with the motion. We will have the Committee members come back on camera please. We will proceed whenever we are ready.

Dimitry Davydow: This is the Dimitry Davydow. I move that the Apple Health Medicaid Program implements the clinical criteria listed on Policy 44.60.30.AA-3 as recommended.

Kevin Flynn: This is Kevin Flynn. I second.

Kavita Chawla: All in favor, please say aye.

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

Kavita Chawla: Any opposed or abstain? Okay. With that the motion carries. Thank you. And Marissa, what are we doing next? Which policy?

Marissa Tabile: This is Marissa. So we will actually be doing the Oncology: Androgen Biosynthesis Inhibitors, which Ryan Taketomo will be on point for that. And I am teeing it up, Ryan, so whenever you are ready, it is good to go.

Ryan Taketomo: Good afternoon. This is Ryan Taketomo. I will be going over the Androgen Biosynthesis Inhibitors Policy. The drugs contained within this policy include brand and generics. Zytiga abiraterone and then brand Yonsa, which is also abiraterone. A little bit of Background before I jump into the clinical criteria. These products are used to treat prostate cancer treatment. First-line is typically androgen deprivation therapy with or without an androgen receptor pathway inhibitor for patients with advanced prostate cancer. There are a lot of different treatment options available and further-line therapy are based on patient-specific characteristics. Treatment options for this type of cancer include radiation therapy, prostatectomy, androgen deprivation, pharmacotherapy, bilateral orchiectomy, chemotherapy, and typically multimodal approaches are used in combination, as mentioned before. So with that, I will jump into the clinical criteria. The first indication we will be going over is metastatic castration-resistant prostate cancer. Both of the Abiraterone products are contained within this indication. And so going through the criteria, abiraterone Yonsa or abiraterone Zytiga may be approved when all the following criteria are met. Criteria 1.) is the patient is 18 years of age or older, and Criteria 2.) is prescribed by or in consultation with an oncologist or urologist, and Criteria 3.) the patient has had a bilateral orchiectomy or is receiving ongoing hormone suppression, for example, GnRH therapy will be used concurrently with the abiraterone product. Criteria 4.) is there is a diagnosis of metastatic castration-resistant prostate cancer, defined by evidence of disease progression despite therapy with a gonadotropin-releasing hormone analog GnRH or a bilateral orchiectomy. And Criteria 5.) the request is for the generic 250 mg tablets, or if the request is for generic abiraterone 500 mg tablets, there needs to be documentation of clinical rationale why the 250 mg tablets would not be an effective regimen. Convenience of taking fewer tablets does not meet medical necessity. The reason we have these particular criteria in this policy is that the 500 mg tablets cost significantly more than the 250 mg tablets. My analysis shows that over the course of a year it roughly falls between $10,000 and $20,000 more per year. So that is why for this particular drug we are pushing towards use of the 250 mg tablets. So for Criteria 7.) if the request is for brand Zytiga or brand Yonsa, then there needs to be documentation of intolerant or contraindication to generic abiraterone, and then note if criteria is met for generic abiraterone, use of 250 mg tablets will be required. And Criteria 8.) abiraterone branded generic will be used in combination with the steroid consistent with FDA labeling. So, for example, in the label it is prednisone with Zytiga and methyl prednisone for Yonsa, and then if all the criteria are

met, the request will be authorized for six months. Moving on to the reauthorization criteria. Yonsa or Zytiga may be approved when all of the following criteria are met. Criteria 1.) is the patient has had a bilateral orchiectomy or continues to receive the GnRH therapy, and that GnRH therapy will be used concurrently. Criteria 2.) is documentation is submitted demonstrating disease stability or a positive clinical response. Examples that meet this may include stabilization of disease, decrease in tumor size, a spread or lack a disease progression. And Criteria 3 is kind of repeating the language in the initial criteria with the generic 250 mg tablet requirements, but I will just read it really quickly. So Criteria 3.) the request is for generic abiraterone 250 mg tablets, or the request is for a generic abiraterone 500 mg tablets, and there is documentation of clinical rationale why 250 mg tablets would not be an effective regimen, or Criteria 5.) the request is for the brand Zytiga or Yonsa, and there is documentation of intolerance or contraindication to generic abiraterone, and if they meet Criteria 2 use generic abiraterone, then the 250 mg tablets will be required. And then Criteria 6.) abiraterone will be used in combination with a steroid consistent with the FDA labeling. And then once these criteria are met, it will be authorized for six months. All right. The next indication is metastatic high-risk castration-sensitive or castration-naive prostate cancer, only Zytiga and generic Zytiga fall under this indication. So Zytiga may be approved brand and generic may be approved when all of the following criteria are met. Criteria 1.) is the patient is 18 years of age or older, and Criteria 2.) it is prescribed by or in consultation with an oncologist or a urologist, and Criteria 3.) is the patient has had a bilateral orchiectomy or ongoing hormone suppression will be used concurrently, and Criteria 4.) diagnosis of metastatic castration-sensitive or castration-naive prostate cancer, and Criteria 5.) the patient has two of the following risk factors. These risk factors come from clinical trials and define what is high risk. So they have to have two of the following: is a Gleason score greater than or equal to 7, which is a grade greater than 2, bone lesions, and/or the presence of measurable visceral metastases, and Criteria 6.) the request is for the generic 250 mg tablets, or Criteria 7.) the request is for generic abiraterone 500 mg tablets, and its documentation of clinical rationale why the 250 mg tablets would not be an effective regimen, or Criteria 8.) the request is for brand abiraterone, and the patient must have had an inadequate response, intolerance, or contraindication to generic abiraterone, and Criteria 9.) if the product is used in combination with docetaxel, then the provider attests that the client has high-volume metastatic burden, and Criteria 10 is abiraterone will be used in combination with prednisone. So once these criteria are met, then the

authorization will be approved for six months. Okay. Moving on to the reauthorization criteria, Zytiga may be approved when all the following criteria met: Criteria 1.) is the patient has either had a bilateral orchiectomy or ongoing hormone suppression will be used concurrently, and Criteria 2.) documentation is submitted demonstrating disease stability or a positive clinical response. Examples include again, stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression, and Criteria 3.) the request is for the generic 250 mg tablets, or Criteria 4.) the request is for generic abiraterone 500 mg tablets, and there is documentation of clinical rationale why the 250 mg tablets would not be an effective regimen, or Criteria 5.) if the request is for the brand Zytiga, and the patient has had an inadequate response, intolerance, or contraindication to generic abiraterone, and Criteria 6.) is abiraterone will be used in combination with prednisone. And if all the criteria met, then the request will be reauthorized for six months. And then moving to the last indication. This one is non-metastatic high-risk prostate cancer. Again only brand and generic Zytiga fall under this indication. So Zytiga may be approved when all the following criteria are met: Criteria 1.) is the patient is 18 years of age or older, and Criteria 2.) is prescribed by or in consultation with an oncologist or urologist, and Criteria 3.) the patient has had a bilateral orchiectomy or ongoing hormone suppression, will be used concurrently, and Criteria 4.) diagnosis of non-metastatic prostate cancer, and Criteria 5.) the patient is in the high-risk or very high-risk group defined by the following: The patient is node-positive, or the patient is node-negative and has two of the following risk factors: these include the Gleason score greater than or equal to 8, tumor stage T3 or T4, and a prostate-specific antigen concentration greater than or equal to 40 ng/mL, or the patient has experienced a prostate-specific antigen doubling time of less than six months, or a prostate-specific antigen greater than equal to 20 ng/mL on androgen deprivation therapy with Criteria 5. Then there is Criteria 6.) which is the request is for a generic abiraterone 250 mg tablets, or Criteria 7.) the request is for generic abiraterone 500 mg tablets, and there is documentation of clinical rationale why the 250 mg tablets would not be an effective regimen, or the request is for brand Zytiga, and the patient must have had an inadequate response, intolerance, or contraindication to generic abiraterone, and Criteria 9.) abiraterone will be used in combination with all of the following: This includes external beam radiotherapy, unless contraindicated, androgen deprivation therapy, and then prednisone or prednisolone. And then once these criteria are met, then the authorization will go for six months. Moving to the reauthorization criteria. Zytiga may be approved when all the following criteria are met: Criteria 1.) is the patient

has either had a bilateral orchiectomy, or ongoing hormone suppression will be used concurrently, and Criteria 2.) documentation is submitted demonstrating disease stability or positive clinical response. Examples again include the stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression, and Criteria 3.) the requests for abiraterone 250 mg tablets, or the request is for generic abiraterone 500 mg tablets, and there is documentation of clinic rationale of why 250 mg tablets would not be an effective regimen, or Criteria 5.) the request is for brand Zytiga, and the patient had an inadequate response, intolerance, or contraindication to generic, and Criteria 6.) abiraterone will be used in combination with all of the following. So again, it is the external beam radiotherapy unless contraindicated, androgen deprivation therapy, and then prednisone or prednisone, and then once these criteria are met, the request will be authorized for six months. And then we just have the Dosing and Quantity Limits, the Background, and then references. So I think we can pull up the end form. Okay. So this form is again used to help facilitate the prior authorization process with providers to help them understand what information we are looking for, and then they will supplement it with chart notes. So I will leave the form up for the Committee to review and then open it up for questions.

Kavita Chawla: Thank you, Ryan. Kavita here. Questions from the Committee for Ryan? And if not, Nonye, do we have any stakeholders?

Nonye Connor: This is Nonye. There are no stakeholders preregistered or with their hands up.

Kavita Chawla: Okay, great.

Nonye Connor: Oh, wait. Did someone raise their hands? This is Nonye. Did I miss it?

Kavita Chawla: Kavita here. I don't see any.

Nonye Connor: Okay. I thought I saw a hand raised. Okay.

Kavita Chawla: I guess we can continue to scroll down on the policy, Marissa, and that way the Committee can review that. Kavita here. I am guessing that extra box there is just a typo in the check all that apply.

Peter Barkett: This is Peter Barkett. I have a question, not about the content of the form, but is this form that some of the people are going to fill out and send in? Or does this link up with an electronic prior authorization system?

Marissa Tabile: This is Marissa. This is a form that the provider would fill out and send in. I don't believe we actually have the functionality to do like EPA's online yet, so we would need physical faxes, I believe, sent in.

Peter Barkett: I thought so. I was just curious. And is EPA -- by the way, I am just curious, does EPA come in, or no timeline yet for that?

Marissa Tabile: This is Marissa. We are getting a new point of sale system in April. I am not sure if Donna is still on. I think there may be EPA functionality, but I might be wrong. So correct me if I am wrong, Donna, on that if you are still on. But I think it may be coming in the pipeline, hopefully with our new vendor.

Kavita Chawla: Okay. Kavita here. And so from the Committee, if no questions or comments or edits for this policy, then we can proceed to the motion. And I will have all our Committee members come back on and turn their cameras on. Yeah. All of you have. Thank you.

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

Laura Beste: [Cross-talk] This is -- go ahead.

Kevin Flynn: Sorry. This is Kevin Flynn. I move that Apple Health Medicaid Program implements the clinical criteria listed on Policy 21.40.60-1 as recommended.

Laura Beste: This is Laura Beste. I second that motion.

Kavita Chawla: All in favor please say aye.

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

Kavita Chawla: Any opposed or abstain? Okay, with that the motion carries. Thank you, Committee. So I am doing a quick time check. So we are a bit behind on our agenda, so what does the Committee think about taking a break for 10 minutes now and then we reconvene? Does that sound reasonable? I see some nodding heads. Okay. So it is 2:54 right, Nonye. So is that okay with you?

Nonye Connor: This is Nonye. Yes, that is okay.

Kavita Chawla: Great. So like 3:04-ish. Okay. 3:04.

Nonye Connor: Yes.

Nonye Connor: All right. Sounds good. We will see you back.

[break]

Kavita Chawla: All right. Are we ready to reconvene? Great. Kavita here. Marissa, do we have an update on the agenda?

Marissa Tabile: This is Marissa. So looking at the agenda, I think we will probably only have time to do like one -- not one class review, but like one set of class reviews. With looking at the schedule, I think the Antidiabetics would probably fit the most appropriately [cross-talk] just kind of based off of the time. So what we will do is we will go through -- I will have Umang do the clinical presentation of the Antidiabetics, and then we will see where that goes from there. If we are right up at time, that is probably all we will have time to do, but -- if we do have additional time, then we will go ahead and review or just at least make a motion for those classes that don't have any updates, and that might put us right at 4. [cross-talk] So yeah, if that works for you all.

Kavita Chawla: Sounds like a great plan.

Marissa Tabile: Okay. So Umang, let me go ahead and pull up your slides for you.

Umang Patel: Awesome, thank you. And if you could just go to Slide 4. Yep, there you go.

Marissa Tabile: And let me put it in presenter mode.

Umang Patel: No problem. While you are doing that, if it is okay, just to give a little bit of background for some of the new Committee folks. Essentially, what happens here is I do try to provide significant clinical updates within the last year or so. As you can see there sometimes you will see repeated names and may wonder what's going on. In our Magellan files and Apple Health PDL files are not always 1:1. For example, we have it listed under Antidiabetics as an umbrella group here, and we will be going over the SGLT-2 inhibitors, the

amylin analogs, the DPP4 inhibitors, and the respective combos, and the GLP-1 agonist and combos as well.

Marissa Tabile: This is Marissa. Sorry, Umang, to interrupt you. If you actually could just do this, and then you can just go straight into the insulins because for the motion everything is going to be all on one, all of the antidiabetics. So you can just go straight into insulins after you are done with this section.

Umang Patel: That sounds good. Let me go ahead and -- okay, that sounds good. We will go ahead. Okay, and so just to provide a little bit of Background here. For diabetes, it is estimated that over 37 million Americans have diabetes, of which 90% to 95% have Type 2, and it is responsible for increased morbidity and mortality. Adequate glycemic control is crucial to minimize chronic microvascular and macrovascular complications. Exogenous insulin supplements deficient levels of endogenous insulin and temporarily restores the ability of the body to properly utilize carbohydrates, fats, and proteins. Multiple insulin products are available and are used as replacement therapy and management of both Type 1 and Type 2 diabetes when glycemic goals are not met with oral antidiabetic agents. In addition to exogenous insulin, there are several pathways by which blood glucose may be regulated in diabetic patients. On the next slide here, now, one thing I try to do for the Committee folks is I try to bold the significant information. As you can see, this guideline is well over a year old. However, I did want to -- I did provide kind of a nice highlight of guideline recommendations. So according to the ADA in 2021, patients using ambulatory glucose profiles glucose management indicators to assess glycemia, a parallel goal is a time and range of greater than 70% with time below range less than 4%. During pregnancy, the ADA recommended target A1C of 6% to 6.5% as reasonable but can be adjusted based on hypoglycemia risk. More frequent aka monthly A1C monitoring may be required. For diabetes technology, an automated insulin delivery system should be considered in adults with Type 1 diabetes, who have the skills to use the device in order to improve time and range and reduce A1C and hypoglycemia. Regarding obesity management, ADA states that lorcaserin should no longer be used as the FDA requested its market withdrawal. The pharmacologic Type 2 diabetes therapy ADA advises to interrupt SGLT-2 inhibitor therapy before scheduled surgery to avoid diabetic ketoacidosis, and this aligns with the label revisions. And for management of CVD in patients with Type 2 diabetes, ADA advises to consider an SGLT-2 inhibitor in patients with reduced ejection fraction to reduce risk of worsening heart failure and CV death. On the next slide here,

continuing guideline updates according to AHA in 2022, they published a scientific statement on comprehensive management of CV risk factors for adults with Type 2 diabetes. In terms of drug therapy, weight loss medications are discussed as adjuncts to diet, physical activity, and behavioral therapy for certain patients with Type 2 diabetes and a BMI of 27 kg/meter squared or more. FDA-approved drugs for weight management with CV safety and A1C lowering include orlistat, lorcaserin, liraglutide, naltrexone/bupropion sustained release, and phentermine/topiramate. Although long-term CV event reduction has not been evaluated, notable CV risk reduction has been demonstrated for liraglutide at lower doses in patients with ASCVD or high CV risk. Additionally, once-weekly semaglutide 2.5 mg has also shown weight loss and CV risk factor improvement. It is FDA-approved for chronic weight management in adults with BMI of 30 kg/meter squared or more or a BMI of greater than 25 kg/meter squared with a comorbid condition. The CV outcome trial data for newer antihyperglycemic agents is also reviewed. Selection of diabetes agents should be individualized based on patient risks and preferences, and BP management lipid-lowering therapies and antithrombotic therapies are also addressed. Continuing on. The ACC, the AHA, and the Heart Failure Society of America published guidelines for the management of heart failure. SGLT-2 inhibitors were given a 2a recommendation in heart failure with mildly-reduced ejection fraction with weaker recommendations in this population for other -- agents. For heart failure with preserved ejection fraction, SGLT-2 inhibitors received a 2a recommendation, mineralocorticoid receptor antagonists a 2b recommendation, and an ARB received a 2b recommendation. All righty. Now according to the American Association of Clinical Endocrinologists last year, the algorithm update separates these recommendations into complications-centric algorithm and a glucose-centric algorithm. It emphasizes a comprehensive approach, including individualized targets for weight loss, glucose, lipid, and hypertension management. AACE supports an HbA1c target of less than or equal to 6.5% for most patients if it can be reached without substantial hypoglycemia or other adverse effects. In the complications-centric algorithm, therapy choice is guided by comorbidity rather than by glycemic target. As such, the algorithm suggests that patients with ASCVD or who are at a very high risk for ASCVD should be initiated on a GLP-1 receptor agonist or SGLT-2 inhibitor, patients with heart failure should be prescribed an SGLT-2 inhibitor, patients with a history of stroke or TIA should be initiated on a GLP-1 or pioglitazone, and patients with CKD should be prescribed an SGLT-2 inhibitor or GLP-1. In all cases, a drug with proven CV benefit is recommended. For these patients, metformin can also

be initiated or continued to achieve glycemic targets. In the glucose-centric algorithm, patients who require glycemic control should begin with lifestyle therapy plus metformin. Additional therapies may be added to achieve A1C target based on individual patient factors. For those who are overweight, obese, or at risk for hypoglycemia, a GLP-1, dual GLP-1/GIP receptor agonist, or SGLT-2 inhibitor is preferred. And for patients with cost or access issues, a TZD, sulfonylurea, or glinide it is preferred. For patients with severe hyperglycemia, basal insulin is preferred in combination with either prandial or GLP-1 or dual GLP-1/GIP receptor agonist. According to the ADA Standards of Care in diabetes last year, they recommend initiation of a pharmacologic therapy along with lifestyle changes at the time of diagnosis for children with Type 2. Metformin is recommended first-line for asymptomatic children with an A1C of less than 8.5%, while those with marked hyperglycemia and an A1C of greater than or equal to 8.5% should be initiated on metformin along with long-acting insulin. If the A1C goals are not met with metformin, the addition of a GLP-1 approved for youth with Type 2 diabetes should be considered in patients 10 years of age or older. Patients who do not meet glycemic targets despite treatment with metformin, a GLP-1 and long-acting insulin should then be initiated on multiple daily insulin injections or an insulin pump. And the current ADA guidelines do not discuss the use of SGLT-2 inhibitors in children with Type 2 diabetes. On the next slide here, the AHA/ACC/ACCP/ASPC/NLA/PCNA Guidelines last year published guidelines for the diagnosis and management for chronic coronary disease. The main takeaway here relevant to the subsections we will be going over is they recommend SGLT-2 inhibitors and GLP-1 in select patients with chronic coronary disease, including groups without diabetes. Okay, now we will be kind of going into the drug-specific updates here. For the first medication here we have Brenzavvy. In January of last year, the FDA-approved this SGLT-2 inhibitor as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes. The limitation of use very similar to the SGLT-2 class in that it is not recommended in patients with Type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis. The precautions are pregnancy, renal and hepatic impairment, as you can see here. Recommended dose is 20 mg once daily taken in the morning with or without food. And the availability is a 20 mg tablet here. Alrighty. And next we have Farxiga. In May of last year, the FDA-approved an expanded indication to reduce the risk of CV death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure. Previously, it was indicated to reduce the risk of CVD death and hospitalization for heart failure in adults with heart failure with reduced

ejection fraction. This medication does have other Indications, as you can see here, to improve glycemic control in adults with Type 2 diabetes, to reduce the risk of hospitalization and heart failure in adults with Type 2 diabetes, with established CV disease or multiple CV risk factors and to reduce the risk of sustained EGFR decline and end-stage kidney disease, CV death, and hospitalization for heart failure and adults with CKD. For some of the newer Committee members, when we go on to drug-specific updates, what I try to do is bold the updates here. So as you can see, Farxiga has an updated Indication, but no changes to Precautions, Dosing, or Formulation here. Okay. Next, we have an Inpefa. So in May of last year, the FDA-approved this dual SGLT-1 and SGLT-2 inhibitor medication for the reduction of the risk of CV death, hospitalization for heart failure and urgent heart failure visits in adults with heart failure, Type 2 diabetes, CKD, and other CV risk factors. In terms of Precautions, pregnancy, as we have seen in this SGLT-2 class, and renal impairment. In terms of Dosing, it is recommended for healthcare practitioners to correct volume status before starting Inpefa at 200 mg daily and titrating it to 400 mg as tolerated. In patients with decompensated heart failure, [audio cuts out] Dosing when patients are hemodynamically stable and withhold medication at least three days, if possible, prior to major surgery procedures. And the Formulation is a 200 mg and 400 mg tablet. Next, we have Synjardy. So this medication has two updates last year. First, in February there was a new Indication that was added to state that the empagliflozin component is indicated to reduce the risk of CV death and hospitalization for heart failure in adults with heart failure. And, secondly, in June of last year, Synjardy was approved for an expanded indication as adjunct to diet and exercise to improve glycemic control in pediatric patients 10 years of age or older with Type 2 diabetes. Previously, it was only in adults. So as you can see, an expanded indication here, and there are no changes in Precautions or Dosing. And as you can see, there are various Formulations for this in tablet formulations with 5/500 mg, 5/1000 mg, 12.5/500 mg, and 12.5/1000 mg of empagliflozin and metformin, respectively. Okay. Next, we have Jardiance. So, again, two updates last year In June of last year, Jardiance was approved for an expanded indication as adjunct to diet and exercise to improve glycemic control in pediatric patients 10 years of age or older with Type 2 diabetes. And in September of last year, it was approved by the FDA to reduce the risk of sustained decline in EGFR, end-stage kidney disease, CV death, and hospitalization in adults with CKD at risk of progression. Again, no changes to Precautions, to Dosing, and Formulations are 10 mg and 25 mg tablets here. Okay. Moving right along. So GLP-1 agonist, specifically, we have Rybelsus. So in January of last year, FDA

approved updated labeling for the 7 mg and 14 mg tablets, allowing use for the first-line treatment for Type 2 diabetes in adults. Again, no changes in Precautions and Dosing. Okay. Now last year, we have an update for Mounjaro. In August, FDA approved a single-use glass vial presentation for all available strengths of Mounjaro. Previously, it was only approved as a single-dose pen, and the Dosage is a 2.5 mg to 15 mg subcutaneously once weekly. So just a new Formulation here. No changes to Indications, Precautions, or Dosing. Next, we have Zituvio. So we are moving right along into the DPP-4 Inhibitors. August of last year FDA approved Zituvio as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes. Again, Limitation of use not recommended in patients with Type 1 and has not been studied in patients with a history of pancreatitis. In terms of Precautions, there is a precaution for pancreatitis and heart failure. Dosing is 100 mg once weekly and can be taken with or without food, and dosage adjustment is recommended for patients with a GFR less than 45 mL/minute. And in terms of Formulations, they come in various strengths of 25 mg, 50 mg, and 100 mg tablets here. Okay. On the next, we have Zituvimet. So in November of last year, FDA approved this DPP-4 inhibitor and metformin combination, sitagliptin and metformin combo to make Zituvimet. And it was approved as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes. As you can see, it probably has its limitations of use of its respective components, first one being not recommended in patients with Type 1 diabetes and has not been studied in patients with a history of pancreatitis. Precautions: BlackBox Warning from its metformin component of lactic acidosis, and it has pancreatitis and heart failure precautions from its DPP-4 inhibitor component. Dosing is orally twice daily with meals. It is an individualized Dosing on the basis of the patient's current regimen effectiveness tolerability, and the maximum dose is 100 mg of sitagliptin and 2000 mg of metformin. And the formulations come in a combination, so it isa 50 mg and 500 mg or 50 mg and 1000 mg of the metformin and sitagliptin, respectively. Okay? Moving right along to Discontinuations of FDA communications. February of last year, Sanofi discontinued distribution of Adlyxin on January 1, 2023, and the product expiration date is September 30, 2023. There are no generics available. Next, in March, AstraZeneca made a business decision to discontinue Onglyza and Kombiglyze XR. And in terms of FDA Communications, first for Ozempic in April of last year, the FDA is reporting availability of the 1 mg, 2 mg, 0.25/0.5 mg products, and the 0.25 mg/0.5 mg product is set to be discontinued. Prescribers were recommended to transition to the 2 mg/3 mL presentation. And lastly in June of last year, for Ozempic, Rybelsus, and Wegovy, FDA released Drug Safety Information

regarding medications containing semaglutide marketed for Type 2 diabetes or weight loss. FDA received reports of compounded products using sodium and acetate salt forms of semaglutide, which have different active ingredients from the approved semaglutide products. Continuing on here, in terms of Ozempic, Wegovy in June of last year, Novo Nordisk issued a statement alerting the public of counterfeit Ozempic pens purchased at a retail pharmacy, which contained insulin glargine rather than semaglutide. The company advises pharmacies to purchase semaglutide products through authorized distributors and encourages patients to check product label and contents against the description provided. A statement by the ASA last year, the American Society of Anesthesiologists, released a statement which suggests to hold GLP-1s prior to surgery for patients undergoing anesthesia due to risk of regurgitation and aspiration of food. Their suggestion is based on anecdotal reports that increased risk may be due to delayed gastric emptying and residual gastric contents. And per ASA, daily GLP-1s should be held on the day of the surgery and weekly GLP-1s should be held for one week prior to the surgery. And lastly, in August of 2023, Novo Nordisk announced that it will continue to restrict started doses of Wegovy into 2024. Okay. Now moving right along, as Marissa stated right before I started, we will be going right through the insulins, as this will all be one motion for the Committee. So going right into the insulins here, we just have a few updates. First, discontinuation. in November of 2023, FDA announced that Novo Nordisk will discontinue manufacturing Levemir 100 unit/mL FlexPen and vials. Discontinuation will occur on April 1, 2024, but supply disruptions are expected to start in mid January. Vials -- will be available up until the end of this calendar year of 2024. And full brand discontinuation -- will occur -- December 31, 2024. And then, lastly, in terms of a new presentation, in June of last year, FDA-approved the 1.6 mL PumpCart cartridge for Fiasp for use in compatible insulin pumps. I am going to pause right there for the Committee.

Kavita Chawla: All right. Questions from the Committee for Umang.

Umang Patel: And I apologize if that was quicker than my normal cadence. I was trying to gift you guys some time.

Kavita Chawla: Appreciate that, Umang.

Peter Barkett: Umang, this is Peter Barkett. I didn't hear anything about canagliflozin and amputation risk, so I assume nothing has changed. Is the conventional

wisdom that that could still be a class effect? Or are we thinking that that is probably more specific to just that particular product?

Umang Patel: I am going to have to look into that, Dr. Barkett, to give you a solid answer on that.

Peter Barkett: Okay.

Kavita Chawla: Here. Peter, I believe the FDA pulled the BlackBox Warning for amputations from canagliflozin. So now it is considered to be].

Peter Barkett: Pulled it from canagliflozin or pulled it from the other SGLT-2 inhibitors? I thought for a while it was on all the SGLT-2 inhibitors, and then it got pulled from everything except for canagliflozin.

Umang Patel: Dr. Barkett, I am confirming what Dr. Chawla said that it was pulled from canagliflozin as well.

Peter Barkett: Oh, gotcha. All right, thanks.

Kavita Chawla: Other questions for Umang? And if not, Marissa, if we can have you pull up the motion. Oh, no. Yes, drug list. Thank you.

Marissa Tabile: This is Marissa. Yes. So I will go over our Antidiabetics drug classes. So you should have a copy of this that was sent to you. I am displaying it here, so feel free to stop me if you have any questions. I will just go through class by class. It can be a little messy. So for the first one, we have the Antidiabetics : Amylin Analogs, and for this class, we have Symlinpen which is pramlintide, and that is preferred. Those are the only products in the class. For Anti-CD3 Antibodies we have Tzield, and that is the only product in the class. It is preferred. For our DPP-4/SGLT-2 inhibitor combinations, it doesn't look like we have any preferred products in this class, so they are all non-preferred. Usually in that case, we really are just wondering and would PA for why can't they take the separate products? Why would they -- we just need justification why they would need the combination product due to cost considerations. So that is the reason why it is non-preferred. For the DPP-4/TZD Combinations, it is the same rationale for these, just why can't they take the separate components, and why would they need the combinations? So we don't have anything preferred in that class. For the DPP-4 inhibitors, the preferred products in this class are -- I am going to try and read these out. So we have

Janumet, Janumet XR, Januvia, Jentadueto, Kombiglyze XR. We have Onglyza. We have the saxagliptin generic and Tradjenta as our preferred products in that class. For the GLP-1 Insulin Combinations, we don't have any preferred products in that class. So nothing is preferred there. That is Soliqua and Xultophy. For our GLP-1 agonists, our preferred products in this class are Bydureon Bcise, Byetta, and I believe it is Victoza. So those are a few of our preferred products. We do have a clinical policy for these products, which we are not going through today, but we do have a clinical policy that applies for those products. For the intermediate-acting insulins, our preferred products in this class are the Humulin N, and that includes the KwikPen formulation. For the long-acting insulins, we have Basaglar, both the KwikPen and the Tempo Pen, the generic insulin glargine, the pen, I believe, and the vial. And then we have Levemir preferred as well. For the pre-mixed insulins, so for the mixed formulations we have Humalog 50/50, the pens and the vials , 75/25, the Humulin 70/30, the generic versions of that, and Novolin 70 -- oh, that's nonpreferred. Um, and it looks like that is it. Oh, and then we have Novolog mix 70/30, the Relion, that is preferred. For our rapid-acting insulins, our preferred products are the Humalog, so we have the KwikPen and the regular adult KwikPen, the junior KwikPen, and the regular KwikPen, and then we have generic insulin lispro preferred. There is KwikPen both junior and adult, and then I believe there is a vial. And then we have Novolog products preferred as well, so the vial, the FlexPen and it looks like the Pen fill. For the short-acting insulins, our preferred products in this class are it looks like Humulin R U-500, and I believe that is it. I think the Humulin R is 100 unit/mL is preferred as well. It just looks odd because there are some blanks. And then for SGLT2s, I can tell you right now we have pretty much -- it is probably easier for me to go through what is non-preferred. So for these products what is non-preferred is the new product, Brenzavvy and the generic bexagliflozin, and then Invocamet XR and segluromet. So these are a lot of like the combination products. And Synjardy XR and Trijardy XR, but for the most part the other products are preferred. Jardiance, Invokana, Synjardy, Farxiga, and the generic. And that is it. I can take any questions anyone has about the PDL.

Greg Hudson: This is Greg Hudson. I just have a brief, I guess, administrative question before we move to motions because I want to make sure I understand the DUR's role, I guess, with this next motion in regard to diabetic treatment.

Marissa Tabile: This is Marissa. Sorry. So what was your question, Greg? I'm sorry, I missed it.

Greg Hudson: Oh, no. And this might, I guess, be more for Kavita or for Leta. I guess I just want to make sure as this being my first meeting that I understand what this is in comparison with the P&T Committee this Drug Utilization Review period, what this motion will be adjusting here if -- as we move forward.

Kavita Chawla: So Kavita here, Greg. So Marissa puts up these medications just so that we have an understanding of preferred versus non-preferred, which we have a little bit more. I don't want to say leverage, but maybe some influence on with DUR compared to P&T, but I think this is more so just so that we understand what is covered and not covered but preferred and non-preferred. And then so with the motion, this applies primarily only to Medicaid population, so it is only the Apple Health Policy, so it is only Medicaid population, not the rest of what HCA covers, so you UMP, L and I, and HCA.

Greg Hudson: Okay. Yes. Thank you for clarifying. [Cross-talk] --

Zoe Taylor: [Cross-talk] Yeah, and do we have -- like, is this a time when we would talk about this formulary or what we would want to change about? Or is that not something that we do now or not at this meeting?

Kavita Chawla: Kavita here. So are you asking about changing meaning, like, what should be on here versus not or what should be [cross-talk]

Zoe Taylor: [Cross-talk] Look, are we having a discussion about this now? Or do we not have a discussion about this list?

Kavita Chawla: Yeah, so it is outside of our scope of view for the reasons that [cross-talk] Donna said in terms of preferred versus non-preferred because a lot of that depends on rebates. So this specific part, what Marissa is showing, is just what review [cross-talk] The part that Umang reviewed is the clinical background and making sure we don't have any questions about that, and then the motion, that is when we will have our final discussion.

Marissa Tabile: Yeah. This is Marissa. You will see, for the newer Board members, the motions for DUR are a little bit different than what you saw for P&T. Our motions for DUR Board you will see in the language. It is not drug-specific like it was for P&T. So like Kavita was saying, we do just show you the AHPDL just so you all can see what the PDL is looking like -- well, a portion of the

PDL -- what that class is looking like as a whole. So then you have an idea of what is preferred and non-preferred. And you can by all means make recommendations for the PDL. So we have had recommendations where the DUR Board recommends that Apple Health has at least one weekly GLP-1 preferred [cross-talk] the selection of the product is up to the discretion of HCA, so you can make different recommendations [cross-talk] --

Zoe Taylor: [Cross-talk] Yeah, that was the kind of thing I was going to say.

Marissa Tabile: Yeah. Like, you can make recommendations for specific formulations that you think should be preferred that maybe are not and things like that, so [cross-talk] --

Zoe Taylor: [Cross-talk] Okay. Yeah, the two things I thought I noticed were -- or that I wanted to check were whether there was a weekly GLP-1 preferred and then whether there was a higher concentration long-acting insulin preferred than U100.

Marissa Tabile: This is Marissa. So yes, we do have a weekly GLP-1 that is preferred, and that is the Bydureon Bcise.

Zoe Taylor: Okay.

Marissa Tabile: Yeah, that is the preferred weekly GLP-1. For the insulins -- sorry, it is very crowded.

Zoe Taylor: No worries.

Marissa Tabile: I thought we did.

Zoe Taylor: There probably is one, like, either Toujeo. Looks like Toujeo is not. If there is no [cross-talk] --

Marissa Tabile: [Cross-talk] No. So it actually looks like we don't have a higher concentration. So we just have [cross-talk] --

Zoe Taylor: [Cross-talk] Okay.

Marissa Tabile: [Cross-talk] regulars right now preferred [cross-talk] --

Zoe Taylor: [Cross-talk] Yeah. Whatever process I should follow to recommend that there be at least one higher concentration preferred, I would love to do that at some point whenever appropriate.

Marissa Tabile: This is Marissa. And you can -- if you are proposing that, you can definitely put that on the table right now, and then if any of the DUR Board Members want to discuss adding that, and if you guys all agree, we can certainly add that to the motion. So I will go ahead and leave it to you, Kavita, for any discussion that the Board wants to have on that.

Kavita Chawla: [Cross-talk] Peter, [cross-talk] --

Peter Barkett: [Cross-talk] Hi. This is Peter Barkett. So I definitely agree with having a long-acting GLP-1 agonist. That makes sense. I am not as sold on a high-concentration long-acting insulin because if you are going to really high-doses of insulin, you need more frequent injections and adjustments anyway, and U500, I believe, is on the preferred list, so I think it is in a little bit of a -- I would consider it a bit of a different boat. I don't feel strongly that we need something like Toujeo on the preferred list.

Zoe Taylor: I use U200 or U300 insulins pretty frequently because I have a lot of patients who are escalating doses in older age because of increasing insulin resistance, and often they are doing like -- or I am inheriting them on really high single-shot regimens that are not appropriate. And the best first thing to -- one first thing you can change, obviously, is splitting it into two shots, but another really helpful next thing to change is to switch them to a higher concentration insulin where they will get better absorption. So even though maybe long-term is the best thing to do is to, like, get them on Jardiance or get them on Ozempic. Those things can be hard to do in the short-term, especially with prior authorizations and things like that, and so I definitely use the U200 and U300 long-acting products. I don't know about other people's experience.

Kavita Chawla: Thank you.

Christy Weiland: This is Christy Weiland. I appreciate that. I manage a lot of diabetes patients and have really high-doses as well. I guess what I am wondering more is if they are if they are using without -- if we went through the step-wise approach, we eventually can get the more potent insulin after using two preferred agents, and I just [cross-talk] --

Zoe Taylor: [Cross-talk] Oh, okay, that makes sense. So you just -- it just doesn't need to be preferred, technically.

Christy Weiland: I guess I am a little concerned about adding it as a preferred based on the cost that it [indistinct] since there are only a few products actually available, and the cost, I think, is quite a bit higher than the standard U100s. I don't know if other people have thoughts around that. I guess [cross-talk] --

Marissa Tabile: [Cross-talk] This is Marissa. So from an HDA perspective, I will say from what I can remember, the cost is significantly different than the 100s.

Zoe Taylor: Okay. So for my patients, I don't know, in the pharma -- we have a pharmacy, like, co-located, so it might just be that I am just sort of shielded by the fact that they already tried two other things, and so that is why it is approved. That is totally fine with me as long as they can get it if they need it.

Kavita Chawla: Kavita here. I think, Zoe, you are right, and that is how all of these policies are typically written, like if they tried two preferred agents, they can then get qualified for a non-preferred agent.

Zoe Taylor: Makes sense.

Kavita Chawla: And I guess, what does the Committee think of it? So I am not very excited about the one long-acting GLP-1 option that we have, the GLP-1 receptor agonist is the Bydureon, which I have never prescribed because the data for that is underwhelming compared to the semaglutide, dulaglutide, and then, of course, tirzepatide is its own thing. So how does the Committee think about that it is the only once-weekly option that we have as preferred?

Christy Weiland: This is Christy Weiland. I feel like we had this conversation before. Maybe it was the P&T when we were doing that. But as I recall, we said there needed to be a once-weekly injection with cardiovascular data [cross-talk] --

Kavita Chawla: [Cross-talk] Oh, yeah, there you go. Yeah, that is right.

Christy Weiland: Yeah, and I think that is what we did. It must have been with the P&T.

Kavita Chawla: You are right. Yeah. So that is a really good point to actually call out that we need a GLP-1RA that has the CVD benefit. Does the Committee agree in making that recommendation to HCA? Oh, sorry? [Cross-talk] --

Laura Beste: [Cross-talk] Can we say the motion as it is currently? This is Laura Beste.

Kavita Chawla: Okay, the motion will be sparse. Kavita here. So I guess because we are kind of lumping together a whole bunch of agents, would it then be appropriate to add a sentence saying at least one long-acting GLP-1 receptor agonist that has cardiovascular benefit has a preferred status on the AHPDL?

Marissa Tabile: This is Marissa. I can probably add that as like a bullet underneath the motion if we want [cross-talk], and then you can just call it out.

Kavita Chawla: Does the Committee agree with that?

Laura Beste: This is Laura Beste. I agree. I think that's a good idea. [Cross-talk]

Zoe Taylor: [Cross-talk] Definitely agree.

Nonye Connor: This is Nonye. And I know, Marissa, you are making adjustments to the motion. I did want to point out that we have a stakeholder that wants to -- that does [laughter] I know [cross-talk] who has their hands up. So, Kat, I am going to allow -- give you permission to talk, and Marissa, I don't know when you guys want to pull Kat in.

Marissa Tabile: This is Marissa. Let me go ahead and just pull the [cross-talk] --

Nonye Connor: [Cross-talk] Bullet -- yeah.

Marissa Tabile: [Cross-talk] the timer, and then Kavita, whenever you are ready, we can do it.

Kavita Chawla: Yeah, certainly. Let's go ahead.

Kat Khachatourian: And Marissa while you are pulling up the timer -- this is Kat Khachatourian, and I am a Washington State Licensed Pharmacist and Medical Account Associate Director with Novo Nordisk. Prior to my testimony, I did want to call the Committee's attention and Umang's attention to the meeting material. There is a Dosing reference to semaglutide 2.5 mg, and the

semaglutide molecule that is Wegovy is only approved for 2.4 mg is the actual dose. And then, additionally, the FDA label is for BMI greater than or equal to 30 or greater than or equal to 27 with comorbid conditions. The BMI greater than or equal to 25 kg/meter squared is only in specific populations. So I just wanted to call attention to that for the Committee's awareness and if there are any edits that need to be made to the documents. So I just wanted to call attention to that.

Kavita Chawla: I appreciate that, Kat. Thank you.

Kat Khachatourian: Of course. And so just to answer the questions. So, again, Kat Khachatourian. I am speaking on behalf of Novo Nordisk. I am a licensed pharmacist. I do not see Medicaid patients, and I am a Washington resident. Conflicts of interest: I am an employee of Novo Nordisk. [cross-talk] Okay, perfect. Thank you. So I would like to request the Committee, as noted during the discussion, add Ozempic, which is the semaglutide injection, and Rybelsus, which is oral semaglutide, to become preferred options for Washington patients. In support of the information that has been discussed in the meeting packet my colleague previously shared during last year's meeting, the class review, the labeled Indications for Ozempic, including reviews of the cardiovascular outcomes trial, SUSTAIN-6, which did demonstrate a 26% relative risk reduction of MACE in patients with established diabetes and cardiovascular disease. Additional information on the Indications, Side Effects, Precautions, and Dosing that has been previously shared is available on the Ozempic package insert, as well as the February 2023 P&T/DUR Meeting minutes. Ss the Committee has recognized, ASCVD is the leading cause of death in the United States, overall, especially in patients with Type 2 diabetes. According to the AHA, adults with Type 2 diabetes have a two to four fold higher risk for cardiovascular morbidity and mortality than adults without diabetes. This accounts for the vast majority of disease burden, including approximately 50% of deaths and over 50% of lifetime medical cost of diabetes complications. As noted in the guideline review, there is a goal to reduce cardiorenal risk in high-risk patients with Type 2 diabetes, noting for patients with ASCVD, GLP-1 receptor agonist with proven cardiovascular benefits should be used, of which liraglutide, semaglutide, and dulaglutide have demonstrated cardiovascular risk reduction in clinical trials. So I respectfully ask that patients gain more than one treatment option for cardiovascular risk reduction and Ozempic become a preferred once-weekly GLP-1 receptor agonist on the PDL, given its potency and the relevant outcomes of glycemic control, weight loss, and cardiovascular protection in

appropriate patients. Next, pertaining to the oral semaglutide approved brand name Rybelsus. Similar to his Ozempic, Rybelsus includes the active ingredient semaglutide; however, it is reformulated to include an absorption enhancer called SNAC. Please refer to the Rybelsus package insert for additional information for Dosing, Adverse Effects, and more. Again, I respectfully ask that Rybelsus become a preferred GLP-1 oral receptor agonist on the Medicaid PDL, again expanding treatment options and provider choice. Thank you for your time, and I am happy to answer any questions you may have.

Kavita Chawla: Thank you, Kat. Any questions from the Committee for Kat?

Peter Barkett: Yeah. This is Peter Barkett here. So, Kat, you mentioned that Rybelsus and Ozempic have the same active ingredient, and you are requesting that both of them be on the preferred list. What is the relative cost of Rybelsus compared to Ozempic?

Kat Khachatourian: So that would be something, Peter, that I would be happy to discuss. I know that that is information that is kept, I think, separate from this discussion, and contracting discussions are typically proprietary. So we would be happy to meet with the Committee and discuss that information as far as gross and net considerations as pertains to Apple Health. I know that doesn't answer your question.

Peter Barkett: Yeah, [cross-talk] I am just struggling to see why we would need both on there as it would seem to be a convenience issue and kind of the exact reason why we have utilization management's right to reduce cost without negatively impacting quality of care, [cross-talk] and if it is the exact same ingredient, I don't know why we would need both, but [cross-talk] --

Kat Khachatourian: And I would defer to the treating provider's experience with patients. There are still some patients who have injection hesitancy, so when thinking about from a clinical inertia and ability to get on an agent with the semaglutide molecule and the cardio protection benefit, which would be adding another option for patients but completely understand your perspective from a molecule standpoint they are the same molecule, so, absolutely, that would be a worthy discussion to have regarding the pricing and contracting capabilities.

Peter Barkett: One other question just out of curiosity, my understanding of the way that Rybelsus was able to go to an oral formulation, other than having the enhancer is basically increasing the number of units of the molecule.

Kat Khachatourian: Yes.

Peter Barkett: And I am curious, does that have any -- you know, we have production issues, supply issues with semaglutide, and I am just curious what impact Rybelsus having so much more of the molecule in order to be able to take it orally has had on those production and access issues.

Kat Khachatourian: Certainly. So that is a valid point because the access issues related to supply were multifold. Number one, the prefilled devices from a pen standpoint, which the Committee did note in the meeting materials, some of the discontinuation of other products in order to enable the actual device to be able to be utilized for patients with diabetes to be able to have access to medication and overcome some of those supply challenges. And from a raw ingredient standpoint, production capabilities are increasing in order to overcome some of the raw material challenges that Novo has encountered. So that is an absolutely valid consideration.

Kavita Chawla: Thank you, Kat. Other questions for Kat? Okay. Any other stakeholders, Nonye?

Nonye Connor: This is Nonye. There is no other stakeholder that has their hand up.

Kavita Chawla: Okay, thank you. Okay, with that, Marissa, if we can bring the motion back up on screen, please. Thank you. And so I think the bullet point we were beginning to work on is at least one GLP-1RA with proven cardiovascular benefit will be included as a preferred agent. [Cross-talk] --

Marissa Tabile: [Cross-talk] This is Marissa. [Cross-talk] So I actually did look at our PDL, and I did want to mention that we do have Victoza preferred without any restrictions -- well, without PA. And that GLP-1 does have cardiovascular benefit to it. I will say in our current policy that we have in order for a patient to get a once-weekly GLP-1 with cardiovascular benefit, they would have to step through the Victoza. So just wanted to make that caveat in that mentioned there, even though it is not evident on our AHPDL right now because it is not the policy. That is what we have in our policy and how we handle those cases.

Kavita Chawla: How does the Committee feel about that? They would have to try liraglutide, and then they would -- basically, the clinician would have to give a good reason for moving to a longer-acting agent. In my practice, I do know that quite a few of my patients respond really well to dulaglutide, and then, of course, semaglutide agents because, number one, it is once weekly, and these are the patients I am trying to prevent them from even getting on insulin. And so the motivation that they are on a once-weekly injectable that has the cardiovascular and nephral benefits is quite motivating for them. So yes, please, Kevin and Christy. So Kevin, first. Please, go ahead.

Kevin Flynn: I just have a question. So it is preferred, but is it that they have to try it first for tolerance to make sure that they can tolerate the GLP-1? Or is it they have to fail in order to get the long-acting? Because I think that distinction would be important for everyone, right? Like, I think it might be reasonable to try just to make sure they tolerate it, but then go on to the long-acting.

Kavita Chawla: Typically that policy -- yeah, please, Marissa, I will let you speak to that.

Marissa Tabile: This is Marissa. So I am not sure exactly. Let me pull up the policy if it says tolerance. There is like a minimum. I believe we have, like, a minimum in there, like minimum days as to how long they have to have tried it in order to be eligible. So it would be [Cross-talk] trial [cross-talk] --

Nonye Connor: [Cross-talk] It is that you have to fail it, yeah [cross-talk] --

Marissa Tabile: [Cross-talk] It will be a trial of 90 days [cross-talk] unless it is contraindicated in a patient, and they can't use liraglutide, then that will be case by case.

Kavita Chawla: Kavita here. So with that 90-day trial, we do have to make -- we as a prescribing provider would have to note on there why liraglutide was inadequate and, hence, we are requesting the once-weekly agent. Kevin, if that answers your question. Go ahead, Zoe.

Zoe Taylor: I think Christy was first.

Christy Weiland: Yep. Thanks. This is Christy Weiland. So, Marissa, typically you have to fail two preferred is my understanding. The steps are [cross-talk] so given that we do have liraglutide on formulary, would they fill that one, and then we

could move to that once-weekly with cardiovascular? Or then are they going to have go to Bydureon, too, and then -- because I mean I want to make sure if we write it that it is [cross-talk] in mind.

Marissa Tabile: This is Marissa, it would just be the one liraglutide because at this time since that is our one preferred agent, that is really the only I guess -- let me reword this. That is the only preferred agent on the AHPDL that has the cardiovascular benefit, so we wouldn't require -- it doesn't clinically make sense for them to have to step through Bydureon because it doesn't have that indication. So, in essence, to answer your question, it would just be that one liraglutide in order for them to be eligible for one of the other once-weekly that does have that indication.

Christy Weiland: Thank you for that. So to clarify that we don't have to write that we want medication available with cardiovascular benefit for that for what you are saying to happen.

Marissa Tabile: Mm-hmm. Yeah.

Christy Weiland: We would still have to build that in.

Kavita Chawla: Go ahead, Zoe.

Zoe Taylor: Yeah, this is Zoe. So I have a patient example of why I think it is so important that we add a semaglutide weekly injection. I have a patient who has schizophrenia and also Type 2 diabetes. and when he was hospitalized for schizophrenia for several months, he was started on Victoza, which in the hospital setting worked fine for him because somebody was administering it to him, or at least handing it to him. and then when he was released from the hospital, he was homeless, and he was no longer able to deal with the Victoza daily injections with alcohol swabs and with unsanitary conditions and also with his mental illness, and so I put in a request for him to switch to Ozempic, which was denied because it was not considered sufficient reasoning, I guess, for why he would fail Victoza as an outpatient given his circumstances, which I completely disagree with. But I just wanted to tell a story that gives an example of why the weekly injection can be so important for some patients.

Kavita Chawla: So thank you for that patient example, Zoe. And so it seems to me that like on the Committee we have both schools of thought here that we would like to have a once-weekly GLP-1 receptor agonist with proven cardiovascular

benefit as a preferred agent. Yes or No, I guess? Should we take a vote on that? How many feel that we should have it as a preferred agent and make that recommendation? So we can do that by raising hands? Okay. So I think five. Okay, so I think that is the majority. So, Marissa, is that something that we can offer as a recommendation?

Marissa Tabile: This is Marissa. Yep. And you can go ahead and say whatever you want, and I will put it on the slide, and we can wordsmith as needed.

Kavita Chawla: Sounds good. So at least one GLP-1 receptor agonist with proven cardiovascular benefit administered once weekly will be included with preferred status. Yeah. There you go. Zoe, I see your hand is raised. Was there another [cross-talk] --

Zoe Taylor: Sorry, no. I didn't mean to have it raised up.

Kavita Chawla: No worries. How does that look to the Committee? I see some thumbs up. Okay.

Peter Barkett: So this is Peter Barkett, and if this is what the Committee wants, I think that is fine. I would be fine with splitting those two up saying at least one weekly GLP-1 on the preferred list and one GLP-1 with proven cardiovascular benefits should be on the preferred list. I don't know that we need an agent with both of those in the same agent. I kind of put that out there. So if five people want that in the same agent, I think that is fine. We will just keep moving on, but if there was anyone who voted that we want both those things and would be fine with them being in different agents, I would just offer that as a potential alternative.

Kavita Chawla: Thank you for that, Peter.

Peter Barkett: Yeah, and part of the reason I am thinking about that is liraglutide is set to go to generic later this year. Liraglutide has a proven cardiovascular benefit, and the GLP-1s, particularly the weekly GLP-1s that are not going generic, are driving quite a bit of increased total cost of care for diabetes. So if we have this on here, then potentially we are going to miss out on avoiding some additional cost for the Apple Health Plan for something that is -- and it is nice to have, particularly when somebody fails a weekly GLP-1, but in many cases, it is a convenience issue.

Marissa Tabile: This is Marissa. So I am glad that you brought that up, Peter, just because we have had GLP-1s come to our attention as of recently. We have done, I believe, an internal analysis as far as the costs for like what would happen if we shift placement of things on our AHPDL in our preliminary analysis. We did find that it is going to have a huge fiscal impact as far as our drugs then for Apple Health. The magnitude of it, I am not quite sure, but I know that it was very, very significant. And I am not able to speak to it because I didn't see it. It is just things what I have heard. But I just want to mention that it will have a very big fiscal impact if we do make a change like this. So just putting that out there.

Peter Barkett: Yeah. I mean to give a sense of the magnitude with the other health plan that I am involved in in their P&T Committee, GLP-1s has ballooned in the last five years, and it is, like, over $200 million annually. It is a lot of money. And in that other health plan, we are looking forward to liraglutide going generic and anticipating positioning that in our algorithms of care. If we keep the word in here, that will significantly mitigate the cost savings of that generic launch.

Kavita Chawla: These are all really great points. Thank you, both. The way I am thinking about it is, one is in within our purview. I think we are making these recommendations on the basis of safety and efficacy, and with that in mind, I do see the A1C-lowering benefit as well as the cardiovascular benefit is stronger with the longer-acting agents than with liraglutide. Liraglutide is still a great agent, but for the right patients it could mean the patient not having to transition to insulin in addition to the GLP-1. So I think as far as clinical benefit goes, I do think that there is enough evidence to support this. And then as Marissa and Donna told us, this will, of course, move forward, and then the final decision remains with HCA to determine whether they will cost-wise be able to include one agent or like this agent or not. But clinically, I feel like there is enough there to support it being called out. What do the other Committee Members think?

Zoe Taylor: This is Zoe. I continue to support what you wrote here on this slide.

Kavita Chawla: So I guess we can take a vote with offering the motion, and we can see how many yeas and nays we have. Okay. Whoever is ready to propose the motion.

Zoe Taylor: I can do a motion. I move that all products in the drug classes listed on Slides 5 and 6 are considered safe and efficacious for their medically-accepted

Indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in these classes may require prior authorization to determine medical necessity. All non-preferred products require a trial of 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. At least one GLP-1 receptor agonist with proven cardiovascular benefit administered once weekly be preferred on the AHPDL. Maybe we should say shall, should be preferred, or must be preferred.

Kavita Chawla: Do we have any Committee members seconding? I don't know if I am allowed to, Marissa. Am I allowed to?

Dimitry Davydow: This is Dimitry Davydow. I second.

Kavita Chawla: Okay, thanks. Okay. All in favor, say aye.

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

Kavita Chawla: Those opposed or abstain.

Peter Barkett: I am going to abstain.

Kavita Chawla: Okay, noted. Any other abstentions or nays? Okay. With that, the motion carries. All right. Thank you so much, Committee. This was a robust discussion today on a whole lot of topics, and we are six minutes over time. Marissa, how do you feel about adjourning today? Or any critical pieces of work left?

Marissa Tabile: This is Marissa. Nope. I think we were able to get through at least what we were able to get through for DUR. So thank you, DUR Board. Welcome to the new DUR Board Members. Nonye, do we have anything? Or Leta, do we have anything logistically that we need to wrap up because then I am going to turn it over to you.

Kavita Chawla: I will call out again Dimitry's service on the Board. Thank you so much. And we all wish you all the very best in your next endeavor.

Dimitry Davydow: Thank you. I appreciate that.

Leta Evaskus: And you have the best backdrop, so.

Kavita Chawla: Yeah! [Laughter]

Leta Evaskus: [Cross-talk] I don't have anything else for today. Nonye, do you?

Nonye Connor: No, I don't have anything else for today.

Leta Evaskus: Okay, thank you guys.

Kavita Chawla: Thank you. With that, we are adjourned. [cross-talk] --

Christy Weiland: Thank you.

Dimitry Davydow: Thanks, everyone.

Kevin Flynn: Goodbye.

Laura Beste: Bye-bye.

[end of audio]