Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
P&T Meeting Notes
February 21, 2018

Dale Sanderson:	We do have one new member here. I wonder if she would mind introducing herself.
Virginia Buccola:	Sure. Good morning. My name is Virginia Buccola. I'm a psychiatric nurse practitioner and I work in community mental health in Lakewood, Washington and I treat children and adults and have a special interest in prenatal population. Thank you for having me.
Dale Sanderson:	I wonder if we could go around the table and introduces ourselves.
Fran McGaugh:	I'm Fran McGaugh from CHPW.
Jennifer Brown:	Hi. I'm Jennifer Brown from Amerigroup.
Piao Ching:	I'm Piao Ching from Coordinated Care.
Petra Eichelsdoerfer:	Petra Eichelsdoerfer United Healthcare.
David Johnson:	David Johnson, Molina Healthcare.
Virginia Buccola:	Again, Virginia Buccola Nurse Practitioner and one of the committee members.
Nancy Lee:	Nancy Lee, committee member.
Catherine Brown:	Catherine Brown, committee member.
Jordan Storhaug:	Jordan Storhaug, committee member.
Dale Sanderson:	Dale Sanderson, committee member.
Susan Flatebo:	Susan Flatebo, committee member.

Leta Evaskus: Leta Evaskus, Health Care Authority.

April Phillips: April Phillips, Health Care Authority.

Donna Sullivan: Donna Sullivan, Health Care Authority.

Ray Hanley: Ray Hanley, Health Care Authority.

Emily Transue: Emily Transue, Health Care Authority.

Doug Brown: Doug Brown, Magellan Medicaid Administration.

Umang Patel: Umang Patel, Magellan.

Dale Sanderson: I'd like to start out with Donna Sullivan.

Donna Sullivan: So good morning. I'm going to talk to you about… just give you a little bit of background around the P&T Committee, as well as the DUR Board. Next slide.

First of all the roles and responsibilities of the staff that you see around the table. You have myself, I'm the Chief Pharmacy Officer with the Health Care Authority. Ryan Pistoresi who is not here today, but is usually at our P&T Committee meetings is our Assistant Chief Pharmacy Officer. He manages the pharmacy… or the public employees' pharmacy benefit for Uniform Medical Plan, as well as our Kaiser Insured Plans and he also represents Washington State on the Drug Effectiveness Review Board which is the evidence-based center that does our research for the P&T Committee. We have Ray Hanley. He is the Prescription Drug Program director. So he's in charge of the oversight of the P&T Committee itself and he manages the cost analysis process when we're making PDL decisions. We have Leta Evaskus who is our Prescription Drug Program analyst. Leta is the miracle worker who makes all these meetings happen and gets you paid and she manages the PDL that is posted online, as well. We have April Phillips who is our Clinical Pharmacist and the Apple Health preferred drug list manager. So she assists with the clinical

policy development and managing the PDL. Amy Irwin who is not here today she's our Medicaid Pharmacy Operations Manager. Some of you might remember Amy from years ago when she supported the pharmacy operations unit. She has rejoined us as the supervisor and she manages the pharmacy operations for our Medicaid Fee-For-Service Program and assists with the data submission and the cost analysis for the Medicaid program.

Other agencies that also attend is Labor & Industries and from Labor & Industries, they're not here today because this is a Drug Utilization Review Board which… we'll get into more detail later, but they don't participate in the DUR portion of our meeting. So they are not here today, but Jaymie Mai is the Pharmacy Manager for Labor & Industries. So she manages the Pharmacy Program for the Worker's Compensation Program. Doug Tuman, who is also a clinical pharmacist he's Jaymie's backup for supporting the Worker's Compensation Program when it comes to the prescription drugs and then Christy Pham is also a pharmacist from Labor & Industries that is responsible for implementing the PDL and helping manage the PDL for the Worker's Compensation Program.

The next slide I want to talk to you about the Drug Effective Review Project. DERP, as we call it, is a collaborative of 13 state Medicaid and public pharmacy programs and they produce evidence-based products that assist us with decision-making. The states that are currently participating are listed and I actually think there might be one or two more that have joined that I just didn't get into this slide.

The next slide I just want to give you some background about the Washington Prescription Drug Program. So the Washington Prescription Drug Program was created in 2003 when the legislature passed a bill creating the PDL and establishing the Washington State P&T Committee. It's a coordinated effort between Health Care Authority's Uniform Medical Plan, which is our self-funded state employee insurance plan, as well as the Medicaid Fee-for-Service and Labor & Industries, the Worker's Compensation Program. The PDL is a subset of each program's overall formulary or preferred drug list so the Washington preferred drug list has about 30 drug classes

on it and all of the programs have to have a comprehensive preferred drug list so we manage the classes outside of what's on the Washington PDL. The goal of the Prescription Drug Program was to develop a state-wide evidence-based preferred drug list and to control prescription drug costs without reducing the quality of care.

So there are several components of the Prescription Drug Program. One is the Endorsing Practitioner Therapeutic Interchange Program, the Pharmacy & Therapeutics Committee, the PDL itself, and then the NW Prescription Drug Consortium and I'll go into detail into those as we're coming up.

So the Endorsing Practitioner Program and Therapeutic Interchange Program it was established when the PDL was passed, the legislation was passed and the… what the legislators had in mind was when we developed the preferred drug list for drugs that were not preferred doctors could sign up to kind of endorse the list or they agreed with the list and what it does is it allows the doctor to determine whether or not therapeutic interchange should occur. So the therapeutic interchange allows a pharmacist to interchange a preferred drug for a prescribed non-preferred drug when it's prescribed by an endorsing prescriber and that they have signed the "may substitute" line. So they kind of made an additional use of the DAW or the "may substitute" or the "dispensed as written" portion of the prescription when you're prescribing. So a retail pharmacist if a non-preferred prescription prescribed by an endorsing provider those prescriptions would reject at the pharmacy and there would be a message instructing the pharmacist to make the interchange. So an example if Nexium was prescribed and it was non-preferred it would reject and it would tell the pharmacist to dispense one of the preferred drugs such as omeprazole. And that's when the doctors wrote… has signed the "may substitute" line. Now if the endorsing prescriber signs the "dispensed as written" line then the prescription would not reject. It would just be covered as normal unless there was some other clinical prior authorization on that non-preferred drug. This was also passed in 2003 when the PDL went into place and the legislators also wanted some protection on certain medications that were… but they didn't feel should be interchanged if a patient had

been established on them so they inserted into the legislation there are classes of drugs, the antipsychotics, antidepressants, antiepileptics, chemotherapy, antiretrovirals, amino suppressive drugs, or treatment for hepatitis C, those medications were all exempted from the therapeutic interchange. So if a patient had already been established on one of those medications we couldn't do interchange on that particular drug. There are about 7200 endorsing prescribers in the state of Washington that have signed up to endorse the list. I always get asked, you know, is that all… what percent of all prescribers have endorsed the list and that's a really difficult question to answer because we have lots of licensed prescribers in Washington State that may not be practicing in the state, but they still have an active license. So we… our database consists of all licensed prescribers, but only 7200 have actually signed up and endorsed the list and are currently active.

So the next slide is the Pharmacy & Therapeutics Committee. So the Pharmacy & Therapeutics Committee is consistent of 10 members and it meets the federal requirements of the Drug Utilization Review Board and the federal requirements of the Drug Utilization Review Board are that they need to be at least one-third, but no more than 51% of actively practicing pharmacists and at least one-third but no more than 51% of actively practicing physicians. So that's how we've come up with the makeup of the DUR board. So we have the four physicians, four pharmacists, the nurse practitioner and a physician assistant. So that allows us to keep that… those percentages in balance. We meet at least quarterly, but really we meet every… when we're in our kind of normal business mode we're meeting every other month because of the single PDL for the Apple Health Medicaid Program we've been meeting monthly since last summer. So I'm hoping that we'll go back to a normal routine starting with April. The charge of the Pharmacy & Therapeutics Committee is to review the reports that are developed by the Drug Effectiveness Review Project and compare the evidence of those drugs for their efficacy and their safety and make recommendations to the state on what drugs should be preferred or, you know, if they are interchangeable, how many should be preferred, those types of recommendations. The P&T Committee does not really go into the

clinical policies on when a drug should be covered. They are really just determining whether or not the drugs should be on the PDL, whether or not they are interchangeable and if there are special circumstances where a certain drug or a certain types of drugs or dosage forms should be made available as preferred. And then you will also indicate to use whether or not the drug class itself is interchangeable or sometimes we've had a drug class that has maybe, you know, several like subclasses underneath it of whether or not they are interchangeable within their subclass or across all of the classes. It's like the diabetes drugs you may have the DPP4s and the GLP1s and the… and so whether or not they are interchangeable across subclasses or just within their own. And then on the next slide we have the Washington Preferred Drug List. So again it is a list of about 30 drug classes and it is used by the agencies, the Health Care Authority, Medicaid and Uniform Medical Plan and then for Labor & Industries with the Worker's Compensation Program. And we began using the list in January of 2004 and I've already said that last one so we are going to move on.

Out of the Drug Effectiveness Review Project comes multiple types of reports and it can be kind of confusing. For the new members I'm going to go through what the types of reports are and for the old members it will just be a briefing of kind of what those reports do and what they mean. So we have new class reviews, we have updates to existing class reviews, we have expanded scan reports for an existing class, we have single drug addendums, and then we have literature scans for those existing drug classes. What we have determined kind of through our policies is that in order for a drug to be considered to be included as preferred on the PDL it has to have gone through a full review. So a full review is the new drug class review, the updated… the update to an existing class and expanded scan or a single drug addendum. And the reason why we say it needs to go through the full review as opposed to the scan is that the scans that are done they are only identifying new information, new studies, new drugs, and new indications that are out there in the literature. They're not actually going in and critiquing the actual evidence. They are just letting us know if there is a significant amount of information that might have come about since the last

time we've reviewed the class to determine whether or not the Drug Effective Review Project the states want to do an update to the class. So each year… actually twice a year the Drug Effectiveness Review Board will review all of the drug classes that they currently manage that have not been archived and they'll do a scan and they'll determine whether or not there will be a full update or not. And then often what we will do as the state individually if there is a couple of new drugs that have come out onto the market where the Drug Effectiveness Review Project itself is not going to update those… or review those drugs or add them to the class then we might commission a single drug addendum where we're just going to have that drug reviewed in order for it to be considered included into the PDL process. I'm going to stop and ask if you guys have any questions because I know I'm going really fast. There will be a test at the end.

So the next… on the next slide the status of drugs on the PDL. So oftentimes we'll talk about, "Well, what happens when we make something preferred or we say something is not preferred or they are interchangeable or not interchangeable?" So a preferred drug by definition, therapeutic interchange doesn't apply because you're not going to interchange a preferred drug for a preferred drug. So all preferred drugs are not subject to therapeutic interchange because they are just covered as preferred. Non-preferred drugs are those that are subject to therapeutic interchange and again they have to be included in a new class report. One of those updated reports, the summary review, single drug addendum in order for therapeutic interchange to apply. So if a drug is not included in one of those types of reports it's considered not reviewed by OHSU and we'll mark that on the online PDL and that means therapeutic interchange doesn't apply and also the DAW doesn't override the try and fail of the preferred products. So drugs that are not included in one of those reports are considered in the class, but again not subject to therapeutic interchange. And they are just covered according to the program benefit. So each individual agency might be able to make that drug preferred or not preferred depending on how they feel it should be placed for their particular program. And then drugs that are outside of the Washington PDL everything except those 30 drug

classes therapeutic interchange doesn't apply to any of those drugs. So it only applies to the drug classes that you are reviewing as the Pharmacy & Therapeutics Committee and allowing interchange to be applied. And the therapeutic interchange also doesn't apply to our managed care plans. As we are moving into the single Apple Health PDL for those drug classes that are on the Washington PDL the managed care plans are not going to be doing therapeutic interchange and neither does our fully insured programs contracted insurance for the public employees so Kaiser and Kaiser Washington. I just wanted to let you know that it really is just the Fee-for-Service Medicaid Program, Uniform Medical Plan and Labor & Industries that is doing therapeutic interchange.

So the next slide we've had some classes, you know, in 2004 when we first started doing the PDL, you know, Lipitor, the proton pump inhibitors, the statins, there were some calcium channel blockers, those were really the expensive drugs that were stressing our budgets and now most of those classes have gone… they are all generics or they are even over-the-counter. So we've started to archive some of those classes. One, you know, the Drug Effectiveness Review Project wasn't updating them. There wasn't a lot of new information coming out in those classes and so we did decide to archive them. So we're not going to bring them back to you unless there is something new that comes out or there might be a new drug where they might be the alternative. We might bring them back. But as we're presenting drug classes for you to archive we will review a final scan of the class or the last updated report and have you vote on whether or not it is appropriate to archive the class. And then you will determine if therapeutic interchange is appropriate and the dispense as written if that is appropriate. And then you'll direct us… we'll ask you to direct us to change preferred status on the drugs based on cost when appropriate without additional clinical review. So if we're looking at ACE inhibitors and one of the prices drops on one of the products or one of them skyrockets, you know, it will allow us to change the PDL without having to bring the class back to you to have you remove it since the evidence really hasn't changed, it's really just the cost of the medications that have changed. And then if we make any changes it

would still be in compliance with your most recent motion. So we would always be following what you had directed us to do as far as the content of the drugs within that particular class. And then the committee or the state can reactive any archived class, you know, whenever you feel that it is appropriate to bring it back just as a refresher. We might bring those back and have you just review them and review the drugs within that class.

And so the next slide is just kind of an overview of the actual process. So you make recommendations based on the evidence that comes out of the Drug Effectiveness Review Project. We do a cost analysis. So we take all of our utilization data from the three different programs and we send it to Milliman, our actuary who does a cost analysis and we'll give them some direction about, you know, which drugs to be preferred and we give them some direction on assumptions of how many people we think would switch from a non-preferred drug to a preferred drug. So we provide input into the analysis, but we don't do it ourselves. And then the staff, the Prescription Drug Program Work Group which consists of the three different programs, we review those cost analyses, the results of those analyses from the actuary and make recommendations to our state agency directors on what we feel should be approved. The agency directors will review that and, you know, either give us approval or ask for more questions. Once the final approval is made we send out a public announcement to the stakeholders letting them know what the final results were for that class. And then the agencies will implement the PDL typically with at least 30 days, sometimes longer before the effective date to give time for each of the programs to notify members that might be adversely impacted by any of the changes that are on the PDL.

So the Drug Utilization Review Board it is required by the federal statute that creates the Medicaid program. So Title 19 of the Social Security Act, specifically in 1927. It's an extension of the P&T Committee. It's an advisory only and it only applies to the Medicaid Program. And then DUR Program really is looking more at clinical criteria and appropriate utilization of drugs, not necessarily… not making decisions on the Washington PDL. You'll review and approve

the Drug Utilization Review Programs proposed by Medicaid and offer guidance and modification on those. Like our clinical policies like the opioid policy that you've reviewed, the hepatitis C, those types of policies and engage in provider education activities when appropriate and in addition to a new role with the Drug Use Review Board we'll be doing… we'll be providing guidance on the Apple Health Medicaid preferred drug list, which is what you've been doing mostly over the course of the last few months. The reason why we kind of have split the Apple Health PDL I guess responsibility out of the P&T Committee and into the DUR Board is because the P&T Committee governs or makes recommendations for Uniform Medical Plan, the public employees and Labor & Industries, the Worker's Compensation Program and in addition to Medicaid. And so we felt it wasn't appropriate for if it was specifically a Medicaid PDL that it really needed to be the responsibility of the Drug Use Review Board to make those recommendations that are specific to the Apple Health PDL. And so that's why we've kind of split the decision-making on those two preferred drug lists.

So the Apple Health PDL was created in a budget proviso just this past legislative session in 2017 and it instructed the Health Care Authority to create a single standard preferred drug list to be used across all managed Medicaid plans and to be implemented on January 1st and we did implement 13 drug classes on January 1st and I think we have.. I would say it has been pretty successful. I haven't heard a lot of complaints from providers and the plans I think are in the same boat. In order to support the Apple Health PDL we joined the top supplemental rebate pool, which is what brings Magellan here to the table with us and going forward for the PDL Umang Patel, the clinical pharmacist with Magellan will be presenting the clinical reviews to the board for development of the Apple Health PDL. So he'll be attending our meetings on a going forward basis. He won't be presenting today, but he will be starting at our next meeting. And then our next implementation phase for the Apple Health PDL is in July and we're going to be implementing a significant number of classes. Depending on how you slice and dice it, it's… when you count it at the subclass level it's probably several hundred. It sounds like a big list, but a lot of those are all generic drugs. A lot

of them are also already on the Washington PDL so it's not a big change. And we'll be bringing to you some clinical policies, mostly that's what we'll be doing next meeting, as well.

So the Apple Health PDL process. Magellan will provide a clinical review of the drug, new drugs, and the drug class. They'll present it to you. You've seen kind of the therapeutic class reviews that have been presented at several of the other meetings and then at the DUR Board meetings you will make those recommendations again on which, you know, if the drugs are interchangeable or if you feel there needs to be, you know, how many need to be preferred, how many need not be preferred? We might also have Magellan just recommend to you based on our utilization and the cost of the drugs so we might actually recommend products… specific products to be preferred. In addition, Magellan will be helping us with looking at our financial trend and utilization and trend and cost as we move forward on a quarterly basis. So we'll probably be bringing more utilization information to you, as well, for those classes that are on the PDL. And then again you'll make a decision for the PDL, the recommendations through a motion and in addition to that you'll make a recommendation on the clinical policies associated with those drugs or those drug classes.

The last slide is just acronyms because we use a lot of acronyms. So this typically this slide will always be in your packet as a cheat sheet. I'm doing my best to try to not talk with using acronyms, but sometimes I do slip up. But this will be in your packet for you to refer to. Any questions? Nope. Okay.

Dale Sanderson: Thank you, Donna.

Donna Sullivan: You're welcome.

Dale Sanderson: We have another new member that has joined us. I wonder if we could give him an opportunity to introduce himself?

Alex Park: Good morning. It's a privilege to be here. My name is Alex Park. I'm an internist in Seattle. I work with Pacific Medical Centers. I'm the

associate medical director the US Family Health Plan that's administered through PacMed and I'm very inspired and impressed by the work of the committee. PacMed has a long history of having internists serve with you. Thomas Vin Reece served with you for many years and prior to me Christopher Smith served a term, I think, that completed last year. So I'm happy to be continuing that tradition.

Dale Sanderson: Thank you. Is Stephanie available?

Leta Evaskus: Stephanie, are you on the line?

Stephanie Christofferson: I am. Are you ready for me?

Leta Evaskus: We are getting the slides up.

Stephanie Christofferson: While you're doing that just to introduce myself. My name is Stephanie Christofferson. I am the pharmacist with Magellan and I'm assisting Umang today in presenting the different therapeutic classes that we'll be reviewing today and for each one of these there will be a very high level overview of each of the classes. We'll look at indications, dosages and formulas and go over some of the guidelines that are still in place. So just let me know whenever you're ready.

Leta Evaskus: We're ready, Stephanie.

Stephanie Christofferson: Okay. I'm going to go ahead and jump right in. The first topic that we will be looking at are the anticonvulsants. You can go to the indication slide, please.

I'll address the next three slides all at once with the indications if you want to go ahead and scan them. When it comes to anticonvulsants there's little to no direct comparative data for the treatment of seizures or really any other indication and the selection of drugs for epilepsy treatment frequently depends on a particular seizure type. On the chart provided, as you can see we've indicated the medications in which they are either monotherapy or adjunct

therapies and also which medications that can be used in the pediatric population. While many patients can be maintained on one drug not all patients are seizure free. If control is not achieved on one drug it is suggested that an alternative medication be attempted before other medications are added to current therapy. The most reason for treatment failure with this drug class is related to non-compliance. So before adding on or changing any therapies of course that should be assessed along with any serum plasma levels that you could possibly obtain with the medications. All the agents in this review except the succinimides, [inaudible] klonopin, Equetrol, Banzel are FDA approved to treat partial seizures. The succinimides, clonazepam and [inaudible] acid derivatives are FDA approved for [inaudible] seizures and then the barbiturates hydantoins, the diazepam rectal [inaudible] acid, Depakote ER and carbamazepines and so on are all indicated for the indication of tonic clonic seizures. I did want to note that Sabril is the only anticonvulsant agent in this review that is indicated for the treatment of infant [inaudible] spasms. As you can see from the chart, as well, there are other indications in which these medications are approved for including bipolar disorder, migraine headaches and neuropathic pain. Next slide.

This takes us through the indications. When we come to dosing and availability again I'll talk as one with the next four slides. Most of the medications are available in a generic and of all the different classes that we have included in here there are generic options available for each one. As you'll note there are medications that are scheduled products in this class. [inaudible] is a schedule 3 controlled substance. The barbiturates and benzodiazepines are schedule 4 and the [inaudible], Lyrica, [inaudible] and [inaudible] are schedule 5. Many of the medications do require multiple dosages per day. However, there are some options in here that do offer once daily dosing which again might be a factor when choosing a medication for a patient. Most of the medications are available in a tablet or capsule form, but there are several medications that are available for folks that cannot swallow capsules such as liquids, chewables and ODT formulations. That information is available in the last column in the dosing and availability charts. I won't go through all the

medications in which that includes. And then finally I just want to point out that diazepam is available in both generic and brand in a rectal formulation or most people are more familiar with the Diastat for that one. Skip down to the guideline section.

I'll go through this briefly. The 2004 American Academy of Neurology guidelines states that Neurontin, Lamictal, Topamax and Trileptal have enough supporting evidence to use as monotherapy in adolescents and adults who are newly diagnosed with partial or mixed seizures. They also state that they do not state that one medication is superior over another. They state that the succinimides, clonazepam and valproic acid derivatives are FDA approved for absence seizures and that lamotrigine may be used for both monotherapy in children newly diagnosed with this condition although it is not included for the condition. For adults and children with Lennox-Gastaut Syndrome the guidelines recommend lamotrigine or [inaudible]. Agents that are FDA approved for adjunct therapy for this indication include clobazam, sulfonate, lamotrigine and banzel. Clonazepam may be used as monotherapy or adjunct therapy and sulfonate should be reserved for use if all other options have been exhausted. And then finally Sabril is the only anticonvulsant in this review that's indicated for the treatment as an infantile for spasms. However, the guidelines do recommend that low dose adrenocorticotropic hormone be used as a treatment of choice prior to using Sabril. For the 2017 International League Against Epilepsy this new guideline really honed in on new classifications of seizures based on three key features including the origin of the seizure, level of awareness during the seizure, and then other seizure features. They have stated that for seizure… the type of seizure onset will help determine the choice of the anti-seizure medication, but they did not endorse one over the other. And then finally for sudden expected death the 2017 American Academy of Neurology and American Epilepsy Association developed guidelines and they had just mentioned that the most notable risk factor for this was generalized tonic clonic seizures, which was found to be a precipitating event for patients that had experienced three or more tonic clonic seizures per year. With that said are there any questions on the anticonvulsants?

Dale Sanderson: Any questions from the committee members? Okay. I would just like to comment that this is being recorded so if you are going to have questions or comments if you could identify yourself, first. Stephanie, go ahead.

Stephanie Christofferson: Okay. The next topic we'll talk about are the anxiolytics. We'll go ahead and go to the indications slide, please.

Essentially in this review you've got benzodiazepines and then the serotonin 1A partial agonist, which is [inaudible]. All the medications do have an FDA approved indication for anxiety disorders. However, as you can see in this chart there are some medications that do treat alcohol withdrawal, also have a diagnosis for… or indication for seizures, muscle relaxants and insomnia. All the medications in this review are a controlled substance with the exception of Buspar which is a non controlled substance. Let's move to dosing and availability, please.

All the medications as you can see are available in a generic formulation and for the diagnosis of anxiety most of the medications are taken multiple times per day. They are available in a tablet or capsule formulation and then also as you can see alprazolam, diazepam and lorazepam do have alternatives available such as liquids and ODTs. If you want to go ahead and move to the guideline slide, please.

The ACFM and APA do share the same recommendations for therapy when it comes to anxiolytics. They recommend Buspar or Buspirone be considered for first line therapy for anxiety as they are not associated with dependency. They also recommend SSRIs or SNRIs for first line therapy, but do realize that the onset of action for these medications is a little bit lengthier anywhere from four to eight weeks. Overall, the guidelines do suggest benzodiazepines as add on therapy especially when the benefits outweigh the risks and they do state that the longer anxiolytics may be a better option due to less risk of abuse compared to the short-acting products. I'll go ahead and stop there if there are any questions.

Dale Sanderson: Any questions from the committee? We have one stakeholder, Kim Laubmeier. You have three minutes.

Kim Laubmeier: Good morning everyone. My name is Dr. Kim Laubmeier and I'm a director of health economics and outcomes research with Sunovion Pharmaceuticals. Thank you for the opportunity to present health outcomes information for eslicarbazepine acetate commercially known as Aptiom. Epilepsy is a serious and potentially fatal neurological condition. In a [inaudible] case study 36% of patients with epilepsy continued to experience seizures despite adequate trials of one or more AEDs. Indeed many patients require switching to a different medication or a combination of medications due to lack of efficacy or intolerable side effects and for these reasons the American Epilepsy Society has stated that "people without epilepsy must have access to and insurance coverage for all AEDs and all their formulations without formulary restrictions." On September 13, 2017 Aptiom received FDA approval for an expanded indication to treat partial onset seizures in patients four years of age and older. Aptiom is dosed once daily and may be taken crushed or whole with or without food. It is not a controlled substance and as recovery is opined therapeutic drug monitoring is not required. I refer you to the full prescribing information for a complete list of warnings, precautions and adverse events.

Recent health outcome studies have examined the effectiveness of Aptiom in real world treatment settings. In a published pooled analysis of five-year follow-up open label, uncontrolled data for more than 2,000 adults and adolescent patients with chronic partial onset seizures as recovery eslicarbazepine acetate was shown to be effective and well tolerated. After 12 months of adjunct treatment 73% of patients remained on therapy, 76% responded and 41% achieved seizure freedom. The median dose of eslicarbazepine acetate was 800 mg per day. Also in a retrospective claims database analysis of 325 adult patients with partial onset seizures as recovery of [inaudible] acetate initiation was associated with approximately 30 and 40% relative risk reduction in rates of all cause and epilepsy specific in-patient admissions respectively in a six-month follow-up

period. In closing, Aptiom may help address an important need in adult and pediatric patients four years of age and older with partial onset seizures and now on behalf of Sunovion Pharmaceuticals I respectfully request that Aptiom be included on the preferred drug list for the Medicaid beneficiaries in the State of Washington and again I thank you for the opportunity to speak today and I'm happy to address any questions.

Dale Sanderson: Thank you. Are there any questions from the committee before we move to provide a motion?

April Phillips: With the Health Care Authority our recommendation is that all products within each class or subclass are considered safe and efficacious and are eligible for preferred status at the discretion of HCA and all non-preferred products require a trial of two preferred products within that class or subclass with the same indication, but different active ingredients before a non-preferred product will be authorized.

Dale Sanderson: So the end of this motion… we can move, but the motion is not complete at the end. So including… to include…

April Phillips: So your motion would be to approve based on a recommendation or amended if you want to maybe add grandfathering or some other issue that you would like to address in your motion.

Amber Figueroa: I think we definitely need to do a grandfathering clause in there for patients who may be on something that's not chosen to be preferred but they are well controlled.

Leta Evaskus: To make changes I have to go to this version.

Nancy Lee: I have a question for Stephanie if she's still on the line. Stephanie, question regarding the anti-epileptic guidelines that you reviewed from 2004. Were there any medications not included in that guideline review that you presented in your table of charts of medications?

Stephanie Christofferson: I do not have that noted in here. I'm sure since then… I mean I could probably go back and tell Donna which medications since 2004 have come out since then, but I have nothing noted at this point in time.

Nancy Lee: Kind of based on that information I would agree with Dr. Figueroa in terms of grandfathering, especially if there are patients who are maybe some of these medications that are well managed or controlled in terms of their seizure therapy.

Amber Figueroa: Are we doing anticonvulsants and anxiolytics under a single recommendation? Okay.

April Phillips: That is something you can call out specifically if you want to have one versus the other differentiated.

Amber Figueroa: I guess I have concerns about benzos and would like a little bit of chat about… my opinion would be to pull them out and give the motion separately because they are two very different classes… groups of… they treat two different types of illnesses. What's the committee's thought on the benzos and anxiety as far as maybe grandfathering and coverage?

Susan Flatebo: I would think we need to say grandfathered in patients that are on, you know, stabilized on their anticonvulsant therapy, but not to grandfather in patients that are on anxiolytics.

Virginia Buccola: I would agree with that statement.

Amber Figueroa: So what would the option be for someone who's been on clonazepam for the last 10 years prescribed by their psychiatrist?

Virginia Buccola: As a psychiatric nurse practitioner I would say that there are many other options that could be explored considering a slow taper would be something that would be highly workable.

Alexander Park: There are some benzodiazepines which are included in the anticonvulsant class, clonazepam and others. I'm curious how the

committee feels about the grandfathering clause for patients who are stable on those medications?

Susan Flatebo: I would think if it's… it would fall under the anticonvulsant grandfather clause if they are taking them for, you know, epilepsy.

Leta Evaskus: Do you want to say anticonvulsant medications or just anti-anxiety, anticonvulsants taken for anxiety?

Woman: No. It should be grandfather patients already on anticonvulsant medications.

Amber Figueroa: Can we just separate it out into two separate motions? One for the anticonvulsants and one for the anxiolytics? I think it will be less confusing.

Dale Sanderson: I certainly have had patients that have been on benzodiazepines for their anxiety disorder, but clearly it was also a significant part of their anticonvulsant therapy, as well.

Susan Flatebo: I think this is tricky just because you look at the drug… what other drug class. So if a patient is taking, you know, an anxiolytic for their seizures, does that fall under the anxiolytic drug class or is it… I mean this is tricky.

Jordan Storhaug: The way I see this working most easily is actually leaving it as a single class and then grandfathering all medications except for the benzodiazepines, which I think are probably the ones that we have more concerns about doing, which would then leave Buspar potentially grandfathered, but then all of the other more traditional anticonvulsant drugs as grandfathered.

Amber Figueroa: So if you have a patient, Jordan, that has well controlled myoclonic seizures on clonazepam then they are going to have to try something else?

Jordan Storhaug: Or I would image they would probably do a prior authorization at that time. That's what that motion would require them to do.

That's the best way I can see to do it, but I admit that it's not perfect either. I do think it is difficult for… at the level of the insurance company to know exactly what the provider is thinking and the history behind that drug and I myself, as a primary care provider with people seeing specialists have a hard time trying to figure out is this your seizure doctor who wants you on this or is this your psychiatrist who wants you on that and that can be very difficult to tease out.

Dale Sanderson: Is the committee satisfied with the motion as written?

Leta Evaskus: Or did you want to go back to the one motion and just call out benzodiazepines?

Dale Sanderson: We have one motion with two subsections.

Amber Figueroa: I think that's fine with me. I mean in reality I'm not sure how many patients are taking benzos for seizures and anxiety so… but I think that's fine with me. It addresses the issue of the benzos. I guess I have a second question, which I don't think we can dictate here, but is there a way to make the short-acting… make sure that none of the short-actings are preferred? I don't think we can make that in the motion, but… to make it more difficult to use that as a first line therapy for anxiety.

Leta Evaskus: Jordan, can you tell me how you worded that?

Jordan Storhaug: Yeah… and then say already on medications with the exception of the benzodiazepine subclass.

Dale Sanderson: Is the committee satisfied with the motion as written?

Susan Flatebo: I second the motion.

Dale Sanderson: All in favor say aye.

Group: Aye.

Dale Sanderson: All opposed same sign. Motion passes.

Nancy Lee: Should we re-read the motion since… oh, nobody made a motion?

Woman: Jordan did.

Jordan Storhaug: I did not read it. I can read it.

Dale Sanderson: Do you want to go back?

Jordan Storhaug: I move that the Apple Health Medicaid Program implement the limitations listed on slide 17 for each drug class listed on slide 16 amended to grandfather patients already on medications with the exception of the benzodiazepines subclass.

Susan Flatebo: I second.

Dale Sanderson: It's official. All in favor say aye.

Group: Aye.

Dale Sanderson: All opposed same sign. Stephanie, we're ready for your next section.

Stephanie Christofferson: Okay. The next group we'll talk about are the cephalosporins and related antibiotics. The first slide looks at the indications. In this review we have four classes including first, second, and third generation cephalosporins and then also the penicillin beta-lactamase inhibitor combinations. As you can see from the chart at the top the medications do treat a wide variety of disease states including community [inaudible] pneumonia, acute exacerbation of chronic bronchitis, acute otitis media, pharyngitis, gonorrhea, skin infections, UTIs, sinusitis, Lyme disease and impetigo. The selection of the product should be based on the indication and the emergence of cephalosporins resistant strains of the various infectious [inaudible]. Go ahead and go to the next slide, please.

All the medications are available in a generic with the exception of Suprax tablets and chewables. Most of the medications are dosed

multiple times daily, which of course could impact patient compliance and maybe a consideration again once using the medication. There are once-a-day medications including cefadroxil, cefdinir, ceflixime and ceftibuten. The medications are available in a variety of formulations which are indicated in the last column including the capsules, tablets, chewables and liquids. Next slide.

That just finishes out the rest of the antibiotics there, the dosing and availability. Move over to the guidelines.

The 2007 American Thoracic Society and Infectious Disease updated guidelines last… like I said in 2007 for community acquired pneumonia they recommend a macrolide or doxycycline in adult patients who are otherwise healthy without risk factors. For adults with comorbidities the first line therapy for community acquired pneumonia may include a respiratory for [inaudible] or a beta-lactam plus a macrolide. Other oral beta-lactam alternatives include cefpodoxime and cefuroxime. Next for childhood community acquired pneumonia the 2014 World Health Organization suggests the use of amoxicillin as the best first line agent in an outpatient setting and they also state that Bactrim may be considered in an alternative setting for some patients. Second line options include the amoxicillin/clavulanate acid combination with or without a macrolide for children that are over the age of three years of age. For acute bacterial rhinosinusitis the 2015 recommendations recommend amoxicillin with or without clavulanic as first line therapy. In patients who have a penicillin allergy they recommend [inaudible] be used. For acute pharyngitis the 2015 guidelines recommend penicillin or amoxicillin. For those who are allergic to penicillin they recommend a course of cephalosporin, clindamycin or chloromycetin or azithromycin therapy. For urinary infections for acute cystitis the empiric antibiotic selection is nitrofurantoin. Bactrim and fluoroquinolone may be considered, but with those medications resistance may be of a concern. And finally cephalosporin and amoxicillin with [inaudible] are appropriate regimens and other agents cannot be used. For skin infections the 2014 recommendations from IDSA for treatment of impetigo is the

use of either topical mupirocin or Altabax. Oral therapy can include either cephalexin or [inaudible]. Any questions on that?

Dale Sanderson: From the committee? None. Go ahead.

Stephanie Christofferson: The next topic is the fluoroquinolones. Go ahead and go to the indications. The oral fluoroquinolones do treat a variety of antimicrobials. The older fluoroquinolones have gram negative activity and they are useful for the treatment of urological infections while the newer products have activity both covering gram negative and gram positive. Many factors must be considered when choosing the most appropriate product for a particular patient including culture and sensitivity information being used when it is available. There's little evidence that exists suggesting clinical outcomes facing tolerance among the different products when they are administered for the appropriate indications. As you can see from the first slide there are several disease states in which the fluoroquinolones are approved for. The newest product is called Baxdela which came out in 2017 and it is indicated for the treatment of acute retrial skin and skin structure infections. This could include MRSA. The medication just provides another treatment option for [inaudible] skin infections.

On the next slide with the dosing and availability the medications most of them are available in a generic and they can be taken anywhere from once daily with the Cipro XR or Levaquin or twice daily with some of the other products including the new product Baxdela. The Cipro and Levaquin are available in a suspension, as well. Next slide.

This looks at the guidelines. Again, as we just discussed the community acquired pneumonia guidelines recommend a macrolide or doxycycline for patients who are healthy and then again with the patients who have [inaudible] diseases the respiratory fluoroquinolone in this case would be recommended such as moxifloxacin or levofloxacin. For anthrax the indicated products here are sitafloxacin, levofloxacin and doxycycline which can be used in adult patients. There's no safety data on the use of Levaquin

beyond 30 days thus they do recommend ciprofloxacin or doxycycline be used as first line therapies. For uncomplicated cutaneous anthrax it's been successfully treated with a single oral antimicrobial drug such as the oral fluocinolone and then also doxycycline can be considered. Again, with the acute bacterial rhinosinusitis clinicians should be prescribing amoxicillin with or without clavulanic as a first line therapy, but when this [inaudible] possible they do recommend that respiratory fluoroquinolone can be used, but again it's not recommended to be the first line agent. And then lastly for acute [inaudible] as we mentioned [inaudible] and Bactrim are appropriate first line therapies, but again if they cannot be used fluoroquinolones can be used but again the resistance and the increased rates of MRSA should be a consideration when choosing these medications as second line therapy. With that said any questions on the fluoroquinolones?

Dale Sanderson: I see none. Go ahead, Stephanie.

Stephanie Christofferson: Okay. The next topic we'll talk about is lincosamides. We'll look at the indications. Clindamycin is indicated for the treatment of serious infections of the respiratory tract and skin and soft tissue structures and it is also widely used for the treatment of infections due to MRSA including community and hospital acquired MRSA infections. Zyvox is bacteriostatic against staphylococcus and enterococcus and [inaudible] against streptococcus. Silvextro has activity against gram positive organisms including staph aureus, including the MRSA and [inaudible] susceptible isolates. When it comes to resistance there have been reports of bacteria becoming resistant to clindamycin. I think less frequently there have been reports also for resistance to Zyvox. So therefore in order to reduce the development of further drugs resistant bacteria maintained effectiveness of the antibiotics. Silvextro has been recommended to only been used in infections in which there's proven susceptibility to the drug. Next slide, please for the dosing and availability.

Clindamycin, as you can see, is taken four times daily where Zyvox and Silvextro are taken twice daily which may be a consideration against the compliance in some patients. Silvextro is not available in

generic unlike the other products and then just a note Zyvox is available in a generic for the suspension where the tablet is not. Next slide for the guidelines.

We'll first look at the soft… I'm sorry, the skin and soft tissue infections for the 2014 IDSA guidelines. The guidelines state that for minor infections they may be [inaudible] treated with penicillin first or second generation oral [inaudible], macrolides, Bactrim or clindamycin. However, simple abscesses they just recommend an incision and drainage [inaudible] rather than therapy. Most community acquired MRSA strains remain susceptible to Bactrim and tetracycline. However, it has been noted that 50% of cases where patients have MRSA they are becoming resistant to clindamycin therapy. This covers for both beta hemolytic streptococcus and community acquired MRSA as needed. The options include clindamycin monotherapy, Zyvox monotherapy, Bactrim or a tetracycline in combination with a [inaudible] such as amoxicillin. At the time of these updates it was noted that [inaudible] was not available. So it was not included with these updates. As we discussed with community acquired pneumonia, again, macrolide with or without a beta-lactam and [inaudible] can be used. For hospital acquired MRSA or community acquired MRSA pneumonia clindamycin… I'm sorry, intravenous [inaudible], oral or intravenous [inaudible] or clindamycin can be treated when the strains are [inaudible]. And then finally for diabetic infections the FDA has approved linezolid for MRSA infections of the diabetic foot. Clindamycin is recommended for mild infections, but sensitivity should first be checked that [inaudible] that clindamycin may be used with levofloxacin or ciprofloxacin in moderate inductions. With that I will ask if there are any questions on the lincosamides section.

Leta Evaskus: Stephanie, would you be able to speak louder? I have you up all the way but it's still kind of hard to hear.

Stephanie Christofferson: Sure. I sure can.

Dale Sanderson: Committee questions at all? I see none. Go ahead, Stephanie.

Stephanie Christofferson: Okay. Next we have the tetracyclines. The tetracycline antibiotics have a similar range of antimicrobial activity and safety profiles and as you can see are treated for a variety of infections. However, the number of uses for these medications are declining due to drug resistance. The tetracycline antibiotics with the exception of doxycycline hyclate 20, doxycycline monohydrate delayed release or minocycline extended-release are indicated for many infections, including ophthalmic infections, Rickettsial infections, respiratory tract infections, sexually transmitted diseases, anthrax, other specific bacterial infections caused by the plague or cholera and they also can be used as an adjunct to penicillin for some organisms such as uncomplicated gonorrhea or syphilis. And lastly they can be used as adjunct therapy for severe acne or acute intestinal ameba infections. Next slide, please.

As you can see on this slide here is additional indications that we have not already discussed. However, I won't review those. I'll just give you a second to look at those.

And then the next slide looks at the dosing and availability of the tetracyclines. All of the generics are available as a generic with dosage frequencies ranging anywhere from once daily to two times daily with some of the delayed release versions of the products and then as you can see many of the other products are just up to four times daily. Most of the medications are available, again, in tablet and capsule formulations. However, doxycycline is available in a liquid formulation. Next slide, please.

The next slide looks at the guidelines. The first one we'll address is the sexually transmitted disease guidelines that were developed by the CDC in 2015. In the guidelines they state that they no longer recommend doxycycline for the treatment of urethritis. Doxycycline is an alternative agent for the treatment of granuloma inguinale. Azithromycin is actually now the preferred agent for this. It is still preferred for the treatment of lymphogranuloma, cervicitis, and infections due to chlamydia. Doxycycline is a part of the treatment regime still for acute epididymitis and proctitis in sexually transmitted rectal infections when gonococcal or chlamydia

infections are presumed to be microbial. And then finally doxycycline and tetracycline are alternatives for the treatment of syphilis when a patient has a severe penicillin allergy. However, it is preferred over tetracycline due to the potential for greater GI side effects associated with the tetracycline. For pneumonia the 2007 American Thoracic Society and Infection Disease Organization, again, we've reviewed these. Again, they recommend the macrolides or doxycycline for healthy individuals and then with comorbid disease states in adults they recommend first line therapy with respiratory fluoroquinolones or beta-lactam plus a macrolide. Doxycycline may be used as an alternative to macrolides in combination with a beta-lactam. The anthrax indication… I'm sorry, guidelines we've already reviewed. Again, it's stating that the doxycycline can be used for initial therapy in inhaled anthrax and that also doxycycline is recommended over lomefloxacin. And then finally for the treatment of acne systemic antibiotics are included at the standard of care for management for moderate to severe acne and then also a treatment-resistant form of inflammatory acne. According to the guidelines doxycycline and minocycline are more effective than tetracycline, but neither product is preferred over another. I'll go ahead and close that. Are there any questions for the tetracyclines?

Dale Sanderson: Any questions at all? I see none. Go ahead.

Stephanie Christofferson: Okay. Next, we'll look at the antifungals, oral. Again, the antifungal agents have a different spectrums of activity and are FDA approved to treat a variety of indications. They are used in the outpatient setting generally for the treatment of fungal infections due to oropharyngeal or esophageal candidiasis, urinary tract infections, superficial skin infections, and then toenail fungal infections. Due to the excellent penetration into the tissues Diflucan is an effective treatment for a variety of the infections and it also lacks the concern about pH dependent absorption that's needed with the cetoconazol product. Vfend has been shown to have similar efficacy to fluconazole in the treatment of esophageal candidiasis. However, more adverse effects have been reported with the medication and intravenous loading dosages are required during the first 24 hours of therapy for all of the infections except the esophageal candidiasis.

For serious fungal infections Cresemba, Noxafil, Ancobon, Vfend, intraconazole and fluconazole can be used for the treatment and/or prophylaxis of various serious fungal infections. To note though Noxafil oral suspension has an indication for the treatment of oropharyngeal candidiasis. One, it is refractory to intraconazole or fluconazole and then also again intraconazole and terbinafine I just wanted to note also have the indication to treat toenail fungus infections. Next slide.

This just looks at the rest of the indications for the products. Give you a second to look at that if you like.

And then the next slide looks at the dosing and availability of the oral antifungals. Cresemba, Onmel, Oravig and Noxafil I did want to note do not have generics available. The dose frequencies vary amongst the products as well as the lengths of therapy, which are dependent on the fungal infections in which they are intended to treat. There are… in the last column as you can see there are a wide variety of availabilities as far as dosage formulations including Troche, tablets, suspensions, capsules and buccal tablets and lozenges. Next slide, please.

This looks at the guidelines. The first set of guidelines is from 2016 on candidiasis from the IDSA which state that treatment of oropharyngeal candidiasis in adults includes clotrimazole troche, miconazole buccal tablets or nystatin for mild disease. And then for moderate to severe oropharyngeal candidiasis and for esophageal disease Diflucan can be used or is recommended. For oropharyngeal fluconazole resistant refractory disease intraconazole solution or Noxafil suspension may be used. In esophageal candidiasis Noxafil, intraconazole or Vfend may be used in patients with fluconazole refractory infections. And then finally for toenail infections usually for mild to moderate disease states topical antifungals can be used. However, the more involved or advanced cases that require systemic therapy griseofulvin, intraconazole or terbinafine can be used. In comparative trials, however, there have been higher success rates with terbinafine compared to intraconazole. And then lastly I just wanted to mention that griseofulvin usage has decreased since the

emergence of the azole fungals and terbinafine. Any questions with the antifungals?

Dale Sanderson: Any committee questions at all? None.

Stephanie Christofferson: Next we'll look at the antifungals that are topical. The first slide looks at the indications. Many of the topical antifungal preparations are available as actually either prescriptions or over-the-counter products. Most fungal infections of the skin can be treated topically. With the exception of Bensal HP, Hongo Cura, and Fungi Nail the agents in this category can be primarily divided into two principle pharmacological antifungal groups which are the [inaudible] and the [inaudible] which essentially work the same by altering the cell membrane of the fungi. In meta-analyses though I will mention that the [inaudible] means cure slightly more infections than the azoles and they are also available over-the-counter now. There is limited data regarding the comparative efficacy and treatment of the various fungal infections and there is also limited data comparing the comparative… the efficacy for the treatment of seborrheic dermatitis. There are some newer products available. The first one is Pedipak, which is indicated for the topical treatment of the amino competent patients in mild to moderate toenail infection or onychomycosis of the fingernails and toenails. It combines existing therapy of the [inaudible] lacquer with Urea, which is thought to increase the penetration of the [inaudible] to the nail bed. The dosing indication, safety and effectiveness for the medication is similar to that of the other products that are available, but also I wanted to mention there is a lack of comparative studies with the ciclopirox, Jublia and [inaudible]. So it's difficult to measure the effectiveness of one product over the other for this indication. Another new product is Dermacinrx Therazole Pak which is indicated to treat [inaudible]. And then Luzu was another new [inaudible] that has similar antifungal properties to the other products that are available. Next slide.

Again, just the rest of the indications. Next slide.

More indications. Next slide.

This looks at the dosing and availability of the topical antifungals. Again, there are generics in this class and OTCs that are available for many of the medications. Administration can vary between the products from once-daily up to four times daily depending on the medication and also the indication in which is being treated. There are also a wide variety of dosage formulations including creams, ointments, gels, lotions and so on. I won't go through the whole list there. There are quite a few, but selection of the dosage formulation is usually dependent on the location of the fungal infection, patient preference, and severity of disease. I will say in general creams and lotions are less effective than ointments for the topical preparations. The ointments are best at delivering the drug to the skin and also for fighting a protective barrier. Next slide.

Again, this just looks at the rest of the dosing availability. Next slide.

Same thing. So I'll go ahead and jump over the guidelines.

There are several agents indicated to treat superficial fungal skin infections, as well as cutaneous candidiasis. The newer agents may offer shorter treatment of duration compared to the older products. Again, there are several agents that are available over-the-counter including clotrimazole, miconazole, terbinafine and tolnaftate. Combination therapies that include corticosteroid are also often times available when there's inflammation present. For onychomycosis there have been significant improvements with treatment of the disease. However, even with therapy approximately 20% of patients still fail on antifungal therapy and actually the treatment therapy of course the therapy can be quite expensive for this indication. Sometimes going up to 48 weeks for therapy. Oral antifungal agents may offer a higher success rate compared to the topical products. However, there are times when prescribers will prescribe both an oral and a topical preparation or antifungal in order to shorten the recovery time and then also lessen the risks of adverse reactions for the medications. I'll go ahead and conclude that with the antifungal topicals. Any questions?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Okay. The next we'll look at are the antivirals and the oral medications. We essentially broke this one up into two different groups. You've got the herpes medications and then the influenza medications. I'll first address the herpes medications. When the antivirals for HSV are used they are used to treat and partially control signs and symptoms of the infection due to initial or recurrent episodes. They can also be given as daily suppressive therapy in order to reduce the frequency in which patients have episodes. But they do not of course eradicate HSV. Acyclovir, famciclovir and valacyclovir can be used for the treatment also of herpes zoster or shingles which can increase after the age of 60. The goal of therapy for this is to reduce the pain in patients and stop viral replication in patients and those with ophthalmic herpes zoster. The antivirals reduce the duration of viral shedding and development of new lesions and then also help promote the healing of the rash. Meta-analyses have shown and also clinical trials have demonstrated that the antivirals also can significantly reduce the duration or incidence of prolonged pain in these individuals. Sitavig is a newer product. It does offer a tablet formulation that has minimal systemic absorption and this is indicated to treat oral hepatic lesions. However, it has not been compared to other formulations. Next we'll look at the flu for indications. As you are aware influenza is most often times self-limiting. However, patients who are very young or very old or in patients who are amino compromised they are more susceptible to the disease and also are more predisposed to secondary complications and sometimes potential fatalities because of the flu. First and foremost vaccinations are considered primary method in which to prevent the flu. However, once one gets the flu there are treatment options available for treatment. All the antivirals for the treatment of influenza should be started as soon as possible and within 48 hours after the illness onset in order to maximize benefits. Benefits being could reduce the flu by one to two days or reduce some of the complications such as getting pneumonia or respiratory failure or death. Prophylactically, according to the CDC, antiviral medications are about 70 to 90% effective in preventing influenza once being exposed. However,

again, they are not recommended if contact with the person that had the flu has been… or has exceeded 48 hours. Tamiflu is approved for the treatment in children two weeks of age and older and for the prevention of influenza in children one age and older and does still remain the drug of choice. Relenza is approved for the prevention of influenza in children as young as five and it is approved for the treatment of influenza in patients seven years and older. I think really with the limitation of Relenza is the fact that it is an inhaler and, again, especially in the pediatric population, coordination with an inhaler and taking the medication can be problematic. And finally Flumadine is not recommended to be used in influenza prophylaxis due to resistance. It's really no longer reviewed, but we do include it in here because it is still an FDA approved indication for the medication. Next slide, please.

This looks at the dosing and availability. Generics are available except [inaudible] and Relenza. Average dosages ranges vary by disease states that one is being treated for. The medications are available in capsules and tablets with acyclovir/Sitavig, Tamiflu and Ranitidine also being available in liquid formulation. As I mentioned, Relenza is an inhaler. Next slide, please.

These are the guidelines. For herpes the CDC states that all three agents are similar in efficacy and side effects. They also do not promote one product over another and they do also mention that oral products are preferred over topical antiviral therapy. For the management of herpes zoster, again, similarly they support the use of any of the three agents and they do not select one agent over another. And then finally I just wanted to mention that with the CDC they do recognize that acyclovir and valacyclovir are approved for treatment of chickenpox. For influenza as we're all aware the CDC monitors influenza viral resistance and publishes recommendations with each season. Again, these guidelines stress the importance of vaccinations and one is needing treatment they recommend either Relenza or Tamiflu. They also note that the Relenza does utilize a complex inhalation device and is not recommended for patients with respiratory disorders. And they also stress the importance of initiating therapy within 48 hours of exposure in order to obtain best

results. And then again, as we mentioned earlier, they do not recommend the use of rimantidine in the U.S. due to viral resistance and lack of influenza B coverage. Any questions with the oral antivirals?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Okay. Next we will look at hepatitis B agents. The ultimate goal, of course, is to eliminate HBV transmission in the U.S. by broadening the recommendations of immunization. However, when treatment is needed the goal is to eliminate or suppress the replication of the HBV and to decrease the risk of progression to cirrhosis and other serious effects of the disease. [inaudible] A, Hepsera, Baraclude, Pegasus, Tyzeka, and Viread are all indicated for initial therapy for chronic hepatitis B. There is a newer product available called Vemlidy which is indicated for chronic HBV infection in adults with compensated liver disease. When selecting medications drug resistance may be something to consider. It's been noted that the Epivir HBV and Hepsera are more susceptible to drug resistance. It has also been noted that Epivir has… even though it's been approved for initial therapy due to rapid resistance the use of other agents may be a consider and in fact there have been studies which have shown that after three years of use resistance can be seen in over 50% of patients. When it comes to Hepsera there have been several trials, some lasting up to 72 weeks in which those trials resistance was not noted. However, it has been reported in case studies. And then finally Baraclude resistance is a little less common but it is still possible and so far there is no clear pattern of resistance with Viread or Vemlidy. Next slide, please.

This looks at dosing and availability. There are generics available for Hepsera, Baraclude and Epivir HBV. The medications are available in tablet formulations with the exception of Epivir HBV and Baraclude which are also available in liquid formulations. And I did want to mention that Tyzeka has been discontinued by the manufacturer. The reason it is being reviewed just case there happens to be some medications still on the shelf, for completeness we do include it, but

eventually as that gets phased out the medication will probably be removed from our review.

Lastly, the last slide looks at guidelines. The 2015 World Health Organization guidelines recommend Baraclude and Viread in adults and children who are 12 years or older and then patients… and then Baraclude also can be used or is recommended in patients who are under the age of 12. They do not recommend Epivir HBV, Hepsera or Tyzeka as first line therapy. I did want to mention that Vemlidy was not reviewed as a part of these guidelines. For the next section the 2015 American Gastroenterological Association their first line agents recommended include Baraclude and Viread. They no longer recommend Hepsera due to the low efficacy in higher resistance that we talked about. And they also do not recommend Epivir unless other agents are inappropriate due, again, to the high resistance of the high drug resistance. Combination therapy they have noted it is usually not recommended for all patients undergoing treatment for chronic HBV. And then they also recommend that issues for consideration for therapy include safety, efficacy and rate of resistance, method of administration and cost. And then last the 2016 AASLD guidelines recommend Baraclude and Viread as first line options. They did also indicate that Vemlidy was not available at the time of publication so it was not included in the review and much like the AGA they also recommend looking at safety and efficacy and cost of the product, as well as patient preference when selecting the medication. Any questions on the hepatitis B section?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Okay. The next we have are the immunosuppressants, oral products. With these products the ultimate goal of the immunosuppressant therapy after organ transplantation is to prevent organ rejection and prolong graft and patient survival by providing an environment of essentially permanent acceptance where the new organ is recognized as self. Following induction therapy at the time of surgery transplant recipients are started on drug regimens that consist of several categories including corticosteroids. Often times multiple agents are used in order to

capitalize on different immune mediated mechanisms and also this [inaudible] times for a lower dosages of the individual agents which could be beneficial in eliminating some of the toxic side effects of the products. Cyclosporine, tacrolimus are effective calcineurin inhibitors with well-established roles due to their more reliable pharmacokinetic profiles which is helpful to a provider because it provides a greater ease of monitoring patients and their drug levels. I also wanted to mention that the tacrolimus products are not interchangeable or substitutable. Cyclosporine has been successfully used to prevent rejection in the heart, liver and renal transplantation, but tacrolimus is often most used instead, especially in renal transplantation patients due to the established nephrotoxic side effects of cyclosporine. However, cyclosporine still is the preferred agent for heart or lung transplants. Azathioprine is also indicated for rheumatoid arthritis but it is not used much anymore and cyclosporine is also indicated for rheumatoid arthritis and refractory plaque psoriasis. I just want to mention that as additional indications for these products. Next slide, please.

For these products, again, most of them are available in generics, however Zortress, Astagraf XL and Envarsus XR do not have generics. Dosages for the products range anywhere from once to twice daily and the medications are available in tablets, capsules and solutions. Next slide, please.

This looks at the guidelines. The 2009 Kidney Disease Improving Global Outcomes guidelines looks at kidney transplant. They recommend initial maintenance immunosuppression with antiproliferative and calcineurin inhibitors with or without corticosteroids. Namely they suggest myophenolate and tacrolimus as first line and agents for kidney transplants. They caution against the use of [inaudible] target of rifamycin inhibitors until the graft function has been established and surgical wounds have been healed. For the 2012 AASLD liver transplant guidelines there's no standard of care designation for liver transplant patients and they just acknowledge that the drug selection and dosing should be individualized for the unique needs of the patient. The 2015 American College of Rheumatology on rheumatoid arthritis

guidelines azathioprine and cyclosporine are not included in this update due to lack of new data since the 2012 criteria and it just states that they are used less due to the emergence of the new biologics that are used for the indication instead. And then finally the 2009 American Academy of Dermatology for plaque psoriasis states that cyclosporine should be considered only in adults that are not immunocompromised after failure with other systemic therapy. So again it's not recommended as a first line therapy for the indication. With that said I'll go ahead and ask if there are any questions on the immunosuppressants?

Dale Sanderson: Any questions from the committee? Any questions on this whole section? We've covered a lot of ground here. I see none.

Stephanie Christofferson: Okay. Thank you.

Dale Sanderson: We have no stakeholders listed. Any input on the motion from the recommendation here?

April Phillips: I just want to clarify. There's a large number bundled together with the motion and at this point it's just a time saving measure rather than having a motion with each drug class since we are reviewing such a high number of drug classes at each meeting. So during your motion if you would like to call something out specific that is your right.

Dale Sanderson: Do we have the recommendation like as listed and then the motion basically accepts that recommendation unless we have any amendments?

Alexander Park: Under the fluoroquinolone section I would be concerned about including delafloxacin. I don't believe it is currently included in any current treatment guideline for skin infection or soft tissue and it's quite new so the safety data in clinical practice is not yet available.

Dale Sanderson: Do we need to call that out specifically in our motion?

Woman: If you choose.

Dale Sanderson: How do you suggest wording for that?

Alexander Park: I guess we could say that we move that the program implement the limitations listed on slide 64 for each drug class listed with the exception of delafloxacin until additional experience of that medication is noted in clinical practice.

Donna Sullivan: When you said with the exception of I didn't hear which… what you said. What are you trying to get at?

Alexander Park: Please let me know if I'm being appropriate here. I'm new to the committee.

Donna Sullivan: Not at all. If there's a particular drug that you think should be non-preferred then you can go ahead and call out that drug and say, you know, in this particular class this drug should be non-preferred or put it on PA and, you know, second line therapy, however you want it to say.

Alexander Park: I would recommend delafloxacin non-preferred and put it under prior authorization.

Donna Sullivan: Okay. So I would just… you can just insert that into the motion.

Amber Figueroa: I think we probably need to make some kind of a grandfathering clause for the hepatitis C drugs.

Donna Sullivan: Yes, please do. And if you… it might be helpful to make the motion to implement the recommendations on slide 64 and then name the drug classes and then whether or not there should be grandfathering in that class just so we have that on the record, you know, which ones you want to definitely have grandfathering and then which ones that HCA could grandfather at our discretion. Some of the ones that you say don't need grandfathering we grandfather them anyways to kind of spread out disruption if there is going to be any.

Susan Flatebo: I would also think that immunosuppressives should also be grandfathered in.

Catherine Brown: I agree.

Leta Evaskus: Could you say that again?

Catherine Brown: Immunosuppressive agents should also be grandfathered in along with the hepatitis B agents.

Nancy Lee: I'd also like to add to bullet point number two for that medication in the tetracycline drug class, the one that is off label use for [inaudible] DH and not really recommended for drug of choice for skin and skin [inaudible] infections called demeclocycline.

Leta Evaskus: The second bullet in the motion or…

Nancy Lee: The second bullet in the motion.

Leta Evaskus: Could you say that again?

Nancy Lee: Um, so the second bullet in the motion I'd like to propose to include demeclocycline.

Dale Sanderson: Do you actually want to specify each class in this motion?

Donna Sullivan: It might be easier just to do this with each class and say, you know, cephalosporins grandfather, not grandfather or grandfather at our discretion and then if you have any limits in the exclusions for cephalosporins and then go to the next class and do the same thing. I think that might be more… a little bit clearer in the direction to us.

Jordan Storhaug: I think we might be there already.

Donna Sullivan: Okay.

Dale Sanderson: Any other amendments we need to make to this motion? I'll go ahead and make the motion then. I move that the Apple Health

Medicaid Program implement the limitations listed on slide 64 for each drug class listed on slide 63. Delafloxacin and demeclocycline should be non-preferred with the PA criteria. Immunosuppressive agents and hepatitis B drugs should be grandfathered.

Susan Flatebo: I second.

Dale Sanderson: All in favor say aye.

Group: Aye.

Dale Sanderson: All opposed same sign. The motion passes. And it's time for a break. So 15 minutes.

Leta Evaskus: 11:05.

Dale Sanderson: 11:05. Yep.

Leta Evaskus: Stephanie, do you want to call back in?

Stephanie Christofferson: Yeah, that's fine.

Leta Evaskus: Great.

Dale Sanderson: If we could come to order, please. I would like to reconvene the DUR Board. Stephanie, we're ready for your next presentation.

Stephanie Christofferson: Okay. Everyone hear me okay?

Dale Sanderson: Yes.

Stephanie Christofferson: Okay. We will first address the short-acting narcotic analgesics. The first slide looks at indications. As you know, pain management needs to be individualized to each individual patient. There are many effective opioid analgesic products available. Some of which differ in the specific opioid or coanalgesics used, the dosage form and duration of action. Likewise, almost all the different medications have a generic product available for them now.

Although some manufacturers market unique strengths of the different combination agents, the minor changes in the doses of acetaminophen, ibuprofen and/or the opioid… and these products have shown to offer little advantage over similar generic combination products. All agents within this class are considered controlled substances and have a boxed warning regarding the serious effects of the use, abuse and so on. Codeine, dihydrocodeine combination products I wanted to mention are a schedule 3. Butorphanol, [inaudible], and tramadol products are a schedule 4 products where all the rest of the products that are within this review are a schedule 2 product. There have also been warnings regarding the concomitant use of opioids with benzodiazepines and other CNF depressants which I'm sure everyone is familiar with, with the media that's surrounding the combination of use. This also would include alcohol. These combinations do create profound sedation respiration depression, coma and death. It's recommend that the combination of these really be avoided if at all possible now. Next slide, please.

This looks at the rest of the indications. We'll go ahead and skip over to the dosage and availability. The next four slides looks at the dosing directions of the medications and the different dosage forms that are available. The list is quite extensive so of course we're not going to review all of those. I will just mention that almost all of the medications are available in tablet, capsule or solution formulations. Fentanyl is available in several dosage formulations that offer alternative routes of administration including buccal, nasal, sublingual, lozenges and so on. When comparing the fentanyl dosage formulations no one formulation has been proven to be more effective than another. But I will just say that the onset of action with the fentanyl products is quicker than some of the other oral formulations just due to the route of administration, which usually takes about 15 minutes to provide onset of pain relief. Hydromorphone and morphine IR are also available in suppository formulations. I wanted to mention that Oxaydo is an immediate-release product opioid analgesic with abuse deterrent properties intended to discourage the abuse of medication. These preventative measures no analgesic effectiveness or advantage over

another product. While it is acknowledged that diversion and misuse of the opioids may be common patients should be evaluated to determine whether or not medications such as Oxaydo are even required. So again patient assessment would be needed. However, it's not recognized as abuse-deterrent formulation by the FDA. Lastly I wanted to mention for this slide that due to the risk of abuse and addiction overdose-related to the transmucosal fentanyl formulations they are included in the [inaudible] program. I'll go ahead and have you skip over to the guideline section.

First we'll talk about guidelines from the CDC. They state as first line therapy, of course, nonpharmacological therapy should be used for the treatment of chronic pain. In instances where that is not effective treatment then they do recommend initiation with the immediate release product over an extended release product due to the side effects and risks of abuse with the longer-acting products. For acute pain the same as chronic pain. They recommend immediate release products at the lowest effective dose and quantity… the quantity dispensed should not exceed that that is expected for the duration of pain, which is typically three days. They mention that greater than seven days therapy is rarely needed. They further specify that doses greater than or equal to 50 morphine milligram equivalents or MMEs per day should prompt assessment of the individuals benefits and risks and that use of more than 90 MMEs per day should be avoided without justification. They also recognize that the use of concomitant benzodiazepines with opioids should be avoided. For the 2017 guidelines from American College of Physicians, again, they also recommend nonpharmacological therapy as first line therapy. In cases when therapy is needed they recommend NSAIDs or skeletal muscle relaxants for acute or subacute lower back pain. For the treatment of chronic low back pain, again, nonpharmacological therapy is recommended first line and then… and those individuals with inadequate response they recommend NSAIDs be first line therapy and tramadol or duloxetine as second line therapy. They state that opioids should only be used essentially as the last line of resort in patients who have failed the prior therapies. And then lastly the American Society of Interventional Pain Physicians they look at pain and they said that

opioids should be used based on an average pain score of moderate to severe. So on a 0 to 10 scale anything that's greater than or equal to a level 4 is when they recommend assessing patients for opioids. They, much like the other organizations, recommend short-acting opioids at the lowest possible effective dose be used first. They also mention that methadone only be used after failure of other opioid therapies and they also state that there is similar effectiveness in a long- and a short-acting opioid, but they do acknowledge that there is greater risk with the long-acting opioids. However, all in all they do not recommend one specific short-acting opioid over another and that was kind of the general theme between all these different organizations and stuff. They don't recommend one opioid over another. With that I'll go ahead and close out the short-acting narcotics unless there are any questions.

Dale Sanderson: We have one question.

Catherine Brown: I just wanted to ask why Xartemis XR is included in this group.

Stephanie Christofferson: Um… I'm assuming just because of the indications for the treatment of pain. It might have to have something to do with… I don't know… Doug, not to put you on the spot, but does it have anything to do with how the drugs in the class are managed from financial perspectives or anything like that?

Donna Sullivan: It might be because it is indicated for acute pain where the other long-actings are not indicated for acute pain.

Dale Sanderson: Any other questions from the committee? I see none. We have the recommendation on page 75.

Leta Evaskus: Dale, are there any stakeholders?

Dale Sanderson: There are no stakeholders. Thank you. Any amendments to the recommendations?

Nancy Lee: I'd like to have the committee consider removing the combination of codeine, carisoprodol and aspirin.

Donna Sullivan: So what do you mean by remove?

Nancy Lee: Require a prior authorization and make it non-preferred.

Donna Sullivan: Okay. Thank you.

Amber Figueroa: I think we had this discussion previously, but acknowledging that they're not really considered safe, you know how it says they are considered safe and efficacious. I don't remember how we did it before but we did something about…

Donna Sullivan: The motion now doesn't state that they are safe and efficacious.

Amber Figueroa: Okay.

Leta Evaskus: Are you thinking about the P&T motions?

Donna Sullivan: I guess in the recommendation it does. So you could just remove the word safe and say "are considered efficacious" if you'd like to do that. I would not want to say that they are not safe just because we try not to say things that go too far outside of what their labeling states. Considered safe and efficacious when used appropriately might be another way to say that.

Dale Sanderson: Given that this is such a significant issue it just seems that we should have some comment in some way that would acknowledge that. I'm open to the committee's recommendations. Is the committee okay with just removing safe and leaving efficacious?

Amber Figueroa: Yes, for me.

Leta Evaskus: Do you want to leave in "when used appropriately" or take that out? Leave it in? Okay.

Donna Sullivan: I just want to point out that I'm… I didn't see… are the fentanyl products in here? We do have fentanyl short-acting on prior authorization so that they are only allowed for pain so that… which

we didn't get here in the recommendation. I just wanted to call that out that we're intending to keep that that way so that they are only used for their labeled indications.

Dale Sanderson: Would someone like to make a motion?

Diane Schwilke: I move that the Apple Health Medicaid Program implement the limitations for the analgesics narcotics shorts listed on slide 75 as recommended. Omit codeine, carisoprodol, aspirin non-preferred with PA criteria.

Jordan Storhaug: I second.

Dale Sanderson: All in favor say aye.

Group: Aye.

Donna Sullivan: All opposed same sign.

Amber Figueroa: Is it called narcotics short for a reason instead of short-acting? I mean the whole class is called that.

Donna Sullivan: I believe that's just a type-o. It should be short-acting.

Amber Figueroa: Okay.

Donna Sullivan: Our official title is opioid short, opioid agonist short-acting. We don't call them narcotics.

Dale Sanderson: With the wording changed everyone in favor say aye.

Group: Aye.

Dale Sanderson: All opposed same sign? Stephanie, go ahead.

Stephanie Christofferson: Okay. Next we'll talk about the lipotropics, other. So most outcomes data supports the use of statins as a primary agent for ADL reduction and for primary and secondary prevention of coronary

heart disease. And as a class they can lower LDL by up to 60%. However, it's been noted that even while on maximum statin therapy some patients cannot adequately lower their LDL levels sufficient enough to reduce their atherosclerotic cardiovascular disease risks. So the addition of non-statin agents can be considered as adjunct therapy. Agents in this class are indicated as adjunct to diet, modifications for the treatment of various dyslipidemias. Most of the medications listed here are indicated for the treatment of hypercholesterolemia or hyperlipidemia. However, Juxtapid, Kynamro, Zetia and Repatha also have FDA improved indications for the treatment of homozygous familial hypercholesterolemia and WelChol, Repatha and Praluent are indicated for heterozygous familial hypercholesterolemia which of course are genetic disorders. Due to the risk of hepatic toxicity Juxtapid and Kynamro are only available through a restricted program under the REMS program. The goal of the program is to educate prescribers on the risks of liver toxicity and restrict access to these agents to patients with a clinical or a laboratory diagnosis consistent with homozygous familial hypercholesterolemia. Compared to other agents in this class Praluent and Repatha are newer agents. They have demonstrated significant efficacy in regards to lowering LDL levels. The American Heart Association advises that the PCFK9 inhibitors can be added to high instance of the statin therapy plus Zetia in patients' familial hypercholesterolemia when dual therapy is not resulting in desired LDL goals after three months. So of course they're not considered a first line therapy. Each class of the non-statin lipotropics provides a unique option for use in patients who cannot reach their target lipid levels or when they cannot tolerate statins. It could be an alternative therapy. Next slide, please.

That just finishes out the rest of the medications and actually the next slide does. You can advance to the dosage and availability slide.

Most of the medications in the class are available by either a tablet, capsule or suspension and they are taken once or twice daily depending on the medication and disease severity. However, there are sub-q medications including Kynamro, Praluent and Repatha. When using Repatha at 420 mg per day I did want to mention the

patient's must use three consecutive subcutaneous injections all within 30 minutes or they do have the ability to use a single-use Pushtronex system that delivers the 420 mg over nine minutes. Praluent and Repatha a little inconvenient in the fact that they have to be refrigerated or they can be kept at room temperature in their original carton up to only 30 days. Praluent should be allowed to warm up to room temperature prior to use. And also the Pushtronex system should be brought to room temperature prior to administration. Do you want to go ahead and advance to the guidelines, please?

The AACE and the ACE published guidelines for dyslipidemia and prevention of cardiovascular disease in 2017. Adults who are the age of 20 or older should be assessed annually. They recommend screening for children who are at risk for familial hypercholesterolemia. At risk children for this condition should be assessed at the ages of greater than 3. Again, between the ages of 9 and 11 and then again at 18 years of age and older. Adolescents who are older than 16 with atherosclerotic cardiovascular disease risks should be evaluated every five years. In regards to drug therapy they do recommend fibrates for the treatment of triglycerides that are greater than 500 mg/dL. Niacin can be used for reducing triglycerides, increasing HDL and then also reducing LDL levels. They recommend the Omega fish oil as an adjunct to fibrate or niacin therapy if it's a necessary medication in order to achieve triglyceride lowering in patients with triglyceride levels that are greater than 500. They recommend bile acid [inaudible] for reducing LDL levels and also for reducing apolipoprotein or apo B and moderately increasing the HDL levels. But do caution that these agents may increase triglycerides. They also note that Zetia is effective as monotherapy in reducing LDL levels and apo B. Particularly in statin intolerant patients. And lastly they do address PCSK9 inhibitors and they state that they can be considered in patients with clinical cardiovascular disease who are not at goal at maximally tolerated statins or those with familial hypercholesterolemia. Overall, they do maintain that statins should be the primary therapy and recommend Zetia addition to statins with additional LDL reduction as needed. For the standards of

medical care and diabetes there's 2007 guidelines that came out from the ADA that state it is reasonable to assess lipid status at the time of diagnosis, at the start of medical evaluation and then every five years after. They recommend moderate or high intensity statin therapy in patients with diabetes based on the patient's age and presence of risk factors. Zetia can be added to moderate intensity statin therapy in patients with acute coronary syndrome and LDL levels that are greater than or equal to 50 or in patients with a history of atherosclerotic cardiovascular disease who cannot tolerate the [inaudible]. They also mentioned that the addition of the PCSK9 inhibitors to maximally tolerate statin doses may be considered at those at higher risk for cardiovascular events who also require additional LDL reduction or who are intolerant to high intensity statin therapy. And then lastly they do recommend against the use of niacin to statin therapy in diabetic patients due to the lack of benefit. With that said I will go ahead and stop there with lipotropics. Are there any questions?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Okay. Next we'll look at the antihypertensive sympatholytics. As you know, hypertension is one of the most common conditions seen in primary care and can lead to myocardial infarction, stroke, renal failure and death if not detected early and treated appropriately. There is strong evidence to support treating hypertensive persons age 60 years and older to blood pressure goals less than 150 over 90, patients younger than 60, adults with diabetes, or adults with non-diabetic chronic kidney disease should have blood pressure goals set to less than 140 over 90. The first two slides here list the sympatholytic agents used in the treatment of hypertension, which includes essentially four different drugs – clonidine, guanfacine, methyldopa and reserpine. As you're probably already aware clonidine is available in both an oral formulation as well as a transdermal formulation in which the patch is applied every seven days. This does offer patients a different treatment approach and may impact compliance since many of the oral products are dosed multiple times per day except for guanfacine and reserpine. There are also combination products as you can see here on the chart

including Clorpres and methyldopa/HCT combination products. The effects for the combination products are additive for blood pressure reduction with the addition of hydrochlorothiazide. I wanted to mention that methyldopa use has diminished due to the use of other drugs with more favorable adverse effect profiles and really that's the same with resperine, as well. Lastly, I just want to mention that all of the products are available in a generic with the exception of Clorpres. Do you want to go ahead and advance to the guidelines?

According to the JNC 8 guidelines, initially therapy for the non-black population includes thiazide-type diuretics, calcium channel blockers, ACE inhibitors or ARBs and then initial therapies for the black population include the thiazide-type diuretic or calcium channel blocker. If goals cannot be reached either due to contraindications or the need for greater than three drugs of the initial therapy the guidelines state that other medications from a different class may be considered at that time. In the ACC guidelines they have the same initial therapy recommendations as the JNC 8 guidelines. They recommend stage 1 hypertension and blood pressure goal of less than 130 over 80. They recommend single-use drug therapy with dose titration and add on therapy as needed. In stage 2 hypertension they recommend initial therapy with two individual agents. Central alpha1 agonists and other centrally acting medications such as sympatholytics are reserved for last line just due to CNS side effects associated with the drugs. I'll go ahead and wrap that up. Any questions on this section?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Next one we'll look at is the sinus node inhibitors. Essentially there's only one drug in this class, which is the Corlanor, but as you know heart failure is a progressive syndrome caused by a change in cardiac structure or cardiac function resulting in failure of the heart to deliver an adequate supply of oxygenated blood to the tissues. The goals included are improving patient symptoms, slowing disease progression and then of course prolonging survival of the patients. Mortality rates have actually declined over the past few decades due to improvements in pharmacotherapy which includes the use of beta

blockers, ACE inhibitors or ARBs. Corlanor is a newer product that is available and it's indicated for the reduction of hospitalization or for worsening heart failure in patients with stable symptomatic chronic heart failure with left ventricular injection fraction less than or equal to 35% who are in sinus rhythm with a resting heart rate of 70 beats per minute or more. They need to be on maximally tolerated beta blockers or have a contraindication to its use. They recommend starting Corlanor at 5 mg twice daily with meals after which the patient should be assessed after two weeks and dose adjustments in 2.5 mg increments in order to achieve a resting heart rate that's desirable between 50 and 60 beats per minute. Thereafter adjustment of the dosages may be necessary up to the maximum dose that can be used. Next slide, please.

We'll look at the guidelines. According to the ACC, AHA and the HFSA guidelines, treatment with an ACE inhibitor or ARB or an ARNI in conjunction with evidence-based beta blockers and aldosterone antagonists in select patients is recommended for patients with heart failure with reduced ejection fraction in order to reduce morbidity and mortality. In patients with chronic symptomatic heart failure class 2 or 3 tolerate ACE inhibitor or an ARB they recommend a replacement with an ARNI to further reduce morbidity and mortality. The guidelines note that there has been one randomized controlled trial that looked at the efficacy of Corlanor in reducing the composite end point of cardiovascular death or hospitalization, but also noted that only 25% of patients in the study were on optimal doses of beta blockers and that given the well-proven mortality benefits of beta blocker therapy they stress the importance of initiating and titrating beta blockers up to the targeted doses as tolerated before assessing the resting heart failure in order for consideration of Corlanor initiation of therapy. In other words it's definitely not a first line therapy. It's an add on therapy when maximum therapies of beta blockers have been used. Any questions on that?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: The next section we have is the vasodilators for coronary. Angina pectoris is a clinical syndrome of coronary artery disease which of course is a common type of heart disease and one of the leading causes of death in the United States. Isosorbide and nitroglycerin ER ointment and transdermal medications have all been approved in the prevention of angina due to coronary disease. The isosorbide products are available in a tablet and capsule formulation whereas the nitroglycerin for the prevention of angina is available in an ER tablet, ointment and transdermal patch. Depending on the product the oral products are dosed once daily up to three or four times daily with the nitroglycerin ER products. The ointment is applied twice daily and the patch is applied once daily for 12 hours and then taken off for the remainder of the 24 hour period. The nitroglycerin lingual formulations are indicated for acute relief of an attack or acute prophylaxis. They are available in several different dosage formulations including translingual sprays, meter dose pumps and sublingual tablets. All the medications are available in the generic except for the Nitro-Bid ointment. Go ahead and move to the guidelines, please.

The ACT in conjunction with the other organizations listed here formed to develop guidelines for stable ischemic heart disease. In their guidelines they state that nitrates are effective in the treatment of all forms of angina. They further state that the long-acting nitrate preparations are beneficial in the treatment when initial therapy with a beta blocker or a non-dihydropyridine calcium channel blocker is contraindicated. Unacceptable side effects to these therapies occur or when additional therapy is needed, but they're not indicated for first line therapy. However, the guidelines do state that all patients should be prescribed sublingual nitroglycerin either tablet or sprays for acute relief in case of an attack. And then also the sublingual formulations should be effective and can be used for the prevention of effort-induced angina when administered prior to action that they believe may cause an issue. With that I'll close out the vasodilators unless there are any questions.

Dale Sanderson: None that I see. We have two stakeholders. Mrs. Jennifer Gram, I believe, from Anthem.

Jennifer Bram: I'm not a stakeholder. I just didn't know where to sign in.

Dale Sanderson: Oh, okay. Thank you. Dr. Sylvia Churchill from Amgen. You have three minutes, please.

Sylvia Churchill: Okay. Thank you. My name is Sylvia Churchill. I've been a pharmacist here in Washington State for over 20 years and I now work with Amgen as a health outcomes and pharmacoeconomics specialist. Thank you for the opportunity to speak today and I'm focusing this on Repatha or evolocumab. Repatha is a fully human monoclonal antibody that inhibits PCSK9 which in turns increases LDL clearance from the body. Repatha and Praluent are the only two agents in this large class with that mechanism of action and the level of LDL reduction with both of these agents is very significant. When given on top of statin therapy PCSK9 inhibitors will decrease LDL levels by an additional 50 to 60%. In addition, Repatha now has published outcomes data in 27,500 patients with ASCVD showing that this decrease in LDL translates to a significant reduction in the incidence of MI, stroke and coronary revascularization. This outcomes data was significant enough that in December of 2017 the FDA added this as an indication to the Repatha PI. This new indication was not mentioned in this presentation here so I'd like to quickly review the recent changes in the Repatha PI. So in addition to adding that indication for improved outcomes Repatha is also now approved for primary hyperlipidemia and it may be given alone or with diet or with other lipid lowering therapies. So for patients who are unable to tolerate a statin Repatha is an approved option. Other recent major changes to the PI relate to the improved safety data. So as a result of additional clinical trial data and long-term safety follow-up the following adverse reactions sections were removed from the Repatha PI in December. The risk of neurocognitive events was removed from the adverse reaction section and this is due to data from the Ebbinghouse Trial which showed that Repatha is non-inferior to placebo in cognitive function domains over a median follow-up of 19 months. The risk of musculoskeletal events was removed from the adverse reaction section. The risk of low LDL levels was also removed from the adverse reaction section. In our

27,500 patient [inaudible] Trial 76% of patients had at least one LDL level of less than 25 mg/dL and these patients had a similar safety profile as patients that had LDL levels greater than 40. We also have new data in severe renal impairment so the PI was changed to state that no dosing adjustment is needed in mild, moderate or severe renal impairment. And finally Repatha is the only PCSK9 inhibitor that is approved for patients with homozygous familial hypocholesterolemia or HOFH. HOFH patients have an extremely high LDL level and very high risk of MI stroke and other CV events.

Dale Sanderson: If you could conclude your talk, please.

Cynthia Churchill: Sure. In summary, the PCSK9 inhibitors have a significantly different mechanism of action and are able to decrease LDLs to a much greater magnitude than many of the other agents in this class. Repatha is the only PCSK9 inhibitor with published outcome data and an FDA approved indication of decreasing the incidence of MI stroke and coronary revascularization. We certainly agree with the guidelines that patients should be optimized on statin therapy before considering the addition of a PCSK9 but for those patients who are already on their maximally tolerated dose of statin and still require significant LDL reduction health care providers should be able to add Repatha to their current regimen to achieve goal LDL and decrease the risk of MI and stroke. Are there any questions? Thank you very much.

April Phillips: I wanted to just clarify on the past one you had a question on the analgesics, narcotics short. How it is, is like the analgesics is the drug class and the narcotic short is the subclass. So the wording is a little confusing, but that's why it is stated that way and the only reason why I'm saying it now is because there are a couple other drug classes that are listed the same way in this motion.

Dale Sanderson: So we have a recommendation as listed. Any amendments from the committee? I'm not seeing any proposed amendments.

Nancy Lee: I'd like the committee to consider, with the exception of the indication for familial hyperlipidemia, the apo B synthesis inhibitors,

and the PCSK9s to be non-preferred with PA just to make sure that patients have really tried and failed a statin to the max effect. And apo B and PCSK9 for familial hyperlipidemia can be used for that indication. So with the exception of that indication I would like to have the committee consider…

Donna Sullivan: I would recommend that you allow us to prefer or to select a preferred PCSK9 inhibitor. We do have them on PA and to require that they try and fail statin therapy first, but it would be preferable to prefer one over the other, if possible.

Nancy Lee: How would you recommend wording that?

Donna Sullivan: I believe… let me look back at the recommendations. I think you could just state that you would like them to be on prior authorization.

Nancy Lee: I would like to recommend that those two drug classes… the apo lipo B synthesis inhibitors and the PCSK9s require prior authorization with the exception of the familial hyperlipidemia. Instead of the lipotropics, put apo lipo protein B synthesis inhibitors.

Amber Figueroa: Does anybody think grandfathering is necessary for any of these classes?

Nancy Lee: I think if patients are on apo lipo B and PCSK9s they should be grandfathered.

Donna Sullivan: I have a question then. Are you saying that they should be allowed to continue a PCSK9 inhibitor or an apo lipo B protein drug or the one that they are actually on? We would not make them go back and trial and fail five statins or something if they had already been approved, but we might request them to switch from one PCSK9 to another.

Alex Park: I would be open to having them switch to another PCSK9.

Donna Sullivan: Okay. Thank you.

Alex Park: If I could make another recommendation for amendment to the motion to make Corlanor non-preferred and require PA given its cost and limited benefit in only a very specific subset of patients who have maximized existing CHF therapy.

Donna Sullivan: So just as a kind of policy thing. I think Corlanor is the only drug within its class. If you want it to not be first line it doesn't mean it has to be non-preferred. When you want something just to be on prior authorization or a second line therapy allow us the ability to make it preferred because if there is a supplemental rebate opportunity it needs to be preferred, but if you direct us to say it's not preferred then we cannot take advantage of that opportunity. But we can always put it on prior authorization if we need to.

Alex Park: Thank you for that clarification. Could we change the amendment to be just requiring prior authorization?

Donna Sullivan: Okay. Thank you.

Dale Sanderson: Would someone like to make a motion here?

Amber Figueroa: I move that the Apple Health Medicaid Program implement the limitations listed on slide 97 for each drug class listed on slide 96 as recommended. The apo B synthesis inhibitors and the PCSK9 inhibitors should be on prior authorization. Corlanor should be on prior authorization.

Catherine Brown: I second.

Dale Sanderson: All in favor say aye.

Group: Aye.

Dale Sanderson: All opposed same sign. Motion passes. Stephanie, go ahead.

Stephanie Christofferson: Okay. Next we'll look at the bone resorption suppression and related agents. Osteoporosis, of course, is characterized by the

deterioration of bone tissue and low bone mass and the primary goal of therapy is to reduce fracture risk. Based on clinical trials in general, bisphosphonates increase bone mineral density approximately 2 to 5%. Calcitonin and raloxifene showed bone mineral density increases of approximately 1 to 2% while Forteo shows the greatest increase in bone mineral density ranging anywhere from 5 to more than 10%. The first two slides list all the indications for the medications. As you can see all the medications are indicated for the treatment of osteoporosis in post-menopausal women with many of the medications also having additional indications as listed. As you can also see from the first two slides most of the medications do have products available that are in a generic formulation. Next slide, please.

This slide looks at the calcitonins. I just wanted to mention that they really are not used anymore due to more effective therapies now being available and also other products that are available; many of which are the injectable products for osteoporosis. The newest product in this class is Tymlos, which gained approval from the FDA for the treatment of osteoporosis in post-menopausal women who are at higher risk for fractures. It does carry a boxed warning including the risks of osteosarcoma much like Forteo does and it should not be used for greater than two cumulative years or in the pediatric population, which is actually... this is the same instructions for use for Forteo, as well. Next slide, please.

This looks at the dosing availability. The bisphosphonates are available in daily, weekly and monthly dosing options. The weekly options include Fosamax, Fosamax Plus D, Actonel, Atelvia and [inaudible], which is a once weekly effervescent formulation of alendronate. It is considered equivalent in efficacy compared to oral once weekly alendronate dosage forms and basically just offers an alternative delivery form for the product. And then finally your monthly options include Boniva and Actonel. There is a significantly higher incidence of abdominal pain that's been recorded for [inaudible] delayed release when administered under fasting conditions compared to the immediate release tablets. Based on currently available studies it appears that bisphosphonates that are

dosed once weekly do promote a greater adherence, as well as longer treatment persistence compared to the daily dosing. However, when compared to the monthly dosing regimens it does not appear to give any greater treatment adherence or persistence in patients. Next slide, please.

This slide looks at the calcitonins. There are two products, the Miacalcin and Fortical. They have the same dosing directions, but again they are not used much anymore due to the other medications being available. Next slide, please.

The last section looks at the medications that have different mechanisms of actions compared to the bisphosphates or the calcitonins. Prolia, Forteo, and Tymlos are all sub-q injections. Prolia is administered by a healthcare professional every six months, which some patients might like due to the convenience of that. Whereas Forteo and Tymlos are daily self-administered sub-q injections. Tymlos is the newest product to the class and it does not need to be refrigerated like Forteo does. I wanted to mention that Prolia is in the REMs program due to risks of hypocalcemia, osteonecrosis of the jaw, atypical femoral fractures and serious infections that can be related to the product. Tymlos and Forteo do have boxed warnings regarding osteosarcoma, as well, and just lists that patients may be at an added risk for development of that. Next slide, please.

This looks at the guidelines. The 2016 guidelines from the AACE and the ACE recommend that alendronate, risedronate and denosumab be used as initial therapy for most patients who are at high risk for fracture. Forteo and Prolia should be considered for patients who are unable to use oral therapy and as initial therapy for patients who are especially high risk of fracture. Raloxifene and ibandronate may be appropriate initial therapy in some cases where patients require drugs with spine-specific efficacy. They also reiterate that there are few patients now that are using the calcitonin products as long-term therapy because of more effective agents being available. Next, from the American College of Physicians their 2017 guideline for the treatment of low bone density and osteoporosis to prevent fractures in men and women. They recommend offering patients treatment in

order to reduce the risk of hip and vertebral fractures in women with known osteoporosis and treatment should occur for five years. The guidelines recommend alendronate, risedronate and denosumab in order to reduce the risk for hip and vertebral fractures in women with known osteoporosis. They do recommend against using estrogen or estrogen with progesterone or raloxifene in patients… in women… in osteoporosis women. Regarding therapy in men they recommend clinicians offer therapy with bisphosphonates. Next from the American College of Rheumatology 2017 guidelines they looked at guidance on managing glucocorticoid-induced osteoporosis in children and adults. In low fracture risk the organization does not recommend the use of pharmacological therapy and only recommends lifestyle modification. In those with moderate to high risk of fracture they recommend oral bisphosphonates as first line therapy. Second line therapy could include IV bisphosphonates, Forteo, Prolia or raloxifene. I did want to also mention that Tymlos was not available at the time of the current treatment recommendations. However, based on the medications indication it may be reasonable to consider other first line therapies, especially given the fact that there is a lifestyle maximum therapy of cumulative two years on this medication. Any questions on the bisphosphonates or bone resorption section? Sorry.

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Okay. Next we'll look at thyroid hormones. The first slide looks at indications. There are three medications and one combination medication for thyroid hormones including porcine thyroid, levothyroxine, liothyronine and then a synthetic combination or Thyrolar. All have the same indication for replacement or supplement for hypothyroidism and it's a pituitary TSH suppressant. Next slide, please.

As you can see most of the agents are available in a generic formulation and are dosed once daily. There are several different strengths available and they are included in tablets and capsule formulations. Next slide, please.

This looks at the guidelines. The American Association of Clinical Endocrinologists and the American Thyroid Association developed guidelines to help prescribers in the treatment of hypothyroidism. Essentially they recommend levothyroxine monotherapy and then they state that it is the main state of therapy for treating hypothyroidism. That treatment is best accomplished using the synthetic levothyroxine sodium, but they do say that because of the uniqueness of the various tablet formulations the current recommendations recommend the use of a consistent preparation in order to minimize the variability from refill to refill. They do not support the use of the combination product with the liothyronine in the treatment of hypothyroidism. And then the desiccant thyroid has not been systematically studied according to the guidelines and they state that the content of the thyroid hormone and the ratio of T4 to T3 can vary in the preparations depending on the brand employed. And there are no controlled trials supporting the preferred use of the desiccant thyroid over the synthetic for the treatment of hypothyroidism. Therefore, the desiccant formulation is not recommended. And then lastly according to the 2016 AACE/ACE guidelines on thyroid nodules, when it comes to the medical treatment for benign nodules they do not recommend levothyroxine therapy. It's also not recommended for the prevention of recurrence after a lobectomy when the TSH levels stay within normal range and they also do not recommend it for preventing recurrence of nodules when the TSH levels are normal. But they do recommend replacement for young patients with subclinical hypothyroidism due to autoimmune thyroiditis. Any questions on the thyroid hormones?

Dale Sanderson: I see none. Go ahead.

Stephanie Christofferson: Okay. Next we'll look at BPH therapies. As you are all probably aware BPH is one of the most common conditions in aging men. Most men with BPH experience only mild or moderate symptoms, but severe BPH can lead to urinary retention and urinary tract infections, as well as renal issues. This especially happens in men who are over the age of 60. The first and second slide represents the

medications indicated for the treatment of the disease state and as you can see from the chart many are available in a generic formulations. There are three classes to consider here, which are the alpha blockers, the five alpha reductase inhibitors and then the phosphodiesterase 5 inhibitors. I also want to mention that you can probably see here in the chart, but Cardura and terazosin also have an indication for hypertension. Next slide.

This just finishes out the indications. Advance to the next, please.

For dosage and availability – all medications are taken daily and are available in either tablet or capsule formulations. While there are no formulations that are liquid, Rapaflo capsules can be opened and the contents can be sprinkled into applesauce or something else similar in order for patients who cannot swallow tablets to receive medication. There are also renal considerations for some of the medications including Rapaflo and Cialis. Next slide, please.

While looking at the American Urological Association 2010 standards, which were then reaffirmed in 2014 patients with mild symptoms of BPH and then also patients with mild to severe symptoms you're not concerned by their symptoms can be managed just by watchful waiting. However, for patients with mild to severe lower urinary tract symptoms secondary to a BPH alpha adrenergic receptor blocker therapy is an appropriate treatment option. However, just to mention head-to-head trials have not distinguished any alpha blocker to be superior compared to the next in terms of effectiveness. The guidelines state that Uroxatral, Cardura, Flomax, and terazosin are appropriate treatment options for all patients and are all equally effective. However, a meta-analysis did show possible better tolerability of Uroxatral and Flomax compared to other products. I did want to mention, however, Rapaflo was not evaluated during this time as clinical literature was not available according to the guidelines. The guidelines also state that the five alpha reductase inhibitors Proscar and Avodart are appropriate and effective treatments for patients with lower urinary tract symptoms associated with the prostate enlargement, but are not appropriate therapy for men with symptoms that do not have evidence of

prostate enlargement. Finally, according to the guidelines combination therapy utilizing an alpha adrenergic blocker and a five alpha reductase inhibitor can be appropriate therapy and effective for patients who not only exhibit lower urinary symptoms, but also define the prosthetic enlargement. With that said are there any questions in the PBH section?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Okay. Next we'll look at the contraceptives, other. Unintended pregnancy rates account for approximately 45% of all pregnancies in the U.S. with higher percentages being amongst the adolescents and younger women. So there's been strategies to prevent unintended pregnancies including looking at contraceptive methods and helping patients to use those methods correctly in order to prevent the pregnancies. So in this section it looks at the IUDs and other implants which are considered long-acting reversible contraceptives or LARCs. These methods are highly effective because they don't depend on the regular compliance from the user. They are appropriate and most women, including adolescents and women who have not had children yet. All women should be counseled about the full range of effectiveness of the contraceptive options for which they are medically eligible so they can help identify an option that would work best for them. All the medications here have an indication, as you can see, full contraception and Depo-Provera does have a generic available. The formulations in the last column include vaginal inserts, transdermal patches, implants and shots. The length of time each product works varies from product to product with the longest being Paragard which should be taken out at the 10-year mark and then the next longest being Mirena and Kyleena which there's a 5-year use for those products. Next slide, please.

This looks at the guidelines. For the U.S. selected practice recommendations for contraceptive use of 2016 they list… they don't select one product as being superior to another one. Again, it states it should be looked at on an individual basis and that they are all effective. Some of them are a little bit more effective, as you can, than others. I think the 1 out of 100 for most of these products in

the intrauterine contraception and implants the injectable is a little less, but still really good. Six out of every 100 women and then the combined hormonal contraceptives 9 out of 100 women. Again, those statistics are based on appropriate use of the medications, which again when their healthcare professional professionally administered the contraceptive… the contraception of those products is… the effectiveness is very high. For the U.S. medical eligibility criteria for contraceptive use in 2016 how their guidelines looked they looked at the safety, effectiveness, availability and acceptability of the products. Then they used eligibility categories based on different disease states and maybe comorbidities of patients and with each one of those products they rate them on basically a 1 to 4 scale. One meaning there's nothing in existence or there's no literature that states that the medication would be inappropriate or not safe for a patient. Category 2 says that it could be appropriate, but patients should be closely monitored. Category 3 is that it is usually not recommended unless there's no other options and then Category 4 is basically it puts the patient's health at risk and it should not be used. But it's a very detailed chart and it goes to all the different patients and their comorbidities and rates them. All in all they have said the effectiveness of contraceptive methods depends on the inherit effectiveness of the method that the patient chooses and on consistent and correct use. They do also state that the IUDs and implants are long-acting and reversible and are highly effective because they do not depend on the regular compliance of the user. But again they don't choose one product over another in their guidelines. Any questions on the contraceptives?

Dale Sanderson: None that I see. Go ahead.

Stephanie Christofferson: Okay. Great. The next section we'll look at the H. pylori treatment. Although theories regarding the pathogenesis of peptic ulcer disease focus on acid hypersecretion, it is now known that hypersecretion is not the primary mechanism by which most ulceration occurs. It appears that H. pylori and then also drug therapy such as NSAIDs disrupt the normal mucosal defense and repair making the mucosa more susceptible to attack of acid. There are several commercially-

available combination therapies available for treatment of H. pylori only one of which Prevpac is available as a generic. Within the last year some other notable drug information that has come out is that previously Pylera was assigned a pregnancy category D, but that language has been updated to comply with the pregnancy and lactation rule stating now that use is contraindicated due to the components of the medication tetracycline and metronidazole not being drugs of choice due to adverse effects to the fetus. And then Omeclamox-Pak and Prevpac labeling were required to include warnings for the potential risk of development of cutaneous lupus erythematosus and systemic lupus SLE due to the PPI components. Next slide, please.

The next slide looks at dosages. As you can see the medications do require additional therapies for the medication and not all of them are available with the different components like a PPR or an H2 blocker wouldn't need to be added for the medications. Most of these products are taken anywhere from 10 to 14 days and I think that's it on that one.

The next slide for completeness we just… some states like to look at the products if they decide not to use the combination products that are commercially available. So this slide is just included in case that's an area of concern for any of our clients so they can look to see whether the individual components in the PPI that make up these different products in case you'd want to go that route. But again we won't review that. It's just kind of more or less for an FYI.

The last slide looks at the American College of Gastroenterology 2017 updates. The guidelines state that all patients with a positive test of active infection should be offered therapy. There are a lot of first line therapies that can be used according to these guidelines. The first one is bismuth quadruple therapy where a PPI, bismuth, tetracycline and nitroimidazole can be used for 10 to 14 days. The guidelines state this is appropriate in patients with a penicillin allergy or those with a previous macrolide exposure. Next they recommend therapy with a PPI clarithromycin, amoxicillin or a nitroimidazole for 10 to 14 days or sequential therapy with a PPI and amoxicillin for 5

to 7 days followed by a PPI clarithromycin and then nitroimidazole for an additional 5 to 7 days. A similar hybrid therapy of a PPI and amoxicillin for 7 days followed by a course of a PPI amoxicillin clarithromycin and nitroimidazole for an additional 7 days is also a first line recommendation according to these guidelines. The use of a fluoroquinolone treatment regimen can also be considered such as a combination of a levofloxacin, PPI and amoxicillin for 10 to 14 days or a PPI and amoxicillin for 5 to 7 days followed by a PPI for quinolone and a nitroimidazole for 5 to 7 days. The guidelines also note that in some regions with low H. pylori resistance, meaning less than 15%, clarithromycin triple therapy which consists of clarithromycin, PPI and amoxicillin are fragile for 14 days can be used. It's also recommended in patients with no previous history of macrolide exposure. But overall the guidelines do suggest that at the end of therapy they recommend testing to confirm that eradication had been successful. Any questions on H. pylori?

Dale Sanderson: None that I see. Go ahead.

Amber Figueroa: At one point there was a one-day treatment with two handfuls of medications. Is that no longer being used or was that never FDA approved in the first place?

Stephanie Christofferson: According to the guidelines that's not something that's recommended and I do not have anything would suggest use of that.

Amber Figueroa: Thank you.

Dale Sanderson: Any other questions? Okay. Go ahead.

Stephanie Christofferson: Okay. Next we will look at phosphate binders. So chronic kidney disease or CKD is a prevalent disease in the U.S. and studies have shown that the control of hyperphosphatemia through dietary phosphorus management, dialysis and phosphate binders is critical to the prevention and delay of renal osteodystrophy in soft tissue calcifications. The first slide lists the medications which are FDA approved indications and as you can see there are many generic options available with Fosrenal and Renvela being the newest

generics available. Indications include the reduction of serum phosphorous in adults with end stage renal disease, control of serum phosphorous in adults with CKD on dialysis and iron deficiency anemia in adults with CKD not on dialysis. There are two medications that were recently receiving new indications including Auryxia which received an indication for iron replacement for the treatment of iron deficiency in anemia with adults with CKD not on dialysis and then also Renvela is now indicated for patients that are 6 years of age or older. Next slide, please.

This slide looks at the dosage and availability of the products. Phoslyra, Fosrenol, Renvela and Velphoro are available in liquids and/or chewable whereas the other products are available in tablets or capsules. Other new information for these products is that Auryxia was previously assigned a Category B, but not its labeling has been updated in compliance with the pregnancy and lactation labeling rules and same with Renvela. It was previously assigned a pregnancy Category C but its labeling rules have also been updated. Next slide, please.

In 2017 the National Kidney Foundation updated guidelines. The guidelines state that the treatment of hyperphosphatemia includes the reduction of dietary phosphorus, phosphate binding therapy and then also removal of phosphorus by dialysis. The guidelines recommend lowering serum phosphate levels in patients with CKD stages 3D through 5D towards a normal range avoiding hypercalcemia in adults and maintaining an age appropriate serum calcium level in pediatric patients. They recommend basing decisions regarding phosphate lowering treatment on progressively or persistently elevated serum phosphate rather than to prevent hyperphosphatemia. They further recommend restricting the dose of calcium-based phosphate binders in adults with CKD stages 3A through 5D and that the choice of phosphate lowering therapy be based on serum calcium level in children's CKD stages 3A through 5D. Lastly they also recommend avoiding the long-term use of aluminum-containing phosphates in these patients. The next set of guidelines from the KDIGO were updated in 2012 and 2014. These guidelines recommend that patients with Stage 3 through 5 CKD with

and without dialysis maintain phosphorous levels within a normal range. And that all patients with CKD stages 3 through 5 and 5D use phosphate-binding agents for the treatment of hyperphosphatemia. The guidelines note that all the phosphate-lowering medications are effective in lowering the serum phosphate levels. Like other guidelines these guidelines state that patients with CKD stages 3 through 5D and hyperphosphatemia restrict the dose of calcium-based phosphate binders in the presence of persistent/recurrent hypercalcemia, arterial calcification, adynamic bone disease and serum PTH levels that are persistently low. In patients with CKD stages 3 through 5D the guidelines strongly recommend avoiding the use of long-term aluminum-containing phosphate binders as they cause neurotoxicities and impair bone mineralization. They state that there is no way to predict a safe aluminum dose. Overall the guidelines note that insufficient… there's insufficient data to endorse the use or the superiority of any one phosphate binder over another. The selection of an appropriate phosphate binder should be individualized and based on various clinical parameters, but not phosphorous-lowering alone. I did want to mention however that Velphoro and Auryxia were not available at the time that this guideline was developed. Any questions on the phosphate binders?

Amber Figueroa: I'm sorry. In the names of these… I don't see aluminum in any of those names. Are they referring to something that's not in this category?

Stephanie Christofferson: Yeah. None of these are included in that. So all of the medications that you see here on the first slide under indications those are all considered safe and effective. Again, with the caveat that Velphoro and Auryxia were not available at the time of the guideline being published.

Amber Figueroa: Thank you.

Dale Sanderson: Any other questions from the committee? I see none. Go ahead.

Stephanie Christofferson: And last we have methotrexate portion. Methotrexate has been used for a wide variety of conditions including psoriasis, rheumatoid

arthritis and polyarticular juvenile idiopathic arthritis. I'll talk as a whole for the next two slides. Otrexup and Rasuvo were approved in October of 2013 and July 2014 respectively to treat psoriasis, rheumatoid arthritis and polyarticular juvenile idiopathic arthritis. They are not approved for neoplastic disease states. There's subcutaneous medications that are self-administered and that are dosed once weekly and are available in an auto injector formulation. Xatmep, which is on the next slide this was approved in 2017 as an oral solution for pediatric patients with polyarticular juvenile idiopathic arthritis, as well as one neoplastic condition acute lymphoblastic leukemia and it is administered once weekly. Other methotrexate formulations are approved not only for these conditions but also for other neoplastic disease states. The medication is available in a variety of formulations allowing for oral, IV, IM or subcutaneous routes of administration. All methotrexate products do carry a boxed warning for serious toxic reactions and death. Fetal death and/or congenital anomalies, severe and sometimes fatal bone marrow suppression, aplastic anemia and so on. So the adverse drug reaction profile for methotrexate products in general are quite extensive. Next slide, please.

This looks at the guidelines for when methotrexate may be used. In psoriasis in 2009 the AAD systematic therapy guidelines for psoriasis note that acitretin, methotrexate and cyclosporine have been used for the treatment of psoriasis for many years with good to excellent results, but that acitretin is the least effective monotherapy. Mild to moderate psoriasis in general can be treated with topical agents particularly corticosteroids whereas the systematic therapies are generally reserved for moderate to severe disease or those with psoriatic arthritis. Multiple trials have demonstrated the benefit of methotrexate in the treatment of psoriasis. However, no randomized trials were found specifically evaluating the route of administration in patients with psoriasis. For rheumatoid arthritis the ACR updated the guidelines for the management of RA in 2015. These guidelines describe the use of [inaudible] in early and established rheumatoid arthritis. Early meaning less than six months and established meaning six months or more. In patients with early symptomatic RA the guidelines recommend the use of disease

modifying anti-rheumatic diseases or DMARD as monotherapy with methotrexate preferred over double or triple therapy in patients who have never taken a DMARD regardless of disease severity. In patients with established RA the ACR recommendations are similar in that they recommend DMARD monotherapy over a TNFi or for DMARD-naïve patients with low disease activity. If the disease activity remains moderate or high despite DMARD therapy the use of combination DMARD and anti-TNF agents such as Enbrel or Remicade a non-TNF biologic or Xeljanz all with or without methotrexate is preferred over DMARD monotherapy. But again when that's needed methotrexate is the preferred therapy. For juvenile idiopathic arthritis, the ACR updated their guidelines in 2013. In these guidelines it states that treatment is dependent on disease activity and the varying degrees of synovitis. The ACR recommends methotrexate leflunomide and NSAID monotherapy in patients without active systemic features with an active joint count of greater than 4. While they recommend NSAID monotherapy or intraarticular glucocorticoid injections for patients with an active joint count less than or equal to 4. In general, ACR recommends [inaudible], glucocorticoid monotherapy or NSAIDs for initial therapy in patients with active systems disease and a varying degree of synovitis. All in all the ACR recommends a variety of treatment choices based on continued disease states, but that methotrexate products are not recommended first line in patients with active systemic disease, but that it is a secondary option which might be available for these patients. With that said I will close out the methotrexate section unless there are any questions.

Dale Sanderson: Any questions from the committee on this last set or anything that Stephanie is doing? I see none. Thank you very much, Stephanie.

Stephanie Christofferson: Thank you.

Dale Sanderson: We do have one stakeholder, Allyson Nelson from Bayer. If you could restrict your comments to three minutes, please.

Allyson Nelson: Good morning. I'm Dr. Allyson Nelson representing Bayer Healthcare to speak about intrauterine contraceptive devices. Bayer

has three IUDs indicated for the intrauterine contraception Mirena, Kyleena and Skyla. Mirena is the only IUD that has an indication for the treatment of heavy menstrual bleeding in women who prefer an IUD for contraception. Bayer's IUDs vary both in size and duration and dose of use. Mirena has initial release rate of 20 micrograms per [inaudible] per day declined to over 10 micrograms per day for five years. Kyleena on the other hand has an average release rate of 9 micrograms per day of [inaudible] over five years. Skyla has an initial release and average release rate of 6 micrograms per days over three years. The Bayer IUDs vary in size as well. The Mirena T-body is 32 mm x 32 mm and is inside of an insertion tube that is 4.4 mm. The Kyleena and Skyla have a smaller T-body. They are 28 mm by 30 mm wide and they are inside of an insertion tube that is 3.8 mm. Mirena, Kyleena and Skyla were all studied in three separate efficacy clinical trials, each enrolling more than 1,000 women. For Mirena the five-year cumulative pregnancy rate was 0.7%. For Kyleena the five-year cumulative pregnancy rate was 1.45%. For Skyla the three-year pregnancy rate was 0.9%. Mirena was also specifically studied to treat heavy menstrual bleeding. In a clinical trial of 160 women half were randomized to Mirena, the other half were randomized to medroxyprogesterone acetate. In the Mirena trials the patients had a baseline of 150 mills blood loss on average and then reduced down to 7 mills of blood loss. This represents a 95% reduction in blood loss. Women receiving MPA experienced a reduction of 21%. Changes in bleeding are to be expected with Mirena, Kyleena and Skyla. During the first three to six months after insertion the number of bleeding spotting days can increase and be irregular. At one year of use, however, the amenorrhea rate defined as no bleeding or no spotting develops at about 20% of Mirena patients, 12% of Kyleena and 6% of Skyla patients. Some of the risks associated with IUDs are perforation, expulsion and pelvic inflammatory disease. Based on a large post marketing study the rate of perphoration for Mirena is 1 in 1,000 in non-breastfeeding women and 6.3 women per 1,000 in breastfeeding women. Expulsion rates in clinical trials were anywhere between 3 and 5% and in clinical trials PID was seen frequently in the first year and more often in the first month and was reported less than 1% in all IUD trials.

Dale Sanderson: Could you conclude your talk, please.

Allyson Nelson: Yes. In conclusion, the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics encouraged the use of implants and IUDs in all [inaudible] patients including [inaudible] women and adolescents. Thank you. Questions?

Dale Sanderson: We will also have the committee look at the submitted stakeholder comments on methotrexate. Any amendments to the recommendation that we have here?

Amber Figueroa: What do you guys think about the armor thyroid?

Dale Sanderson: What is your suggestion?

Amber Figueroa: Well, there are no controlled trials and it's not recommended by the AACE. Having said that I have patients that prefer that, but they can pay cash in my opinion.

Nancy Lee: I agree. I'm also under the impression… I was trying to… I researched this a couple of weeks ago as well. My understanding is it's not… even though it has an FDA indication it's not actually FDA approved. Is that…

Donna Sullivan: If it wasn't FDA approved then Medicaid wouldn't be allowed to cover it. So I don't think that that is an accurate statement.

Nancy Lee: Okay. I just couldn't find it on the FDA.gov website in the drug section. That's all.

Leta Evaskus: Is that accurate? You want to make it non-preferred?

Susan Flatebo: As far as the contraceptives go when it says non-preferred they are all like classed together, patches, IUD, implants. How are they… as far as like two non-preferred, what is a preferred and what is a non-preferred on the contraceptives? Or is that our duty here to say?

Donna Sullivan: I'm just trying to find where it's at. What you're looking at.

Amber Figueroa: I agree with that. I think we should say something like "with like delivery mechanism" or something like that.

Donna Sullivan: Can you go to the slide, Leta? I'm not exactly sure what she's looking at. I guess what's your question?

Susan Flatebo: I'm assuming the cost on an IUD with insertion is probably significantly more than the patch. So how do you determine which one is preferred or non-preferred of these? Since they are all lumped together on this slide.

Donna Sullivan: I don't remember. Doug, I'm going to call you guys out. Are they all… I forget what we recommended for these. Are they almost all preferred on the contraceptives? I think there's at least one of each one. I mean with the contraceptives most of them are covered under family planning and we get the 90% match. So oftentimes most of them are all preferred. I don't remember off the top of my head exactly which ones we are recommending. We don't necessarily prefer one method over another method, but we would have… if there's multiple products within a method we would potentially have a preferred… like a preferred IUD or a preferred implant or a preferred vaginal product. Does that answer your question?

Susan Flatebo: Somewhat although since they are all grouped together then does that mean… I guess you're saying if they are going with an IUD, one of those IUDs is preferred?

Donna Sullivan: Let me look it up.

Susan Flatebo: Again, if the provider prescribes a patch… as far as like the class itself they are not interchangeable. You wouldn't go from a patch to IUD or…

Donna Sullivan: And we're not doing interchange. There's no therapeutic interchange in these particular drugs because they are not on the

Washington PDL. So that is not an issue. Let me look for contraceptives.

Amber Figueroa: I think the hang-up is that the recommendation is that all non-preferred products require a trial of two preferred products and we just want to make sure that each different delivery system there's at least one preferred product so that if someone wants a patch they wouldn't be told they had to get an IUD or vice-versa.

Donna Sullivan: The way I have them broken up into how they will be coded in our system is that the IUDs will be their own class, as well like a patch, an implant, an injectable. So they are all individual classes within themselves. But Magellan lumps them all into this kind of generic other class because they're not the oral or transdermal products. I actually have them broken out if you want to know by the combination contraceptives, oral, the biphasic, the triphasic, the continuous, the extended cycle, the transdermal vaginal IUD and implants. I think that's all.

Amber Figueroa: So we don't need to adjust anything on…

Donna Sullivan: I don't think so. So if there was a preferred product it would be within its method. So we wouldn't make you go from a triphasic oral to a monophasic oral. It's all within how I have them broken out into their subclasses.

Amber Figueroa: Sorry I'm being the one being the devil's advocate here. I circled the Cialis on the BPH. First of all because I didn't know that it was indicated for that and second of all because I'm concerned about it being used for different indications.

Donna Sullivan: So we have that on prior authorization and I don't know if we're looking at that today. We'll be looking at that clinical policy for BPH this afternoon or after lunch. It is on prior auth. I think as we kind of move forward think in your head that if you want something to be on prior auth we can direct it to be on prior authorization while we're doing this process and then we will bring you a clinical policy on what that PA criteria actually is either… well, today we already

planned to so it will be today at another meeting so that you can just say this needs to be on PA and then we can go off and do our research and try and come up with what the appropriate clinical criteria would be as opposed to trying to do it right here in our heads. Then we'll bring it back to you to review and modify as needed and approve it.

Amber Figueroa: So for clarification we do not need to say Cialis should be on the PA because it already is? Or does it…

Donna Sullivan: You should still say that it should be on PA. That would be helpful.

Dale Sanderson: If there are no other amendments would someone like to entertain a motion?

Susan Flatebo: I also think that the Rapaflo on the BPH treatments since that's a newer agent and should also be on PA. The silodosin…

Alex Park: Can I ask a question to Donna? Is Forteo currently preferred among the parathyroid hormone analogs?

Donna Sullivan: Right now for fee-for-service we don't have a preferred… we don't have a PDL in that particular class. I couldn't tell each… one of the plans would have to tell you individually how they have them covered and I don't know if you know off the top of your heads. David?

David Johnson: It's covered under prior authorization.

Dale Sanderson: Again, calling for any amendments. If not, would someone like to entertain a motion?

Susan Flatebo: I move that the Apple Health Medicaid Program implement the limitations listed on slide 133 for each drug class listed on slide 132 as recommended. Armor thyroid should be non-preferred. Cialis and silodosin should be on PA.

Dale Sanderson: A second?

Catherine Brown: I second.

Dale Sanderson: All in favor say aye.

Group: Aye.

Dale Sanderson: All opposed same sign. With that the motion passes. We are running significantly behind. So we have an hour for lunch and our projected adjournment is going to be closer to 4:00.

Donna Sullivan: And it's up to your prerogative if you want to take a full hour or if you want to shorten lunch to a half hour. It's up to you.

Dale Sanderson: I'd be find with shortening it unless there's any objections from the committee. Thirty minutes would get us 30 minutes earlier.

Leta Evaskus: The second part probably won't be a full two hours.

Dale Sanderson: All right. So a 30-minute lunch. Come back here at 1:15.

Donna Sullivan: Sounds good.

Dale Sanderson: Okay. So be it.

April, whenever you're ready.

April Phillips: Sorry about that. I'm going to go over some policies that we worked with the managed cares into kind of everybody agreeing on. We're going to kind of show you what we've done and then at the very end of everything we'll ask if you guys accept it or reject it.

So the first one we're going to start with is the antihyperuricemic agents. Specifically on this first one the Uloric… I'm sorry, I'm going to destroy drug names. Zurampic and Krystexxa – what we're requiring is a diagnosis for symptomatic hyperuricemia associated with gout confirmed by one of the following items that are listed below. We are also requiring at least three gout flairs in the

previous 18 months and then potentially removing any medications that may be causing or effecting any… precipitating any gout attacks be discontinued or changed, if possible. And then we would like to see a history of failure and we define failure as normalizing the uric acids to less than 6 mg/dL or contraindicated or intolerant to at least three months of allopurinol at maximum tolerated dose.

For the next slide we just have a few little things for each drug. On the uloric we are asking that there is no history of cardiovascular disease. On the Zurampic per the labeling it's to be used in combination with the allopurinol and Duzallo is currently a combination already prepared of the previous the Zurampic and the allopurinol. On that one we're requesting information that there's no history of severe renal impairment. For the Krystexxa history of failure, contraindication or intolerance to uloric and either of the Zurampic or Duzallo and no history of G6PD deficiency.

For our next policy I want to point out there are a couple of spelling errors and I will note those and take responsibility for them.

Jordan Storhaug: Your second point with the antihyperuricemics agents they have to be inadequately controlled gout flairs? Can you tell me what that means? Are you saying that they have to not improve from their gout flair?

April Phillips: So what we're requesting on that is they are inadequately controlled either by colchicine or NSAID. So if they had a gout flair and it wasn't improved by either of those options then that's considered a gout flair that wasn't previously treated. So if they've had three of those in the past then we will…

Donna Sullivan: I forget where we landed on this but allopurinol is not on here so I'm thinking that, if I'm missing something let me know, but I believe that they would have had to try and fail… oh, it's down here as number 4. They also have to have tried and failed allopurinol. So it's not just the colchicine and the NSAIDs. So they would have to be on a therapeutic dose of allopurinol and still be having flairs in order to

get the other three drugs and I think that's what we are trying to get at. Does that better answer your question?

Jordan Storhaug: That's what I thought you were trying to get at, but the wording didn't make me sure if that's what you were going for or not.

April Phillips: I apologize. Serious stage fright. So even though I've talked to all of you I'm very intimidated right now. So for the BPH agents the preferred first line agents are not going to require prior authorization. And then the non-preferred first line agents are going to require a history of failure, contraindication or intolerance to at least two preferreds which obviously didn't require a prior authorization and if you're requesting a brand product that has generic available we're going to ask for clinical justification why none of the generics can't be tried.

The policy criteria is for the Cialis, diagnosis of BPH, history or failure or intolerance to both of the following… or one medication from both of the following classes, a four-week trial of the alpha-1 adrenergic blockers and then at least a six-week trial of the 5-alpha reductase inhibitors and this is where I'm going to point out my spelling mistake. It should be Alpha and not Apha, not even sure that's a word. We are also limiting the dose to 5 mg a day or less.

Donna Sullivan: Do you mean… I thought I heard you say greater than six-week trial of the 5-alpha reductase inhibitors, but it says six months. So I just want to clarify it.

April Phillips: Yes, sorry. At least a six-month trial.

Nancy Lee: Six weeks or six months?

April Phillips: Six months.

Jordan Storhaug: So to clarify what is printed is correct?

April Phillips: Yes. And then for the agents for Gaucher disease so for the diagnosis of type 1 Gaucher disease for adult patients with any of the

following symptoms: moderate to severe anemia, significant hepatomegaly, skeletal disease, symptomatic disease or thrombocytopenia. For Zevesca and Cerdelga require a treatment with enzyme-replacement therapy unless ineffective, not tolerated or contraindicated. And for Cerdelga only requires testing of the CYP2D6 genotype and that we are looking for extensive metabolizer, intermediate metabolizer or poor metabolizer. And just for everybody's knowledge ultra-rapid metabolizer don't necessarily get a therapeutic effect from this medication. I only point it out because I didn't realize there was an ultra-rapid.

For diagnosis for type 3 Gaucher disease we are looking for a neurologic finding consistent with the type 3 Gaucher disease, which are listed on here as examples. And then the same thing with any of the following symptoms – moderate to severe anemia, significant hepatomegaly, skeletal disease, symptomatic disease or thrombocytopenia. Are there any questions on this policy at this time?

So moving on to the next one, the chronic GI motility medications. Specifically Lotronex and Viberzi diagnosis of IBS with diarrhea. We're looking for… you've ruled out the GI obstruction. Also greater than or equal to one of the following symptoms just for medical necessity – frequent or severe abdominal pain or discomfort, frequent bowel or urgency or fecal incontinence, disability or restriction of daily activities due to the IBS with diarrhea. It's also limited to adult patients 18 years or older with a history of the… and failure of two of the conventional therapies listed below.

The next slide is regarding Amitiza, Linzess or Trulance for chronic constipation more specifically IBS with constipation, chronic idiopathic constipation or advanced illness or terminal illness receiving palliative care. Once again 18 years or older and a trial of at least two of the conventional therapies and GI obstruction has been ruled out.

And finally for Movantik, Relistor and Symproic diagnosis of opioid-induced chronic constipation for chronic non-cancer pain 18 years

and older and failure contraindication or intolerance to two of the conventional therapies listed below and GI obstruction ruled out.

Amber Figueroa: April, on some of these they don't have a time, you know, they have to have tried this for however long. Is that just going to be subjective or…

April Phillips: I don't believe we decided on the limit on that.

Donna Sullivan: It would be helpful on some of these of what you guys would think would be an adequate trial. If you could let us know and then we can amend the policy to include that. Sometimes it is difficult to tell what… on some drugs what an adequate trial really should be from a clinicians' perspective.

April Phillips: And so for our next policy for the hereditary angioedema agents – diagnosis of hereditary angioedema documented… documentation of the serum C4 and the serum C1 inhibitors that are below lower limits of normal. With the history of moderate to severe attacks and so we would also like to not see used in combination for acute attacks none of the following medications are used in combination with each other for prophylaxis of attacks, those two products not used in combination. And there's no evidence of known or… no evidence of medication known to cause angioedema either they've been discontinued or changed when possible. And for this one we are looking for it to be prescribed by or in consultation with a specialist. Are there any questions on that policy?

So for the asthma immunomodulators specifically the Cinqair, the Fasenra and Nucala diagnosis of severe asthma with eosinophilic phenotype. We're looking for documentation of blood eosinophil count as one of the following: greater than or equal to 150 micrograms in the cells per microgram in the prior 6 weeks, or greater than or equal to 300 cells per microgram in the prior 12 months. We're also looking for severe asthma as defined by one of following: the FEV less than 80% predicted, two or more bursts of systemic corticosteroids in the past 12 months or poor symptom control as defined by the ACQ or the ACT scores. For try and fail our

failure is defined as remains symptomatic after two to six weeks of a high dose inhaled corticosteroid or contraindication or intolerance to. And used in combination with additional asthma controller medications. And not to be used in combination with other monoclonal antibodies for the treatment of asthma. And then once again prescribed by or in consultation with a specialist. These particular medications also have age limits on them. The Fasenra and the Nucala are for at least 12 years old where the Cinqair is for at least 18 years old.

Susan Flatebo: So you have a diagnosis of severe asthma, but then the third bullet point says uncontrolled or inadequately controlled. Does that mean the diagnosis of severe asthma needs to be uncontrolled or inadequately controlled?

April Phillips: Yes. Like you said the uncontrolled or inadequately controlled severe asthma. So with the trial of the asthma controlled medications.

Susan Flatebo: Okay.

April Phillips: And for Nucala only it has recently gotten a new indication for EPGA, formerly known as Churg-Strauss syndrome. That particular syndrome has received more information so now it's defined as EPGA. With symptoms, which include two of the following: the documentation of the blood eosinophilic count as following: white blood cells outside of the blood vessels, migratory spots or lesions on a chest x-ray, acute or chronic sinusitis and damage to one or more nerve groups. We also are requesting a history of filler contraindication or intolerance to corticosteroids or immunosuppressants. The maximum dose for this indication is no more than 300 mg every four weeks and prescribed by or in consultation with a specialist. The age limit on this particular diagnosis is at least 12 years old.

And for Xolair the diagnosis is a little bit different of moderate to severe persistent allergic asthma for age 6 years… or age at least 6 years old who remain symptomatic after two to six weeks,

contraindication or intolerance to medium to high dose inhaled corticosteroids, positive skin test or in vitro reactivity to a perennial aeroallergen, FEV1 is less than 80% of predicted, pre-treatment serum IgE level is between 30 and 1,500 IU/mL, or diagnosis of chronic idiopathic urticarial greater than or equal to 12 years of age, history of failure, contraindication or intolerance to H1 antihistamines, not used in combination with other monoclonal antibodies for the treatment of asthma and prescribed by or in consultation with a specialist. Are there any questions on this policy?

And finally for the movement disorder agents diagnosis of one of the following: the chorea associated with Huntington's disease, tardive dyskinesia, they have to be at least 18 years of age and then not used in combination with other VMAT2 inhibitors and prescribed by or in consultation with a neurologist.

Virginia Buccola: I'm curious about the prescribed by a neurologist or in consultation with neurology. I'm wondering about expanding to psychiatric providers. We see a good percentage of… the presentation of TD.

April Phillips: That makes sense. Tardive dyskinesia is common with typical antipsychotics. And so on the next page we've got… each drug class has a little bit different… so specifically for the Austedo less than or equal to 40 mg per day and no hepatic impairment or concurrent use or recent discontinuation of MAOIs. For the Ingrezza it's only approved for the diagnosis of tardive dyskinesia and dose of less than or equal to 80 mg per day. We are also looking for no history of QT syndrome or arrhythmias associated with prolonged QT intervals or a history of renal impairment. For the Xenazine one of the following diagnosis with the dose limits: chorea associated with Huntington's disease less than or equal to 50 mg. For doses greater than 50 mg we are requiring genotyping of the CYP2D6 to determine if the client is intermediate or extensive metabolizer. The diagnosis of tardive dyskinesia is technically an off label use. However, it is part of our compendia. It is compendia so it is a supported indication.

Dale Sanderson: Is that a neurologist in consultation? Above, I mean we… those of us in psychiatry see lots of people with tardive dyskinesia. We're pretty good at it. Is there a reason why you [inaudible] neurologist?

April Phillips: I made note of that because I didn't think of it in the policy. We were just… went with neurologist for the Huntington's disease.

Nancy Lee: I just wanted to point out a type-o for the Ingrezza. The second bullet point less than or equal to the symbol.

April Phillips: Sorry. Yes. I told you there would be a couple of those. And then with the Xenazine no hepatic impairment or concurrent use or recent discontinuation of MAOIs. Are there any questions on this? I've gotten a few notes and will take care of those.

Amber Figueroa: Just going back addressing my previous comment about length of therapy, going back to those GI motility agents. I don't know… some of that stuff is over-the-counter stuff so I don't know if… I don't know if you want us to comment on what we think an appropriate trial period is, but on slide 8 and slide 9, 10.

April Phillips: Yes. If you have feedback, please feel free to provide it.

Jordan Storhaug: Amber, do you have a suggestion?

Amber Figueroa: I think four weeks for most of these. I mean maybe not the sertraline, but most of them you're going to get an idea as to whether or not it's going to help.

Jordan Storhaug: I would think even in two weeks I'd expect most of the change for that. So two to four weeks sounds very reasonable.

Donna Sullivan: So even though we do require those medications that are over-the-counter they are still covered products. So we would still be able to tell if they had been on it and then also looking at, you know, chart notes, as well for documentation of OTC use.

Dale Sanderson: Is there a motion that you would like us to consider?

April Phillips: Yeah. If you want to go through any stakeholder comments and that way you have all the background information?

Dale Sanderson: Yeah. Sure. So we have four stakeholders. Lisa Stroup. Again, please three minutes only, please.

Lisa Stroup: Hi. My name is Lisa Stroup. I'm from Neurocrine Biosciences medical affairs and thank you for the chance to speak about Ingrezza. Ingrezza is a highly selective [inaudible] transporter to or VMAT2 inhibitor with long-term safety and efficacy data up to 48 weeks of treatment and it is the first FDA approved treatment for tardive dyskinesia in adults. TD is a persistent and disabling condition associated with prolonged exposure to dopamine receptor blockers including antipsychotic and antiemetic agents. Hallmark symptoms include involuntary movements of the face, trunk and/or extremities and they are often irreversible even after the offending medication is discontinued. Patient's with TD are typically diagnosed and treated by a psychiatrist, psychiatric nurse practitioners and less often neurologists. The FDA recommended dosing for Ingrezza is 40 mg once daily for one week increasing to 80 mg once daily at week two. It's taken orally with or without food and is the only VMAT2 inhibitor with no black box warning or contraindications. Ingrezza's safety was evaluated in three six-week double blind placebo controlled studies and included 445 patients. The most commonly reported adverse reaction greater than or equal to 5% and twice the rate of placebo was somnolence. Ingrezza may cause an increase in the QT interval although the degree of this QT prolongation is not clinically significant at concentrations expected with recommended dosing. Importantly there was no safety signal for increased depression or suicidality in these groups. Ingrezza's efficacy was evaluated in a randomized double blind placebo controlled six-week trial on 234 patients age 18 to 85. All previous diagnosed with schizophrenia, schizoaffective disorder or mood disorder and who had moderate to severe TD as determined by clinical observation and diagnosed using the clinically accepted DSM for criteria. All the patients remained on their usual stable doses of psychotropic medications throughout the trial. The study examined two doses of

Ingrezza, 40 and 80 mg once daily versus placebo. The primary efficacy endpoint was the mean change from baseline in the abnormal involuntary scale at the end of week six as scored by blinded central video raters. Open label follow-up continued for 42 weeks followed by a four-week wash out period. Nearly 90% of patients completed the six-week placebo controlled phase at which time a mean reduction in AIM score for the 80 mg group was significantly reduced relative to placebo with a decrease of 3.2 points versus .1 points in placebo respectively. This reduction on the AIMs was maintained during the 48-week extension phase. Careful examination of multiple psychiatric scales revealed psychiatric stability across the 48 weeks of treatment. In summary, Ingrezza is the first FDA approved for adults with tardive dyskinesia and has long-term efficacy and safety data up to 48 weeks of treatment. Thank you. Any questions?

Dale Sanderson: I do have a question. In your studies did you tease out the length of time that people had tardive dyskinesia? So you've got someone who has been… has had TD for 20 years as opposed to someone who has it for two months.

Lisa Stroup: I don't have a good answer to that because it's really hard to get clear timelines in these patients. It was a very complicated, messy patient population just by their very nature. Many have chronic mental illness, two-thirds of them had schizophrenia. They have been on any typical and atypical antipsychotic you can imagine. So getting an accurate diagnosis was difficult. We did do post hoc analyses looking at severity at baseline and that sort of thing. We didn't see any difference between the groups. So we did look at lots of other parameters, but it was very hard to get length of time since true diagnosis.

Dale Sanderson: All right. Thank you. Maria Agapova?

Maria Agapova: Hi. Good day. My name is Maria Agapova. I'm the medical outcomes liaison for Teva Pharmaceuticals and I'm just adding to the body of evidence some key safety findings for Austedo deutetrabenazine and I hope that the committee ensures access for

the Washington State patients with tardive dyskinesia and chorea associated with Huntington's disease. As you may already know a box warning exists for the use of Austedo but this box warning applies to the patients with Huntington's disease and those at risk of depression suicidality. The efficacy of Austedo for chorea was associated with… sorry, chorea associated with Huntington's disease was established in one Phase 3 perspective double-blind randomized placebo controlled trial [inaudible] and the safety of Austedo was further established using an open label single arm two cohort long-term study ARC HT. In ARC HT 82 study subjects rolled over from first HT study within one week washout period. Thirty-seven of those patients switched overnight from a stable dose of tetrabenazine to Austedo. At week 54 total maximum chorea score reduced by 4.1 and 3.0 units in the rollover and the switch cohorts respectively. Exposure adjusted incidence rates for patients reporting [inaudible] were similar in the rollover and switch cohorts and similar to the rates observed in the shorter first HT trial. The most common [inaudible] were falls, somnolence and depression. Those numbers were very small and there were no new safety signals within one year of treatment. Independently there was an indirect treatment comparison which is a statistical analysis done between Austedo and tetrabenazine in the treatment of HT associated chorea looking at tolerability differences. Deutetrabenazine demonstrated significantly lower incidence rates for overall adverse events, moderate severe adverse events than tetrabenazine. Although not statistically significant deutetrabenazine resulted in a greater risk of mild [inaudible] specifically with greater incidence of coughing and diarrhea. Deutetrabenazine demonstrated significantly overall… fewer overall dose reduction and dose reduction suspensions due to AEs than tetrabenazine. In tardive dyskinesia the efficacy of Austedo was established in two 12-week randomized double-blind placebo-controlled multi-center trials ARM and AIM TD conducted in 334 ambulatory patients with tardive dyskinesia. At completions subjects were eligible to roll into the REM TD open trial single arm long-term safety study. At week 54 mean improvement and AIM score was 5.1 in the 78 enrolled patients. Additionally the proportion of patients that were much improved or very much

improved by the [inaudible] of global impression of change assessment at week 54 with 72%. Long-term exposure of Austedo resulted in similar exposure just in incidence rates of adverse events to those seen in the short-term treatment trials and there was no evidence of increased depression, anxiety, suicidality, akathisia, restlessness, somnolence and sedation or [inaudible] after long-term exposure. So given that we're looking at a very small population, looking at prevalence… use prevalence of 0.137% of HT and in the .013% overall U.S. prevalence of patients being treated with a VMAT2 inhibitor for instance a specific agent was also around 0.0136%. We ask that you continue to give access to patients for… with these two disease conditions to Austedo. Thank you. Any questions?

Dale Sanderson: Lisa Sniderman-King?

Lisa Sniderman-King: Thank you. I'm Lisa Sniderman-King with Medical Affairs at Sandfi Genzyme. Prior to this I was a genetic counselor at the University of Washington where I was involved in the management of gaucher patients, about 25 of them for about 11 years. Gaucher disease is a rare autosomal recessive disorder caused by [inaudible] enzyme deficiency. Symptoms of Gaucher disease type 1 include enlarged liver and spleen, hematologic abnormalities and bone disease. Severity of symptoms may vary among patients with the same genotype and even among patients within the same family. Enzyme replacement therapy is a long-standing therapeutic approach to treat gaucher disease type 1. Cerezyme and Sandfi Genzyme [inaudible] replacement product approved in 1994 and indicated for pediatric and adult patients with type 1 gaucher disease who have anemia, [inaudible], bone disease, enlarged liver or spleen. Two clinical trials and outcomes data published from the gaucher disease registry started in 1991. Cerezyme has been shown to reduce the [inaudible], improve bone mineral density and lessen bone pain and decrease frequency of bone crises.

Approximately 15% of patients develop IGG antibodies to Cerezyme during the first year of therapy. In the clinical trial and post marketing experience 13.8% of patients experienced adverse events

judged to be related to Cerezyme. Symptoms suggestive of hypersensitivity have been noted in approximately 6.6% of patients. Substrate reduction therapy with an oral small molecule is another therapeutic approach to treat Gaucher disease type 1. A first line substrate reduction therapy Cerdelga was approved by the FDA in August of 2014 and is indicated for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers, intermediate metabolizers or poor metabolizers in an FDA clear test. In a Phase 3 clinical trial of naïve adult Gaucher type 1 patients, Cerdelga significantly improved hepatic splenomegaly, anemia and thrombocytopenia compared to placebo. During the long-term extension period significant improvements were also seen in patients originally on placebo at nine months and incremental improvements were seen in patients originally on Eliglustat out to 18 months. In a second Phase 3 study of one year, Cerdelga met the criteria for non-inferiority to Cerezyme in adult Gaucher type 1 patients previously stabilized on enzyme replacement therapy. Patients in the long-term extension period continued to show stability of the same disease parameters out to four years. Cerdelga is available in 84 mg capsules. The dosing and management of drug/drug interactions is dependent on the patient's metabolizer status. Cerdelga is not recommended in patients with pre-existing cardiac disease or for patients taking certain concomitant medications. The most common adverse reactions in more than 10% during the two registration trials were fatigue, headache, nausea, diarrhea, back pain, pain in extremities and upper abdominal pain. Recommendations for the use of Cerdelga and Gaucher type 1 patients including recommendations for monitoring have been published.

In conclusion, to allow for appropriate management for individual Gaucher disease type 1 patients we request that the State of Washington allow open access for commercially available treatments in the Gaucher disease class including Cerezyme and Cerdelga. Thank you. I'll take any questions.

Dale Sanderson: Jesse Hong?

Jesse Hong: Thank you. My name is Jesse Hong. I'm the medical science liaison with Purdue Pharma. I'm here to provide public testimony for Symproic naldemedine tablets. Symproic is indicated for the treatment of opiate-induced constipation in adult patients with chronic non-cancer pain including patients with chronic pain related [inaudible] cancer or is treatment who do not require frequent opiate dosage escalation. Symproic is indicated… contraindicating patients with no or suspected gastrointestinal obstruction or patients at increased risk of recurrent obstruction. Recommended dosage for Symproic is 0.2 mg orally once daily at any time of the day with or without food. Symproic can be used with or without laxatives. Patients receiving opioids for less than four weeks may be less responsive to Symproic and Symproic shall be discontinued if treatment with opioid medication is continued. OIC, opiate-induced constipation is a distinct form of constipation as we have discussed earlier as defined as a change when initiating opiate therapy from baseline bowel habits that is characterized by any of the following: reduced bowel [inaudible] and frequency, development of worsening or straining to pass bowel movement, a sense of incomplete rectal evacuation, or harder stool consistency. In adult patients with chronic non-cancer pain taking opioids the prevalence of OIC ranges from approximately 40 to 50%. Symproic is in the [inaudible] new opioid receptor antagonists [inaudible] that help to address the underlying mechanism of OIC. It inhibits the peripheral effects of opioid medication by blocking their action on new opioid receptors within the GI tract. This particular mechanism leads to decrease in the constipation effect of opioids.

In our clinical trial in two 12-week randomized double-blind placebo-controlled trials in adult patients Symproic provided statistically significant increases from baseline compared to placebo in multiple end points including proportion, spontaneous bowel movement, frequency of SBM and then spontaneous bowel movement without staining and complete SBMs. The most common adverse reactions were abdominal pain, diarrhea, nausea and gastroenteritis.

Symproic was also studied in a long-term 52-week randomized double-blind placebo-controlled pivotal safety trial where adult

patients with chronic non-cancer patients in OIC could remain on their previous stable laxative regimen thus we were able to receive the indication for it to be taken with or without laxatives. The safety profile of Symproic compared to placebo was similar regardless of laxative use and was similar to the two 12-week studies. Thank you very much for your time and consideration that you, Washington State will consider adding Symproic to the preferred drug list. Thank you. Any questions? Thank you.

April Phillips: Can we ask that you guys make a motion to approve, reject any changes to the policies that we presented? Sorry, we did make the changes that you had provided earlier.

Catherine Brown: I had one other additional question I just thought of around the chronic GI motility. Would you also want to have a stipulation that they are on an opioid? I don't see that listed there and it makes sense?

Donna Sullivan: So you're speaking to the one of… where the indication is for chronic constipation due to opioid use? Yes, we can add that.

Alex Park: Could we return to the antihyperuricemic agents? I had a couple… sorry.

Leta Evaskus: Catherine, does that look okay?

Catherine Brown: Yes.

Susan Flatebo: Since we're on this one right now the trial of two to four weeks, should we even have a length of time? Because if it's chronic constipation and they are going three or four days without a bowel movement, I mean I would say it is up to the discretion of the provider saying they've tried two other conventional therapies and they're not working. I don't know if I like that it has to have a trial of a timeline in there for this particular class.

Dale Sanderson: I'm also concerned about the wording you just added. It sounds like… there are going to be patients that need this medication that aren't on an opioid.

Donna Sullivan: These drugs are only indicated for opioid-induced constipation.

Dale Sanderson: Okay.

David Johnson: Just to clarify, the requirement for an opioid is for the diagnosis of opioid-induced constipation. If they have a diagnosis of IVSC or something like that then that doesn't apply. Just for the diagnosis at the top of the slide, correct? Okay.

Susan Flatebo: I wasn't even thinking about this being the opioid-induced constipation so you could probably leave it in for this slide. Yes, that's fine. I was thinking general.

Donna Sullivan: So to David's point were you saying that the diagnosis of opioid-induced constipation implies that they're on an opioid already?

David Johnson: I think that's what Catherine's concern was that if they have that diagnosis but they're not taking opioids… they need to be taking an opiate on a regular basis and have that diagnosis.

Donna Sullivan: Okay.

David Johnson: I also would say if you make some sort of clarification on prerequisites because they are all OTCs. If you could be clear, because we can't… yes, they're covered, but they don't have to be. So if you want to say documented claims of [inaudible] versus she bought it over the counter or whatever. Clarification would be good because does it have to be in the chart note? Does it have to be a claim? Can it just be written on the PA form? Grandma said so, etc. This group… any time you have OTCs the PA gets really problematic unless the criteria is really clear.

Woman: You have to be clear on what kind of documentation you're expecting because if it is okay for it to be that the provider attests to

it when they call in a PA, that's very different from we have to have a claim in our system. A claim in our system means it has to have been recent enough that they were under our plan at the time and they might have tried it five years ago.

Donna Sullivan: I think that that's giving it maybe a little too much detail for the committee to determine. I think that if they just give us guidance on how long the treatment we can decide on the documentation and how we're going to administer that.

Nancy Lee: I just wanted to comment on Susan's comment, as well as the timeframe. I'm not tied to one way or the other. I just pulled up two [inaudible] goals on like Linzess to kind of take a look at what the baseline patient population whether or not they were on a stool softening agent while they were getting… or enrolled in this study and I couldn't really find much information other than that Rome 3 criteria was used. So it wasn't very clear as to like what the baseline patient population like how long they were on it. So I was just trying to find further information to help guide us. I guess I will defer to the Health Care Authority to point to that.

Alex Park: I think to the point of the… I think Susan's concern about the patient comfort level and safety with regard to the length of time that you're trialing the over-the-counters I think… I don't see on the slide right now, but I see in my paperwork here that GI obstruction, etc. has been ruled out. I think that's important to keep. It's on the second page of that slide.

Donna Sullivan: I would prefer that we just say two weeks, if we want it to be two weeks, or four weeks if we want it to be four weeks, because if somebody had tried it for two weeks we couldn't reject it and say, "No, you have to try it for four weeks". So I think the minimum for two weeks would be fine and that would get to Susan's point about, you know, they have gone for two weeks without a bowel movement you might be really concerned. They have at least tried one of the products for a week or two products one week each or something like that.

Alex Park: I'm happy to accept that.

Donna Sullivan: Okay.

Leta Evaskus: I noticed that on these three different GI slides we have it written differently. So GI motility chronic, its history of failure at least two weeks trials. The next one is history of failure, contraindication or intolerance. That's for chronic constipation and then the opioid-induced is at least two weeks trial. Is that okay?

Donna Sullivan: We'll make them all the same for the final, to two weeks.

Leta Evaskus: Alex, did you have a different flyer?

Alex Park: Yes. Returning to the antihyperuricemic agents I wondered if we could add a couple clarifications? For Duzallo when we say severe renal impairment I believe it's creatinine clearance of less than 30.

Donna Sullivan: Are you on slide 2 or 3?

Alex Park: This is slide 3. I think it is somewhat vague. I think it would be useful to clarify what type of renal impairment we're referring to. So it should not have creatinine clearance less than 30. Or you could say creatinine clearance has to be greater than 30. For Zurampic I would think that we would also want to offer providers the options to have it used with Uloric as well as allopurinol. For the Zurampic only a specification we have currently used in combination with allopurinol and I would recommend adding Uloric, as well.

Donna Sullivan: Is it Uloric or allopurinol? Or used with Uloric and allopurinol?

Alex Park: Uloric or allopurinol. Yeah. Or you could just say xanthine oxidase inhibitor if you wanted to have the class, but I think that's fine the way it is. And then for Krystexxa I'd recommend saying history of failure, contraindication or intolerance to allopurinol, or Uloric, or Zurampic, or Duzallo. You probably want to add Zurampic… some kind of language indicating that Zurampic would have to be combined with one of the other xanthine oxidase inhibitors.

April Phillips: So originally it was Uloric and Zurampic. So do you want to specify Uloric…

Alex Park: You could say allopurinol or Uloric and then have the Zurampic because that has to be used with one of the other preceding drugs. And then I would add a comma after Zurampic.

April Phillips: Does that make sense to everybody? The changes?

Alex Park: That looks fine to me. And then I had one other comment on slide 2. Because many providers often look to these guidelines as some form of clinical information it would be useful to add, under bullet point two, inadequately controlled by colchicine, corticosteroids or NSAIDs. Corticosteroids are now first line for acute gout flair, as well.

April Phillips: Are there any other comments or feedback? Then if we can get a final motion to accept.

Dale Sanderson: Do you need a written motion or should we just say all in favor of accepting your clinical review?

April Phillips: Yes, I would say go with that.

Dale Sanderson: As amended?

April Phillips: Correct.

Dale Sanderson: I'll make that motion. I move to accept… we move to accept the clinical review that you have provided given the amendments that have been made. Is there a second?

Jordan Storhaug: I second.

Dale Sanderson: All in favor say aye.

Group: Aye.

Dale Sanderson: All opposed same sign. It passes and I think we're done. So the meeting is adjourned.